# Palliasjon i kreftomsorgen – medullakompresjon & skjelettmetastaser – litteratursøk oppsummert forskning – screeningliste

## Medullakompresjon

1 Tulloch I, Georges H, Phadke R, Hardwidge C. **A thoracic extradural chordoid meningioma: a unique case report and literature review**. Br J Neurosurg 2018:1-3.

**Abstract:** We describe the unique case of a patient being diagnosed with a thoracic extradural chordoid meningioma following her presentation with mild lower limb pyramidal weakness and a T8 sensory level. This is the first report of an extradural chordoid meningioma being identified in the thoracic spine. The tumour was successfully resected through a posterior thoracic laminectomy approach. Post-operatively, her neurological deficit resolved and to date she has not experienced a radiological recurrence. In this report, we review the literature and discuss this unusual tumour's characteristics and prognostic significance. Copyright © 2018 The Neurosurgical Foundation

2 Teyssonneau D, Gross-Goupil M, Domblides C, Haaser T, Pointillart V, Daste A, et al. **Treatment of spinal metastases in renal cell carcinoma: A critical review**. Critical Reviews in Oncology-Hematology 2018;125:19-29.

**Abstract:** Kidney cancer is the 9th most common cancer in men and the 14th most common in women worldwide. Renal cell carcinoma (RCC) constitutes 90% of all malignancies of the kidney. RCC, is known to be highly vascular and relatively radioresistant. Bone metastases are one of the most common metastatic sites and occur in around 30% of RCCs. They significantly impact the quality of life of patients causing pain and pathological fractures. Spinal metastases represent a particular case with regard to symptoms and treatment. Indeed, neurological pain is often added to the nociceptive pain caused by metastases. More importantly, neurological impairment can be seen, caused by spinal cord or nerve root compression (MSCC). Due to close contact with the spinal cord, the treatment of spinal bone metastases is challenging and requires a multidisciplinary approach. Specific treatment is currently focused on 4 main avenues which are surgery, radiotherapy, interventional radiology and systemic treatment. In June 2017 we carried out an extensive search on PubMed, Web of Science, and Cochrane Library to review the various treatment options and to establish a treatment strategy. This article presents the result of our critical review of the literature, given our expertise in the field.

3 Rich SE, Chow R, Raman S, Liang Zeng K, Lutz S, Lam H, et al. **Update of the systematic review of palliative radiation therapy fractionation for bone metastases**. Radiother Oncol 2018;126(3):547-57.

**Abstract:** PURPOSE: Radiation therapy is an effective modality for pain management of symptomatic bone metastases. We update the previous meta-analyses of randomized trials comparing single fraction to multiple fractions of radiation therapy in patients with uncomplicated bone metastases.

METHODS: A literature search was conducted in Ovid Medline, Embase, and Cochrane Central Register. Ten new randomized trials were identified since 2010, five with adequate and appropriate data for inclusion, resulting in a total of 29 trials that were analyzed. Forest plots based on each study's odds ratios were computed using a random effects model and the Mantel-Haenszel statistic.

RESULTS: In intention-to-treat analysis, the overall response rate was similar in patients for single fraction treatments (61%; 1867/3059) and those for multiple fraction treatments (62%; 1890/3040). Similarly, complete response rates were nearly identical in both groups (23% vs 24%, respectively). Re-treatment was significantly more frequent in the single fraction treatment arm, with 20% receiving additional treatment to the same site versus 8% in the multiple fraction treatment arm (p<0.01). No significant difference was seen in the risk of pathological fracture at the treatment site, rate of spinal cord compression at the index site, or in the rate of acute toxicity.

CONCLUSION: Single fraction and multiple fraction radiation treatment regimens continue to demonstrate similar outcomes in pain control and toxicities, but re-treatment is more common for single fraction treatment patients.

4 Rajah G, Rapp A, Discolo E, Eltahawy H. **Surgical decompression for recurrent cord compression in cancer: a case series and review of the literature**. Neurol Res 2018:1-6.

**Abstract:** Spine metastases affect a significant number of cancer patients each year, with the spine being the third most common location for cancer spread. As patients live longer with improved treatments, the opportunity for recurrence at previously treated sites increases. Here, we describe seven patients with recurrent, compressive, metastatic spine tumors at previously surgically treated sites that required additional surgical intervention with manipulation of at least one rod. Five of the patients had recurrence including adjacent levels while two had recurrence solely at the previously decompressed level. The patients remained ambulatory for an average of 31.2 months after the initial surgery. We also discuss the role of adjuvant treatment in these patients and review the literature. Copyright © 2018 Informa UK Limited, trading as Taylor & Francis Group

5 Paniagua-Collado M, Cauli O. **Non-pharmacological interventions in patients with spinal cord compression: a systematic review**. J Neurooncol 2018;136(3):423-34.

**Abstract:** Spinal cord compression is a complex and challenging condition that greatly affects the quality of life. Non-pharmacological techniques have only been studied to a very lesser extent; although they are evidence to be beneficial. We performed Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) analysis of the scientific literature in several databases (Medline, Cochrane, Scopus, Cuiden, Pubmed, Lilacs and Embase); using the following keywords: spinal cord compression, spine compression, mobilization, positioning, brace and bracing. Eleven studies met the inclusion criteria and were finally included in the systematic review. 3 of them were related to metastatic spinal cord compression, 5 to spinal cord compression due to other causes and the last 3 of them regarded the health professional's knowledge in oncology patients. In all cases, it seems possible to manage spinal cord compression by using external mobilization and braces and that this treatment is beneficial to patients. Positioning plays a massive role in the disease and can improve or worsen the condition when used improperly; the supine position is overused and can have a negative impact both physically and psychologically. Non-pharmacological interventions could be useful for pain management, cardiovascular alterations and patients' well-being. One randomized clinical trial demonstrated that massage therapy, using either broad compression massage or light contact touch massage improved pain control. There is an urgent need of randomized clinical trials with these interventions in order to achieve an improved care of these patients.

6 Liu YH, Hu YC, Yang XG, Lun DX, Wang F, Yang L, et al. **Prognostic Factors of Ambulatory Status for Patients with Metastatic Spinal Cord Compression: A Systematic Review and Meta-Analysis**. World Neurosurg 2018;04:04.

**Abstract:** BACKGROUND: This study aimed to identify prognostic factors for functional outcome of metastatic spinal cord compression (MSCC).

METHODS: All full texts in English regarding the prognostic factors for functional outcome of MSCC, published between January 2007 and October 2017, were identified using the electronic databases PubMed, Embase, and the Cochrane Library. An exploratory meta-analysis was also conducted when appropriate data were available.

RESULTS: A total of 25 studies, involving 4897 patients, met the inclusion criteria. Overall, 69.7% of patients across all studies were able to walk postoperatively compared with 49.0% preoperatively. Moreover, 84.7% of the patients maintained ambulation after treatment. Motor function was significantly associated with ambulatory status before treatment, time of developing motor deficits, interval from symptom to surgery, and preoperative performance status.

CONCLUSIONS: Ambulatory status before treatment, interval from symptom to treatment, and time of developing motor deficits can be considered as the most significant prognostic factors for posttreatment ambulatory status. Spinal metastasis should have a higher priority, and immediate intervention should be started before the development of irreversible neurologic deficits. Moreover, short-course radiotherapy might be a good option for patients with a limited life span. Consequently, the identified prognostic factors can be regarded as a preoperative assessment tool to predict neurologic outcome and guide clinical treatment for individual patients with MSCC. However, the retrospective nature of this study with low-quality evidence must be taken into account when interpreting these results, and further research is needed to identify prognostic factors.

7 Konig L, Herfarth K. **Benefit of radiotherapy in patients with plasmacytoma and multiple myeloma. [German]**. Onkologe 2018:1-5.

**Abstract:** Background: Treatment options for patients with plasmacytoma or multiple myeloma should be discussed in an interdisciplinary context. This systematic review focusses on the importance of radiotherapy in multiple myeloma and plasmacytoma. Objective: Summary of local radio-oncological treatment options for patients with plasmacytoma and multiple myeloma. Material and methods: A systematic literature search and analysis was performed to summarize the current evidence on the topic. Results: Patients with plasmacytoma should be primarily treated with curatively dosed radiotherapy with or without surgery. Irradiation concepts may vary depending on risk factors and manifestation (solitary bone plasmacytoma vs. solitary extramedullary plasmacytoma). Although local control rates are high after radiotherapy, progression to multiple myeloma frequently occurs. In patients with multiple myeloma radiation is mainly used in palliative settings for pain relief, prevention of fractures or in patients who suffer from neurological symptoms due to spinal cord compression. Irradiation dose and fractionation should be selected based on treatment indications and the general condition of the patient. Conclusion: Although most patients receive systemic treatment at initial diagnosis, approximately 40% of patients with multiple myeloma will require radiation during the course of disease. While radiation is mainly used for palliative reasons in patients with multiple myeloma, it represents the primary and curative treatment option in patients with plasmacytoma. Copyright © 2018 Springer Medizin Verlag GmbH, ein Teil von Springer Nature

8 Hadden NJ, McIntosh JRD, Jay S, Whittaker PJ. **Prognostic factors in patients with metastatic spinal cord compression secondary to melanoma: a systematic review**. Melanoma Res 2018;28(1):1-7.

**Abstract:** Melanoma is one of the most common primary tumours associated with metastatic spinal cord compression (MSCC). The aim of this review is to identify prognostic factors specifically for MSCC secondary to melanoma. A systematic search of literature was performed in MEDLINE, Embase and the Cochrane Library to identify studies reporting prognostic factors for patients with MSCC secondary to melanoma. Two studies, involving a total of 39 patients, fulfilled the inclusion criteria. The variables associated with increased survival were receiving postoperative radiotherapy, receiving chemotherapy, perioperative lactate dehydrogenase level less than or equal to 8.0micro kat/l, preoperative haemoglobin level more than 11.5mg/dl, an interval of 4 or more years between melanoma diagnosis and skeletal metastasis, absence of further skeletal metastases, absence of visceral metastases, Eastern Cooperative Oncology Group Performance Status of 2 or less, two or fewer involved vertebrae, being ambulatory preradiotherapy and an interval of more than 7 days between developing motor deficits and radiotherapy. The variables associated with good functional outcome were slow development of motor dysfunction, good performance status and being ambulatory before radiotherapy. The most important prognostic factors for survival are Eastern Cooperative Oncology Group Performance Status of 2 or less and absence of visceral metastases. There is a lack of studies looking specifically at prognostic factors for patients with MSCC secondary to melanoma, and the number of patients involved in the existing studies is small.

9 Galgano M, Fridley J, Oyelese A, Telfian A, Kosztowski T, Choi D, et al. **Surgical management of spinal metastases**. Expert Rev Anticancer Ther 2018;18(5):463-72.

**Abstract:** INTRODUCTION: Metastatic spinal disease is a source of significant morbidity in patients with cancer. Recent advancements in adjuvant oncologic therapy has led to increased survival for many patients who harbor neoplastic disease. As a result of this, the chance of developing metastatic spinal disease over the course of a cancer patient's lifespan has increased. Symptomatic metastatic spinal disease can cause significant morbidity including severe pain, neurologic deficit, and loss of ambulation. Current treatment of these patients typically involves the use of multiple modalities, including surgery, radiation, and chemotherapy. Areas covered: An extensive literature review was performed to support the author's opinion on the matter of surgical management of spinal metastatic disease. Pubmed was utilized as a primary search engine. Expert commentary: Despite advances in chemotherapy and radiation therapy, surgery remains a mainstay in many of these patients, particularly with those with either significant metastatic spinal epidural compression or spinal instability. This review discusses the surgical management of metastatic spinal disease including a framework for decision making and technical considerations when deciding to operate on these patients.

10 Zhang Z, Pu F, Shao Z. **The skeletal-related events of denosumab versus zoledronic acid in patients with bone metastases: A meta-analysis of randomized controlled trials**. Journal of Bone Oncology 2017;9:21-4.

**Abstract:** Objective The meta-analysis was used to evaluate the skeletal-related events (SREs) and efficacy of denosumab versus zoledronic acid (ZA) in patients with bone metastases. Methods The data of this meta-analysis study were searched from PUBMED, EMBASE, Cochrane Library, Web of Science with Conference Proceedings, Elsevier and China National Knowledge Infrastructure (CNKI) databases till August 2017. Two independent reviewers reviewed the reference lists of relevant articles. The fixed-effects model and random-effects model were used to summarize relative estimates and 95% confidence intervals (CIs) according to the heterogeneity of the included studies. Results Three randomized controlled trials (RCTs) including 4050 patients were identified in this meta-analysis study. The pooled analysis showed that denosumab could significantly reduce SREs, series SREs [Odds Ratio (OR) = 0.84; 95% CI, 0.74-0.95, I<sup>2</sup> = 0%, P = 0.008] in patients with bone metastases as compared with ZA. Similar results of spinal cord compression SRE and surgery to bone SRE were obtained with (OR = 0.84; 95% CI, 0.70-1.01, I<sup>2</sup> = 0%, P = 0.07) and (OR = 0.92; 95% CI, 0.78-1.08, I<sup>2</sup> = 0%, P = 0.28) separately, radiation to bone SRE (OR = 0.72; 95% CI, 0.46-1.10, I<sup>2</sup> = 11%, P = 0.13) and pathological fracture SRE (OR = 0.78; 95% CI, 0.35-1.73, I<sup>2</sup> = 25%, P = 0.54) showed similar results, there were no significant difference between denosumab and ZA in patients with bone metastases. Conclusion Denosumab was more effective than ZA in reducing the incidence of SRE in patients with bone metastases. Copyright © 2017 The Authors

11 Vayne-Bossert P, Haywood A, Good P, Khan S, Rickett K, Hardy JR. **Corticosteroids for adult patients with advanced cancer who have nausea and vomiting (not related to chemotherapy, radiotherapy, or surgery)**. Cochrane Database of Systematic Reviews 2017;7:CD012002.

**Abstract:** BACKGROUND: Nausea is a common symptom in advanced cancer, with a prevalence of up to 70%. While nausea and vomiting can be related to cancer treatments, such as chemotherapy, radiotherapy, or surgery, a significant number of people with advanced cancer also suffer from nausea unrelated to such therapies. Nausea and vomiting may also cause psychological distress, and have a negative impact on the quality of life of cancer patients; similarly to pain, nausea is often under-treated. The exact mechanism of action of corticosteroids on nausea is unclear, however, they are used to manage a number of cancer-specific complications, including spinal cord compression, raised intracranial pressure, and lymphangitis carcinomatosis. They are also commonly used in palliative care for a wide variety of non-specific indications, such as pain, nausea, anorexia, fatigue, and low mood. However, there is little objective evidence of their efficacy in symptom control, and corticosteroids have a wide range of adverse effects that are dose and time dependent. In view of their widespread use, it is important to seek evidence of their effects on nausea and vomiting not related to cancer treatment.

OBJECTIVES: To assess the effects of corticosteroids on nausea and vomiting not related to chemotherapy, radiotherapy, or surgery in adult cancer patients.

SEARCH METHODS: We searched CENTRAL, MEDLINE Ovid, Embase Ovid, CINAHL EBSCO, Science Citation Index Web of Science, Latin America and Caribbean Health Sciences (LILACS), Conference Proceedings Citation Index - Science Web of Science, and clinical trial registries, from inception to 23rd August 2016.

SELECTION CRITERIA: Any double-blind randomised or prospective controlled trial that included adults aged 18 years and over with advanced cancer with nausea and vomiting not related to chemotherapy, radiotherapy, or surgery were eligible for the review, when using corticosteroids as antiemetic treatment.

DATA COLLECTION AND ANALYSIS: All review authors independently assessed trial quality and extracted data. We used arithmetic means and standard deviations for each outcome to report the mean difference (MD) with 95% confidence interval (CI). We assessed the quality of the evidence using GRADE and created a 'Summary of findings' table.

MAIN RESULTS: Three studies met the inclusion criteria, enrolling 451 participants. The trial size varied from 51 to 280 participants. Two studies compared dexamethasone to placebo, and the third study compared a number of additional interventions in various combinations, including metoclopramide, chlorpromazine, tropisetron, and dexamethasone. The duration of the studies ranged from seven to 14 days. We included two studies (127 participants) with data at eight days in the meta-analysis for nausea intensity; no data were available that incorporated the same outcome measures for the third study. Corticosteroid therapy with dexamethasone resulted in less nausea (measured on a scale of 0 to 10, with a lower score indicating less nausea) compared to placebo at eight days (MD 0.48 lower nausea, 95% CI 1.53 lower to 0.57 higher; very low-quality evidence), although this result was not statistically significant (P = 0.37). Frequency of adverse events was not significantly different between groups, and the interventions were well tolerated. Factors limiting statistical analysis included the lack of standardised measurements of nausea, and the use of different agents, dosages, and comparisons. Subgroup analysis according to type of cancer was not possible due to insufficient data. The quality of this evidence was downgraded by three levels, from high to very low due to imprecision, likely selection bias, attrition bias, and the small number of participants in the included studies.

AUTHORS' CONCLUSIONS: There are few studies assessing the effects of corticosteroids on nausea and vomiting not related to chemotherapy, radiotherapy, or surgery in adult cancer patients. This review found very low-quality evidence which neither supported nor refuted corticosteroid use in this setting. Further high quality studies are needed to determine if corticosteroids are efficacious in this setting.

12 Trodello C, Pepper JP, Wong M, Wysong A. **Cisplatin and Cetuximab Treatment for Metastatic Cutaneous Squamous Cell Carcinoma: A Systematic Review**. Dermatol Surg 2017;43(1):40-9.

**Abstract:** BACKGROUND Cutaneous squamous cell carcinoma (cSCC) is the second most common form of skin cancer and metastasizes in 2% to 5% of cases. OBJECTIVE Systematic evaluation of published cases of metastatic cSCC (mSCC) treated with cisplatin or cetuximab from 1989 to 2014. MATERIALS AND METHODS A literature search was performed to identify cases of mSCC treated with cisplatin or cetuximab. Patient demographics, tumor characteristics, response rates, and disease-free survivals were extracted. RESULTS A total of 60 cases of mSCC treated with cisplatin and 9 cases treated with cetuximab reported in the literature from 1989 to 2014 were included in the analysis. Patients treated with cetuximab obtained a complete response of 67%, an overall response of 78%, and a median disease-free survival of 25 (range 3-48) months. Patients treated with cisplatin obtained a complete response of 22%, an overall response of 45%, and a median disease-free survival of 14.6 (range 3-112) months. CONCLUSION Head-to-head prospective clinical studies between cetuximab and cisplatin are needed to determine which is more efficacious. In addition, prospective tumor registries and randomized controlled trials should be developed in order to establish the ideal systemic regimen in cSCC. Copyright © 2016 by the American Society for Dermatologic Surgery, Inc. Published by Wolters Kluwer Health, Inc. All rights reserved.

13 Roque IFM, Martinez-Zapata MJ, Scott-Brown M, Alonso-Coello P. **WITHDRAWN: Radioisotopes for metastatic bone pain**. Cochrane Database of Systematic Reviews 2017;3:CD003347.

**Abstract:** BACKGROUND: This is an update of the review published in Issue 4, 2003. Bone metastasis cause severe pain as well as pathological fractures, hypercalcaemia and spinal cord compression. Treatment strategies currently available to relieve pain from bone metastases include analgesia, radiotherapy, surgery, chemotherapy, hormone therapy, radioisotopes and bisphosphonates.

OBJECTIVES: To determine efficacy and safety of radioisotopes in patients with bone metastases to improve metastatic pain, decrease number of complications due to bone metastases and improve patient survival.

SEARCH METHODS: We sought randomised controlled trials (RCTs) in MEDLINE, EMBASE, CENTRAL, and the PaPaS Trials Register up to October 2010.

SELECTION CRITERIA: Studies selected had metastatic bone pain as a major outcome after treatment with a radioisotope, compared with placebo or another radioisotope.

DATA COLLECTION AND ANALYSIS: We assessed the risk of bias of included studies by their sequence generation, allocation concealment, blinding of study participants, researchers and outcome assessors, and incomplete outcome data. Two review authors extracted data. We performed statistical analysis as an "available case" analysis, and calculated global estimates of effect using a random-effects model. We also performed an intention-to-treat (ITT) sensitivity analysis.

MAIN RESULTS: This update includes 15 studies (1146 analyzed participants): four (325 participants) already included and 11 new (821 participants). Only three studies had a low risk of bias. We observed a small benefit of radioisotopes for complete relief (risk ratio (RR) 2.10, 95% CI 1.32 to 3.35; Number needed to treat to benefit (NNT) = 5) and complete/partial relief (RR 1.72, 95% CI 1.13 to 2.63; NNT = 4) in the short and medium term (eight studies, 499 participants). There is no conclusive evidence to demonstrate that radioisotopes modify the use of analgesia with respect to placebo. Leucocytopenia and thrombocytopenia are secondary effects significantly associated with the administration of radioisotopes (RR 5.03; 95% CI 1.35 to 18.70; Number needed to treat to harm (NNH) = 13). Pain flares were not higher in the radioisotopes group (RR 0.74; 95% CI 0.27 to 2.06). There are scarce data of moderate quality when comparing Strontium-89 (<sup>89</sup>Sr) with Samarium-153 (<sup>153</sup>Sm), Rhenium-186 (<sup>186</sup>Re) and Phosphorus-32 (<sup>32</sup>P). We observed no significant differences between treatments. Similarly, we observed no differences when we compared different doses of <sup>153</sup>Sm (0.5 versus 1.0 mCi).

AUTHORS' CONCLUSIONS: This update adds new evidence on efficacy of radioisotopes versus placebo, <sup>89</sup>Sr compared with other radioisotopes, and dose-comparisons of <sup>153</sup>Sm and <sup>188</sup>Re. There is some evidence indicating that radioisotopes may provide complete reduction in pain over one to six months with no increase in analgesic use, but severe adverse effects (leucocytopenia and thrombocytopenia) are frequent.

14 Macherey S, Monsef I, Jahn F, Jordan K, Yuen KK, Heidenreich A, et al. **Bisphosphonates for advanced prostate cancer**. Cochrane Database of Systematic Reviews 2017;2017 (12) (no pagination)(CD006250).

**Abstract:** Background: The prevalence and incidence of pain and skeletal complications of metastatic bone disease such as pathologic fractures, spinal cord compression and hypercalcemia is high and an important contributor to morbidity, poor performance status and decreased quality of life. Moreover, pathologic fractures are associated with increased risk of death in people with disseminated malignancies. Therefore, prevention of pain and fractures are important goals in men with prostate cancer at risk for skeletal complications. Objectives: To assess the effects of bisphosphonates in men with bone metastases from prostate cancer. Search methods: We identified studies by electronic search of bibliographic databases including the Cochrane Controlled Trials Register and MEDLINE on 13 July 2017 and trial registries. We handsearched the Proceedings of American Society of Clinical Oncology (to July 2017) and reference lists of all eligible trials identified. This is an update of a review last published in 2006. Selection criteria: We included randomized controlled studies comparing the effectiveness of bisphosphonates in men with bone metastases from prostate cancer. Data collection and analysis: Two review authors independently extracted data and assessed the quality of trials. We defined the proportion of participants with pain response as the primary end point; secondary outcomes were skeletal-related events, mortality, quality of life, adverse events, analgesic consumption and disease progression. We assessed the quality of the evidence for the main outcomes using the GRADE approach. Main results: We included 18 trials reporting on 4843 participants comparing the effect of bisphosphonate administration to control regimens. Primary outcome: there was no clear difference in the proportion of participants with pain response (RR 1.15, 95% CI 0.93 to 1.43; P = 0.20; I<sup>2</sup> = 0%; 3 trials; 876 participants; low quality evidence). In absolute terms, bisphosphonates resulted in a pain response in 40 more participants per 1000 (19 fewer to 114 more). Secondary outcomes: bisphosphonates probably reduced the incidence of skeletal-related events in participants with prostate cancer metastatic to bone (RR 0.87, 95% CI 0.81 to 0.94; P = 0.27; I<sup>2</sup> = 19%; 9 trials; 3153 participants; moderate quality evidence). In absolute terms, bisphosphonates resulted in 58 fewer SREs per 1000 (85 fewer to 27 fewer). We found no clinically relevant differences in mortality (RR 0.97, 95% CI 0.91 to 1.04; P = 0.43; I<sup>2</sup> = 1%; 9 trials; 2450 participants; moderate quality evidence). In absolute terms, bisphosphonates resulted in 16 fewer deaths per 1000 (47 fewer to 21 more). Outcome definition of quality of life and the measurement tools varied greatly across trials and we were unable to extract any quantitative data for meta-analysis. Bisphosphonates probably increased the number of participants affected by nausea (RR 1.19, 95% CI 1.00 to 1.41; P = 0.05; I<sup>2</sup> = 0%; 9 trials; 3008 participants; moderate quality evidence). In absolute terms, bisphosphonates resulted in seven more cases of nausea per 1000 (0 fewer to 14 more). Bisphosphonates probably increased the number of renal adverse events (RR 1.65, 95% CI 1.11 to 2.46; P = 0.01; I<sup>2</sup> = 0%; 7 trials; 1794 participants; moderate quality evidence). In absolute terms, bisphosphonates resulted in 22 more renal adverse events per 1000 (4 more to 50 more). We found no clear difference in the number of participants with osteonecrosis of the jaw between groups (RR 1.92, 95% CI 0.75 to 4.90; P = 0.17; I<sup>2</sup> = 0%; 5 trials; 1626 participants; very low quality evidence). In absolute terms, bisphosphonates resulted in seven more cases with osteonecrosis of the jaw per 1000 (2 fewer to 29 more). We observed no clinically relevant difference in the proportion of participants with decreased analgesic consumption (RR 1.19, 95% CI 0.87 to 1.63; P = 0.28; I<sup>2</sup> = 37%; 4 trials; 416 participants). Statistical analysis revealed that bisphosphonates probably reduce the number of participants with disease progression (RR 0.94, 95% CI 0.90 to 0.98; P = 0.006; I<sup>2</sup> = 0%; 7 trials; 2115 participants; moderate quality evidence). In absolute terms, bisphosphonates resulted in 36 fewer cases of disease progression per 1000 (71 fewer to 7 fewer). Findings of our predefined subgroup and sensitivity analyses were no different from those of the primary analyses. Authors' conclusions: Based on low quality evidence, there may be no clinically relevant difference in the proportion of men with pain response between bisphosphonates and control regimens in men with bone metastases from prostate cancer. Bisphosphonates probably decrease the number of skeletal-related events and disease progression. These benefits need to be weighed against the increased risk of renal impairment and nausea in men receiving bisphosphonates. Future studies should explicitly evaluate patient important outcomes such as quality of life and pain by using standardized and comparable assessment tools. Copyright © 2017 The Cochrane Collaboration. Published by John Wiley & Sons, Ltd.

15 Lutz S, Balboni T, Jones J, Lo S, Petit J, Rich SE, et al. **Palliative radiation therapy for bone metastases: Update of an ASTRO Evidence-Based Guideline**. Pract Radiat Oncol 2017;7(1):4-12.

**Abstract:** Purpose The purpose is to provide an update the Bone Metastases Guideline published in 2011 based on evidence complemented by expert opinion. The update will discuss new high-quality literature for the 8 key questions from the original guideline and implications for practice. Methods and materials A systematic PubMed search from the last date included in the original Guideline yielded 414 relevant articles. Ultimately, 20 randomized controlled trials, 32 prospective nonrandomized studies, and 4 meta-analyses/pooled analyses were selected and abstracted into evidence tables. The authors synthesized the evidence and reached consensus on the included recommendations. Results Available literature continues to support pain relief equivalency between single and multiple fraction regimens for bone metastases. High-quality data confirm single fraction radiation therapy may be delivered to spine lesions with acceptable late toxicity. One prospective, randomized trial confirms both peripheral and spine-based painful metastases can be successfully and safely palliated with retreatment for recurrence pain with adherence to published dosing constraints. Advanced radiation therapy techniques such as stereotactic body radiation therapy lack high-quality data, leading the panel to favor its use on a clinical trial or when results will be collected in a registry. The panel's conclusion remains that surgery, radionuclides, bisphosphonates, and kyphoplasty/vertebroplasty do not obviate the need for external beam radiation therapy. Conclusion Updated data analysis confirms that radiation therapy provides excellent palliation for painful bone metastases and that retreatment is safe and effective. Although adherence to evidence-based medicine is critical, thorough expert radiation oncology physician judgment and discretion regarding number of fractions and advanced techniques are also essential to optimize outcomes when considering the patient's overall health, life expectancy, comorbidities, tumor biology, anatomy, previous treatment including prior radiation at or near current site of treatment, tumor and normal tissue response history to local and systemic therapies, and other factors related to the patient, tumor characteristics, or treatment. Copyright © 2016 American Society for Radiation Oncology

16 Lin N. **Spinal metastases: A comparison of stereotactic body radiotherapy (SBRT) and conventional radiotherapy**. J Med Radiat Sci 2017;64 (Supplement 1):89.

**Abstract:** Background: The primary treatment for spinal metastases is conventional palliative radiotherapy. However, due to the risk of myelopathy, the radiation dose is limited by the spinal cord, and reirradiation can present challenges. Hence, stereotactic body radiotherapy (SBRT) has emerged as an alternative treatment method. In particular, SBRT has the potential to escalate the biologically effective radiation dose without exceeding the spinal cord tolerance.1 Objectives: To compare SBRT and conventional radiotherapy treatment for spinal metastases. Methods: A literature review of studies that discussed radiotherapy for spinal metastases was conducted. It focused on three main criteria to determine technique superiority: clinical outcomes, toxicity and practical issues. Results: The main goals for treatment of spinal metastases are to increase local control, relieve pain, decrease the likelihood of spinal cord compression and improve quality of life. A randomised controlled trial (RCT) by Braam et al.2 comparing conventionally fractionated radiotherapy and SBRT is ongoing; however, there are no current RCT results available yet. However, single arm studies of SBRT have shown relatively high rates of local control with minimal toxicity.3,4,5 Conclusion: SBRT treatment of the spine has been shown to be effective and safe; however, careful patient selection is very important. Nevertheless, conventional radiotherapy still plays an integral role in the palliative management of patients with spinal metastases. RCTs comparing both modalities with long-term follow-up should be conducted.

17 Leven D, Meaike J, Radcliff K, Qureshi S. **Cervical disc replacement surgery: indications, technique, and technical pearls**. Curr Rev Musculoskelet Med 2017;10(2):160-9.

**Abstract:** Purpose of review: Cervical disc replacement (CDR) is a surgical option for appropriately indicated patients, and high success rates have been reported in the literature. Complications and failures are often associated with patient indications or technical variables, and the goal of this review is to assist surgeons in understanding these factors. Recent findings: Several investigations have been published in the last 5 years supporting the use of CDR in specific patient populations. CDR has been shown to be comparable or favorable to anterior cervical discectomy and fusion in several meta-analyses and mid-term follow-up studies. Summary: CDR was developed as a technique to preserve motion following a decompression procedure while minimizing several of the complications associated with fusion and posterior cervical spine procedures. Though success with cervical fusion and posterior foraminotomy has been well documented in the literature, high rates of mid- and long-term complications have been clearly established. CDR has also been associated with several complications and challenges with regard to surgical technique, though improvements in implant design have lead to an increase in utilization. Several devices currently exist and vary in terms of material, design, and outcomes. This review paper discusses indications, surgical technique, and technical pearls and reviews the CDR devices currently available. Copyright © 2017, Springer Science+Business Media New York.

18 Kumar A, Weber MH, Gokaslan Z, Wolinsky JP, Schmidt M, Rhines L, et al. **Metastatic Spinal Cord Compression and Steroid Treatment: A Systematic Review**. Clin Spine Surg 2017;30(4):156-63.

**Abstract:** STUDY DESIGN: Systematic review.

OBJECTIVES: We conducted a systematic review of the literature to answer the following questions regarding the use of steroid therapy in metastatic spinal cord compression (MSCC): 1. In cases of MSCC, what is the effect of steroid administration before definitive radiotherapy or surgery on ambulatory status, bowel and bladder function and survival? 2. What steroid dosing regimens are associated with the best outcomes concerning neurological symptoms and complication prevention in cases of MSCC?

SUMMARY OF BACKGROUND DATA: Currently, there is significant variation in the initial bolus dose, daily maintenance dose and duration of treatment when steroids are used as a bridge to definitive therapy for MSCC.

METHODS: A literature search following PRISMA guidelines was conducted in June 2016, using Medline via Ovid SP, Medline via PubMed, Embase, Biosis Previews and the Cochrane Library. Search terms used in each database varied slightly to optimize results. All generic steroid formulations were included along with spinal cord compression or myelopathy combined with metastatic or malignant tumors. Papers discussing acute traumatic causes of spinal cord compression were excluded, as were papers discussing cord compression from nonmetastatic tumors or epidural lipomatosis. Subjects were limited to adult humans undergoing definitive treatment with radiotherapy or surgery.

RESULTS: Of the 309 papers retrieved, 66 full text studies were reviewed and 6 papers were found to address the stated questions.

CONCLUSIONS: There is a paucity of high quality literature evaluating the use of steroids in MSCC. On the basis of the evidence available an initial 10 mg intravenous bolus of dexamethasone followed by 16 mg PO QD has been associated with fewer complications compared with 100 mg bolus and 96 mg QD. Weaning of steroids should occur rapidly after definitive treatment. Risk of gastric bleeding or perforation can be managed with the routine use of proton-pump inhibitors.

LEVEL OF EVIDENCE: Level IIIa.

19 Kraal K, Blom T, van Noesel M, Kremer L, Caron H, Tytgat G, et al. **Treatment and outcome of neuroblastoma with intraspinal extension: A systematic review**. Pediatric Blood and Cancer 2017;64 (8) (no pagination)(e26451).

**Abstract:** We performed a systematic review to define the long-term health problems and optimal treatment strategy for patients with neuroblastoma with intraspinal extension. Of 685 identified studies, 28 were included in this review. The burden of long-term health problems is high; a median of 50% of patients suffered from neurological motor deficit, 34% from sphincter dysfunction, and 30% from spinal deformity. The currently available literature remains suboptimal as a guide for treatment of NBL with intraspinal extension. More well-designed, prospective studies are needed to determine the optimal treatment strategy. Copyright © 2017 Wiley Periodicals, Inc.

20 Clarke MJ, Molina CA, Fourney DR, Fisher CG, Gokaslan ZL, Schmidt MH, et al. **Systematic Review of the Outcomes of Surgical Treatment of Prostate Metastases to the Spine**. Global spine j 2017;7(5):460-8.

**Abstract:** STUDY DESIGN: Systematic review.

OBJECTIVE: Surgical decompression and reconstruction of symptomatic spinal metastases has improved the quality of life in cancer patients. However, most data has been collected on cohorts of patients with mixed tumor histopathology. We systematically reviewed the literature for prognostic factors specific to the surgical treatment of prostate metastases to the spine.

METHODS: A systemic review of the literature was conducted to answer the following questions: Question 1. Describe the survival and functional outcomes of surgery or vertebral augmentation for prostate metastases to the spine. Question 2. Determine whether overall tumor burden, Gleason score, preoperative functional markers, and hormonal naivety favor operative intervention. Question 3. Establish whether clinical outcomes vary with the evolution of operative techniques.

RESULTS: A total of 16 studies met the preset inclusion criteria. All included studies were retrospective series with a level of evidence of IV. Included studies consistently showed a large effect of hormone-naivety on overall survival. Additionally, studies consistently demonstrated an improvement in motor function and the ability to maintain/regain ambulation following surgery resulting in moderate strength of recommendation. All other parameters were of insufficient or low strength.

CONCLUSIONS: There is a dearth of literature regarding the surgical treatment of prostate metastases to the spine, which represents an opportunity for future research. Based on existing evidence, it appears that the surgical treatment of prostate metastases to the spine has consistently favorable results. While no consistent preoperative indicators favor nonoperative treatment, hormone-naivety and high Karnofsky performance scores have positive effects on survival and clinical outcomes.

21 Chow R, Hoskin P, Chan S, Mesci A, Hollenberg D, Lam H, et al. **Efficacy of multiple fraction conventional radiation therapy for painful uncomplicated bone metastases: A systematic review**. Radiother Oncol 2017;122(3):323-31.

**Abstract:** Background: Radiation therapy is effective for painful uncomplicated bone metastases, with multiple fraction radiation therapy (MFRT) administered frequently. The optimal dose for MFRT to yield maximum pain relief remains unclear. The aim of this systematic review was to determine pain response across MFRT doses. Methods: A literature search was conducted in Ovid MEDLINE(R) <1946 to July Week 3 2016>, Embase Classic & Embase <1947 to 2016 Week 30> and Cochrane Central Register of Controlled Trials <June 2016>. Pain response rates and the side effects for MFRT doses were extracted. Results: From the 3719 articles identified from the search, 17 were included for quantitative synthesis. 22.5 Gy/5 had the highest overall response (OR) rate, 30 Gy/15 had better complete response (CR) rate and 20 Gy/2 had better partial response (PR) rate. Only 4 of the 17 included studies directly compared MFRT doses with each other - one reported marginally-better OR for 24 Gy/6 over 20 Gy/2; another found 20 Gy/10 to be slightly more efficacious than 30 Gy/15 and 22.5 Gy/5 for OR. Two randomized trials compared 20 Gy/5 and 30 Gy/10 - one favored 20 Gy/5 while the other concluded 30 Gy/10 to be the better option. The overall rate of GI toxicities, nausea, and vomiting did not differ greatly between MFRT doses. Conclusion: No major difference exists between the schedules and toxic events studied in these trials. This is consistent with the wealth of randomized data which show no dose response for pain relief after radiotherapy for metastatic bone pain. Copyright © 2017 Elsevier Ireland Ltd

22 Ben Salah N, Bou-Fakhredin R, Mellouli F, Taher AT. **Revisiting beta thalassemia intermedia: past, present, and future prospects**. Hematology 2017;22(10):607-16.

**Abstract:** Background: The spectrum of thalassemias is wide ranging from thalassemia minor, which consists of mild hypochromic microcytic anemia without obvious clinical manifestations, to thalassemia major (TM), which is characterized by severe anemia since the first years of life and is transfusion dependent. Thalassemia intermedia (TI) describes those patients with mild or moderate anemia. Objective: To describe the genetic features and major clinical complications of TI, and the therapeutic approaches available in the management of this disease. Methods: Publications from potentially relevant journals were searched on Medline. Results and discussion: Over the past decade, the understanding of TI has increased with regard to pathophysiology and molecular studies. It is now clear that clinical presentation and specific complications make TI different from TM. It is associated with greater morbidity, a wider spectrum of organ dysfunction and more complications than previously thought. Conclusion: TI is not a mild disease. The interplay of three hallmark pathophysiologic factors (ineffective erythropoiesis, chronic anemia, and iron overload) leads to the clinical presentations seen in TI. New treatment modalities are currently being investigated to broaden the options available for TI management. Copyright © 2017 Informa UK Limited, trading as Taylor & Francis Group.

23 Al Tamimi M, Aoun SG, Gluf W. **Spinal Cord Compression Secondary to Epidural Fibrosis Associated with Percutaneously Placed Spinal Cord Stimulation Electrodes: Case Report and Review of the Literature**. World Neurosurg 2017;104:1051.e1-.e5.

**Abstract:** Spinal cord stimulation is a safe method for treating chronic pain syndromes. Spinal cord stimulators can be placed either surgically by creating a laminectomy defect for paddle leads or percutaneously by inserting electrodes. They are usually not associated with major complications. There have been several reports of epidural fibrosis formation after paddle lead placement but only 1 case of excessive fibrosis following percutaneous lead placement. We describe the unique case of excessive cervical fibrosis formation with creation of tolerance phenomenon, clinically significant stenosis, cord compression, and myelopathy after percutaneous lead placement, which improved after surgical removal of the implant. We also reviewed the PubMed and Medline databases for all cases of significant epidural fibrosis related to spinal cord stimulator lead placement, including both surgically implanted paddles and percutaneously implanted leads. This is an uncommon complication after placement of spinal cord stimulators, but it can carry a clinically significant impact and be the source of severe morbidity. It should especially be suspected if the successful placement of the device is followed by development of a "tolerance" phenomenon, with progressive loss of satisfactory pain control and development of new myelopathic symptoms. Copyright © 2017 Elsevier Inc.

24 Zuckerman SL, Laufer I, Sahgal A, Yamada YJ, Schmidt MH, Chou D, et al. **When less is more: The indications for mis techniques and separation surgery in metastatic spine disease**. Spine (Phila Pa 1976) 2016;41(Supplement20):S246-S53.

**Abstract:** Objective. The aim of this study was to review the techniques, indications, and outcomes of minimally invasive surgery (MIS) and separation surgery with subsequent radiosurgery in the treatment of patients with metastatic spine disease. Summary of Background Data. The utilization of MIS techniques in patients with spine metastases is a growing area within spinal oncology. Separation surgery represents a novel paradigm where radiosurgery provides long-term control after tumor is surgically separated from the neural elements. Methods. PubMed, Embase, and CINAHL databases were systematically queried for literature reporting MIS techniques or separation surgery in patients with metastatic spine disease. PRISMA guidelines were followed. Results. Of the initial 983 articles found, 29 met inclusion criteria. Twenty-five articles discussed MIS techniques and were grouped according to the primary objective: percutaneous stabilization (8), tubular retractors (4), mini-open approach (8), and thoracoscopy/endoscopy (5). The remaining 4 studies reported separation surgery. Indications were similar across all studies and included patients with instability, refractory pain, or neurologic compromise. Intraoperative variables, outcomes, and complications were similar in MIS studies compared to traditional approaches, and some MIS studies showed a statistically significant improvement in outcomes. Studies of mini-open techniques had the strongest evidence for superiority. Conclusions. Low-quality evidence currently exists for MIS techniques and separation surgery in the treatment of metastatic spine disease. Given the early promising results, the next iteration of research should include higher-quality studies with sufficient power, and will be able to provide higher-level evidence on the outcomes of MIS approaches and separation surgery. Copyright © 2016 Wolters Kluwer Health, Inc. All rights reserved.

25 Toquart A, Graillon T, Mansouri N, Adetchessi T, Blondel B, Fuentes S. **[Management of spinal metastasis by minimal invasive surgery technique: Surgical principles, indications: A literature review]**. Neurochirurgie 2016;62(3):157-64.

**Abstract:** INTRODUCTION: Spinal metastasis are getting more frequent. This raises the question of pain and neurological complications, which worsen the functional and survival prognosis of this oncological population patients. The surgical treatment must be the most complete as possible: to decompress and stabilize without delaying the management of the oncological disease. Minimal invasive surgery techniques are by definition, less harmful on musculocutaneous plan than opened ones, with a comparable efficiency demonstrated in degenerative and traumatic surgery. So they seem to be applicable and appropriate to this patient population.

MATERIAL AND METHODS: We detailed different minimal invasive techniques proposed in the management of spinal metastasis. For this, we used our experience developed in degenerative and traumatic pathologies, and we also referred to many authors, establishing a literature review thanks to Pubmed, Embase.

RESULTS: Thirty eight articles were selected and allowed us to describe different techniques: percutaneous methods such as vertebro-/kyphoplasty and osteosynthesis, as well as mini-opened surgery, through a posterior or anterior way.

DISCUSSION: We propose a surgical approach using these minimal invasive techniques, first according to the predominant symptom (pain or neurologic failure), then characteristics of the lesions (number, topography, type...) and the deformity degree. Whatever the technique, the main goal is to stabilize and decompress, in order to maintain a good quality of life for these fragile patients, without delaying the medical management of the oncological disease.

26 Tilley D, Kerba M, Kostaras X, Fairchild A. **Development of provincial palliative radiotherapy guidelines**. Radiother Oncol 2016;120 (Supplement 1):S62.

**Abstract:** Purpose: Radiotherapy (RT) practice variability in the palliative setting is well-documented. Clinical practice guidelines inform standardized, evidence-based, beneficial practice, while simultaneously discouraging unnecessary or potentially harmful practices. The process of creating provincial palliative RT clinical practice guidelines is associated with multiple challenges. We describe the unique approach required in aligning multidisciplinary goals as compared to traditional tumour sitespecific guidelines. Methods and Materials: Radiation oncologists from the provincial Palliative Care Tumour Team, along with guideline specialists from the Guideline Resource Unit, formed the primary guideline working group tasked with updating the Palliative RT guidelines. Tumour site specific representatives (ex. Central Nervous System Tumour Team) were incorporated as needed, as well as experts in supportive care, on a guideline by guideline basis. For each guideline, a systematic literature review was conducted to identify relevant evidence. Recommendations were initially developed within the primary working group, then revised in collaboration with experts from other disciplines. Once working group consensus was reached, guideline recommendations were circulated to all radiation oncologists and Palliative Tumour Team members for input. After several rounds of feedback and modifications, provincial consensus was reached. Results: Initially, one RT guideline had been created for all provincial palliative RT recommendations. These guidelines have since been split into smaller, more functional palliative RT guidelines: 1) Brain Metastases; 2) Bone Metastases and Spinal Cord Compression; 3) Bleeding and Gastrointestinal Obstruction; and 4) Superior Vena Cava Obstruction, Dyspnea, and Hemoptysis. The majority of recommendations were either modified or new due to advancements in research or changes in consensus based approaches. In total, 70 recommendations were approved. Recommendations were supported by a range of evidence from high (level one evidence) to low quality (consensus opinion). Conclusions: By combining the newly updated palliative RT guidelines with an educational intervention, variations in practice may be mitigated. Using our model, similar efforts can be undertaken in other jurisdictions.

27 Srinivasan VM, Fridley JS, Thomas JG, Omeis I. **Nuances in Localization and Surgical Treatment of Syringomyelia Associated with Fenestrated and Webbed Intradural Spinal Arachnoid Cyst: A Retrospective Analysis**. World Neurosurg 2016;87:176-86.

**Abstract:** INTRODUCTION: Intradural spinal arachnoid cysts (SACs) are among many etiologies for syringomyelia. Consequentially, neurologic symptoms arise such as pain, gait disturbance, and bladder dysfunction. Identification of SAC on magnetic resonance imaging (MRI) can be challenging, as SACs can be fenestrated or in the form of fine webs.

METHODS: Imaging and clinical data for 7 patients who underwent surgical treatment for SAC associated with syringomyelia were reviewed. All previous publications of this pathology were reviewed via MEDLINE search.

RESULTS: Seven patients with a mean age 59 years were found to have a SAC causing syringomyelia. Intraoperative exploration confirmed SAC appearances of fine webs or a fluid-filled loculation impinging on the spinal cord. Common presentations were back pain, gait disturbance, and bladder incontinence. Diagnosis was made by MRI, although in 3 cases, the SAC was not identified on the initial review. Computed tomography myelogram was performed in one case due to the enlarged syringomyelia and lack of obvious spinal cord compression. Thoracic laminectomy/laminoplasty was performed for all patients, centered at the level of a subtle indentation of the cord; the syringomyelia proper was not directly addressed. Postoperatively, all patients had complete resolution of their symptoms with MRI demonstrating resolution of the syringomyelia.

CONCLUSIONS: Careful evaluation of the MRI can demonstrate subtle indentation of the cord at the caudal or cephalad end of the syringomyelia and may obviate the need for additional imaging. Meticulous arachnoid dissection and establishment of good CSF flow is sufficient for resolution of the syringomyelia, averting the need for more aggressive procedures.

28 Sheehan C. **Defining spinal instability and methods of classification to optimise care for patients with malignant spinal cord compression: A systematic review**. Radiography 2016;22(1):77-83.

**Abstract:** The incidence of Malignant Spinal Cord Compression (MSCC) is thought to be increasing in the UK due to an aging population and improving cancer survivorship. The impact of such a diagnosis requires emergency treatment. In 2008 the National Institute of Clinical Excellence produced guidelines on the management of MSCC which includes a recommendation to assess spinal instability. However, a lack of guidelines to assess spinal instability in oncology patients is widely acknowledged. This can result in variations in the management of care for such patients. A spinal instability assessment can influence optimum patient care (bed rest or encouraged mobilisation) and inform the best definitive treatment modality (surgery or radiotherapy) for an individual patient. The aim of this systematic review is to attempt to identify a consensus definition of spinal instability and methods by which it can be classified. Copyright © 2015 The College of Radiographers.

29 Ost P. **How to optimise the potential of SBRT**. Radiother Oncol 2016;119 (Supplement 1):S292-S3.

**Abstract:** Radiotherapy is a well-established treatment for painful vertebral metastases. Multiple prospective studies report pain response rates of 50 to 90%. Based on randomized studies, 8 Gy in a single fraction is the standard of care for painful uncomplicated bone metastases. Despite the lack of a dose response relationship for pain control, there is good rationale for dose escalation with the aim to improve upon existing rates of local tumour control and pain control. Stereotactic body radiotherapy is ideally suited to safely escalate the dose and improve tumour control. In order to optimize the potential of SBRT, adequate patient selection and specific technical considerations should be taken into account. PATIENT SELECTION Several considerations should be taken into account before delivering SBRT for vertebral metastases. A first consideration is the life expectancy of the patient, which should be evaluated with validated scoring systems (e.g. NRF score, Recursive partitioning analysis index, PRISM). Patients with a short life expectancy in need for palliative radiotherapy should be managed with short effective radiotherapy courses. In patients with longer life expectancy local control might be an important end point potentially requiring a higher radiotherapy dose. A second consideration is the characteristic of the vertebral metastasis and divides the metastases into uncomplicated or complicated. A systematic review suggested the following working definition for uncomplicated bone metastases: those unassociated with impending or existing pathologic fracture or existing spinal cord compression or cauda equina compression. Although this definition looks straightforward it is still variable to interpretation and might be incomplete. The Spinal Instability Neoplastic Score (SINS) might help us estimate the risk of vertebral fracture limiting SBRT to stable and potentially unstable metastases. Different definitions of spinal cord compression are available with the minimum evidence for cord compression being indentation of the thecal sac at the level of clinical features. Finally, other aspects such as, primary tumour type, other metastases, symptoms, practical considerations, current systemic treatment and previous radiotherapy' should be taken into TECHNICAL CONSIDERATIONS For treatment simulation several options are available for patient immobilization. Independent of the system used, the patient must be positioned in a stable position capable for reproducibility of positioning, allowing the patient to feel as comfortable as possible. A typical CT scan length should extend at least 10 cm superior and inferior beyond the treatment field borders (slice thickness of <=2.5 - 3 mm). CT contrast will help visualize the soft tissue and adjacent normal tissues. The International Spine Radiosurgery consortium developed a consensus guideline for target volume definition. MRI images are mandatory for delineation. Axial volumetric T1 and T2 sequences without gadolinium are a standard with <=3 mm slice thickness. Contouring of norm al tissue should be standardized for example: start contouring at 10 cm above the target volume to 10 cm below the target (RTOG 0631). Different fractionation schedules exist with variable total doses. None of the proposed schedules is proven to be superior to another. In case of single fraction, the doses vary between 16 and 24 Gy, with a strong trend for increasing pain relief with higher radiation doses, particularly with doses >= 16 Gy. In case of fractionated radiotherapy, doses vary between 7-10 Gy for a 3 fraction schedule and between 5-6 Gy for a 5 fraction schedule. Most centers prescribe the dose (Dpr) to a % volume of the PTV. A PTV dose coverage of <80% of the Dpr should be avoided (RTOG 0631). This Dpr. should be prescribed to the isocenter or periphery of target. To minimize the risk for toxicity it is advised to strictly adhere to the published dose-constraints keeping in mind that they are mostly unvalidated. Control and correction of the patient and tumor position should be done with vol metric or stereoscopic X-ray imaging at least before each treatment fraction. Extensive recommendations and guidelines for a stereotactic or high precision QA program, supplementing the QA program for linear accelerators can be found in literature and should be followed (e.g. AAPM TG 101 report). OUTCOME The International Bone Metastases Consensus Working Party developed guidelines for the assessment of endpoints of palliative radiotherapy of bone metastases. It is recommended to follow the proposed definitions of pain assessment and pain response. Toxicity should evaluated at follow up visits using standardized criteria such as the National Cancer Institute (NCI) Common Terminology Criteria for Adverse Events (CTCAE) v.4.0.

30 Nakamura N. **Palliative radiotherapy for painful bone metastases**. Ann Oncol 2016;27 (Supplement 7):vii65.

**Abstract:** Radiotherapy is a highly successful modality to palliate pain due to bone metastases, with mild adverse effects and short treatment durations. According to previous metaanalyses, response rates and complete response rates were 59-73 and 23-34%, respectively. The median period until pain relief is 3-4 weeks, while the median period until a pain increase is 5-6 months. For uncomplicated painful bone metastases, which are defined as the presence of painful bone metastases that are not associated with impending or existing pathological fracture or existing spinal cord or cauda equine compressions, multiple randomized trials have shown that a single 8-Gy fraction regimen is equally effective as multiple fraction regimens, such as 20 Gy in 5 fractions or 30 Gy in 10 fractions. A single fraction regimen is equally effective not only in terms of response rates of pain relief but also in the period until a pain increase, incidence of spinal cord compression, incidence of pathological fracture, quality of life, as well as acute and late adverse effects. Therefore, a single fraction regimen is applicable not only for patients with a poor prognosis but also for those with a good prognosis. For patients with complicated bone metastases, multiple fraction regimens are recommended. Multiple fraction regimens are also recommended for patients with neuropathic pain. For patients who have recurrent or persistent pain after radiotherapy, reirradiation of the same sites is also effective. The response to the first irradiation is not a predictive factor of the response to reirradiation. Radiopharmaceuticals such as Strontium-89 are an important option for multifocal painful bone metastases, of which the number of anatomical sites is too high to reasonably be treated with external beam radiotherapy. Stereotactic body radiotherapy (SBRT) for spinal metastases should be used only within clinical trials.

31 Molina C, Goodwin CR, Abu-Bonsrah N, Elder BD, De la Garza Ramos R, Sciubba DM. **Posterior approaches for symptomatic metastatic spinal cord compression**. Neurosurg Focus 2016;41(2):E11.

**Abstract:** Surgical interventions for spinal metastasis are commonly performed for mechanical stabilization, pain relief, preservation of neurological function, and local tumor reduction. Although multiple surgical approaches can be used for the treatment of metastatic spinal lesions, posterior approaches are commonly performed. In this study, the role of posterior surgical procedures in the treatment of spinal metastases was reviewed, including posterior laminectomy with and without instrumentation for stabilization, transpedicular corpectomy, and costotransversectomy. A review of the literature from 1980 to 2015 was performed using Medline, as was a review of the bibliographies of articles meeting preset inclusion criteria, to identify studies on the role of these posterior approaches among adults with spinal metastasis. Thirty-four articles were ultimately analyzed, including 1 randomized controlled trial, 6 prospective cohort studies, and 27 retrospective case reports and/or series. Some of the reviewed articles had Level II evidence indicating that laminectomy with stabilization can be recommended for improvement in neurological outcome and reduction of pain in selected patients. However, the use of laminectomy alone should be carefully considered. Additionally, transpedicular corpectomy and costotransversectomy can be recommended with the expectation of improving neurological outcomes and reducing pain in properly selected patients with spinal metastases. With improvements in the treatment paradigms for patients with spinal metastasis, as well as survival, surgical therapy will continue to play an important role in the management of spinal metastasis. While this review presents a window into determining the utility of posterior approaches, future prospective studies will provide essential data to better define the roles of the various options now available to surgeons in treating spinal metastases.

32 Laufer I, Zuckerman SL, Bird JE, Bilsky MH, Lazary A, Quraishi NA, et al. **Predicting Neurologic Recovery after Surgery in Patients with Deficits Secondary to MESCC: Systematic Review**. Spine (Phila Pa 1976) 2016;41 Suppl 20:S224-S30.

**Abstract:** STUDY DESIGN: Systematic literature review and expert survey OBJECTIVE.: The aim of this study was to determine factors associated with neurologic improvement in patients with neurologic deficits secondary to metastatic epidural spinal cord compression (MESCC). Clear understanding of these factors will guide surgical decision-making by helping to elucidate which patients are more likely to benefit from surgery and how surgeons can increase the probability of neurologic and functional restoration.

SUMMARY OF BACKGROUND DATA: Surgical spinal cord decompression has been shown to improve neurologic function in patients with symptomatic MESCC. However, prognostication of neurologic improvement after surgery remains challenging, owing to sparse data and complexity of these patients.

METHODS: PubMed and Embase databases were searched for relevant publications. PRISMA Statement guided publication selection and data reporting. GRADE guidelines were used for evidence quality evaluation and recommendation formulation.

RESULTS: Low-quality evidence supports the use of the duration and severity of neurologic deficit as predictors of neurological recovery in patients with MESCC. Low-quality evidence supports the use of thoracic level of compression and previous irradiation as adverse predictors of neurological recovery. Nearly all of the AOSpine Knowledge Forum Tumor members who responded to the survey agreed that ambulation with assistance represented a successful surgical result and that duration of ambulation loss and the severity of weakness should be considered when trying to predict whether surgery would result in restoration of ambulation.

CONCLUSIONS: Review of literature and expert opinion support the importance of duration of ambulation loss and the severity of neurologic deficit (muscle strength, bladder function) in prediction of neurologic recovery among patients with symptomatic MESCC. Efforts to reduce the duration of ambulation loss and to prevent progression of neurologic deficits should be made to improve the probability of neurologic recovery.

Level of evidence: 2.

33 Huang D, Du X, Liang H, Hu W, Hu H, Cheng X. **Anterior corpectomy versus posterior laminoplasty for the treatment of multilevel cervical myelopathy: A meta-analysis**. International Journal Of Surgery 2016;35:21-7.

**Abstract:** PURPOSE: To compare the effectiveness between anterior corpectomy (CORP) and posterior laminoplasty (LAMP) for the treatment of multilevel cervical myelopathy.

STUDY DESIGN: Systematic review and meta-analysis.

METHODS: We searched MEDLINE, EMBASE, PubMed, OVID, Web of Science and the Cochrane Central Register of Controlled Trials databases for all relevant articles that compared the two operations for the treatment of multilevel cervical myelopathy. Exclusion criteria were non-controlled studies, combined anterior and posterior surgery, follow-up <1 year and patients with tumors, trauma, soft disc herniation or previous surgery. The following outcome measures were extracted: Japanese orthopedic association (JOA) score, neurological recovery rate, surgical complications, reoperation rate, operation time and blood loss.

RESULTS: 7 high quality studies were included in the meta-analysis. There was no significant difference in preoperative JOA score [P > 0.05, WMD 0.31 (-0.16, 0.79)] and complication rate [P > 0.05, OR 1.26 (0.82,1.94)] between the two groups. Significant less reoperation rate [P < 0.05, OR 8.16 (3.10, 21.51)], operation time [P < 0.05, WMD 67.94 (50.69, 85.20)] and blood loss [P < 0.05, WMD 170.06 (80.05, 260.08)] were found in posterior LAMP group. Whereas, patients in anterior CORP group obtained a better postoperative JOA score [P < 0.05, WMD 2.02 (1.61, 2.43)] and neurological recovery rate [P < 0.05, WMD 7.22 (0.36,14.08)] than that in posterior LAMP group.

CONCLUSIONS: Anterior CORP has a higher postoperative JOA score and neurological recovery rate compared with posterior LAMP. However, significant higher reoperation rate, operation time and blood loss should be taken into consideration when anterior CORP is used. High-quality RCTs with long-term follow-up and large sample size are needed.

34 Hoes K, Hatanpaa K, Raisanen J, Gluf W. **Epidural spinal cavernous hemangioma and hybrid vascular subtype**. Clin Neuropathol 2016;35(6):368-74.

**Abstract:** Aim: To demonstrate less common pathologies of purely epidural spinal tumors that should be considered when noted on MRI prior to surgery. To expand the differential diagnosis of purely epidural spinal tumors and comment on their surgical implications. Material and methods: We report on two patients from our institution with rare pathology. We also utilized PubMed to concisely review the literature concerning purely epidural vascular lesions akin to the cavernous hemangioma. Results: We describe common clinical presentations, radiographic findings, histopathologic characteristics and treatment algorithms relevant to the rare pure spinal epidural cavernous hemangioma and a newly described compound hemangioma subtype. Conclusion: Epidural spinal tumors are relatively common entities, though lesions isolated to the epidural space without origination in the vertebral body or as part of neurologic presentation of metastatic disease, are much less common. Less common pathologies may be missed in the initial differential diagnosis with treatment implications at surgery. Copyright © 2016 Dustri-Verlag Dr. K. Feistle.

35 Health Quality O. **Vertebral Augmentation Involving Vertebroplasty or Kyphoplasty for Cancer-Related Vertebral Compression Fractures: A Systematic Review**. Ont Health Technol Assess Ser 2016;16(11):1-202.

**Abstract:** BACKGROUND: Cancers that metastasize to the spine and primary cancers such as multiple myeloma can result in vertebral compression fractures or instability. Conservative strategies, including bed rest, bracing, and analgesic use, can be ineffective, resulting in continued pain and progressive functional disability limiting mobility and self-care. Surgery is not usually an option for cancer patients in advanced disease states because of their poor medical health or functional status and limited life expectancy. The objectives of this review were to evaluate the effectiveness and safety of percutaneous image-guided vertebral augmentation techniques, vertebroplasty and kyphoplasty, for palliation of cancer-related vertebral compression fractures.

METHODS: We performed a systematic literature search for studies on vertebral augmentation of cancer-related vertebral compression fractures published from January 1, 2000, to October 2014; abstracts were screened by a single reviewer. For those studies meeting the eligibility criteria, full-text articles were obtained. Owing to the heterogeneity of the clinical reports, we performed a narrative synthesis based on an analytical framework constructed for the type of cancer-related vertebral fractures and the diversity of the vertebral augmentation interventions.

RESULTS: The evidence review identified 3,391 citations, of which 111 clinical reports (4,235 patients) evaluated the effectiveness of vertebroplasty (78 reports, 2,545 patients) or kyphoplasty (33 reports, 1,690 patients) for patients with mixed primary spinal metastatic cancers, multiple myeloma, or hemangiomas. Overall the mean pain intensity scores often reported within 48 hours of vertebral augmentation (kyphoplasty or vertebroplasty), were significantly reduced. Analgesic use, although variably reported, usually involved parallel decreases, particularly in opioids, and mean pain-related disability scores were also significantly improved. In a randomized controlled trial comparing kyphoplasty with usual care, improvements in pain scores, pain-related disability, and health-related quality of life were significantly better in the kyphoplasty group than in the usual care group. Bone cement leakage, mostly asymptomatic, was commonly reported after vertebroplasty and kyphoplasty. Major adverse events, however, were uncommon.

CONCLUSIONS: Both vertebroplasty and kyphoplasty significantly and rapidly reduced pain intensity in cancer patients with vertebral compression fractures. The procedures also significantly decreased the need for opioid pain medication, and functional disabilities related to back and neck pain. Pain palliative improvements and low complication rates were consistent across the various cancer populations and vertebral fractures that were investigated.

36 Guan J, Yuan ZC, Liu B. **Research progress of <sup>125</sup>I seeds implantation for metastatic spinal tumors. [Chinese]**. Chinese Journal of Cancer Prevention and Treatment 2016;23(20):1392-7.

**Abstract:** OBJECTIVE: The primary therapy for spinal metastases patients is to relieve the pain, improve quality of life and the prognosis. Brachytherapy, especially <sup>125</sup>I seeds for treating spinal metastases showed a greater advantage. This paper summarized the recent researches of the <sup>125</sup>I Particle Therapy in the mechanisms of spinal metastases, the impact on the human body and the surrounding tissues and the related clinical applications for the treatment of spinal metastases. METHODS: Relevant articles were searched with "<sup>125</sup>I seed, brachytherapy, molecular biology, spinal metastases, et al" as keywords in pubmed, CNKI, Wanfang, VIP, CBD database from 2000 to 2016. Totally 39 papers were selected and analyzed according to the inclusion criteria as follows: the molecular biology mechanisms of <sup>125</sup>I seeds for treating cancer, the effect of <sup>125</sup>I seeds implantation on body and surrounding tissue, the <sup>125</sup>I seeds implantation for treating spinal metastases'efficacy and prognosis, and the exclusion criteria are as follows: the experimental design is unreasonable, non-randomized controlled trials, the total number of samples or the total number of cases is less than 15 cases. RESULTS: <sup>125</sup>I seeds brachytherapy can effectively kill tumor cells, the organ function of vital organs and spinal cord nerve function had no significant effect, and can effectively relieve neuropathic pain. <sup>125</sup>I seeds in the treatment of spinal metastases, a higher local control rate of the tumor, pain relief effect is obvious, can relieve spinal cord compression symptoms; <sup>125</sup>I seeds implantation combined with vertebroplasty in the treatment of spinal metastases can also be Further increase the rate of pain relief and restore the stability of the spine, a superposition effect and complementary advantages. Spinal metastases osteolytic destruction involving the small joints leading to spinal instability and the emergence of more severe symptoms of spinal cord compression in patients with <sup>125</sup>I seeds can be combined with surgical treatment, is a minimally invasive, safe, effective, concurrent Low incidence of disease treatment, effective relief of pain, improve spinal nerve function, local tumor control, reconstruction of spinal stability.CONCLUSIONS: Compared with conventional External radiation therapy, <sup>125</sup>I seeds brachytherapy for the spinal metastases provides a new way for treatment. It has advantage, but still needs further researches in order to get better treatment effect. Copyright © 2016, Editorial Board of Chinese Journal of Cancer Prevention and Treatment. All right reserved.

37 Groenen KHJ, Pouw MH, Hannink G, Hosman AJF, Van der Linden YM, Verdonschot N, et al. **The effect of radiotherapy, and radiotherapy combined with bisphosphonates or RANK ligand inhibitors on bone quality in bone metastases. a systematic review**. Journal of Orthopaedic Research Conference 2016;34(Supplement 1).

**Abstract:** INTRODUCTION: Without treatment, patients with bone metastases may suffer from debilitating skeletal complications such as pathological fractures or, when vertebrae are affected, neurological complaints such as spinal cord compression [1]. The clinical experience of many clinicians is that radiotherapy (RT) strengthens bone due to re-calcification. However, scientific data underlining this stabilizing effect are scarce. Bisphosphonates (BPs) and RANKL inhibitors have already been shown to play a role in improving bone strength [2, 3]. The effect of combining RT, BPs, and RANKL inhibitors on bone quality is, however, unknown. As these treatments have different mechanisms of action, these treatment combinations might prevent pathological fractures and possible accompanying neurological problems more effectively. Therefore, the aims of this systematic review were to assess the effects of (1) RT, (2) RT combined with BPs, and (3) RT combined with RANKL inhibitors, on bone quality and bone strength parameters in bone metastases originating from solid tumors. METHODS: Pubmed, EMBASE and the Cochrane Library were searched for articles concerning the effect of RT or RT combined with either BPs or RANKL inhibitors on bone mineral density, bone quality and bone strength in patients with solid bone metastases. Any type of study design and type and dose of RT, BPs and RANKL inhibitors were allowed. Only articles in English, German, or Dutch were included. Outcome measures related to bone quality and bone strength were extracted and subsequently divided in five principal outcome categories: 1) Radiologic response (any qualitative description of re-calcification), 2) bone density (any quantitative description of bone density), 3) micro-architecture, 4) bone strength, and 5) pathological fractures. The Quality Assessment Tool for Quantitative Studies (QATQS) [4] was used to assess methodological quality. Data were analyzed qualitatively. RESULTS: The search strategy retrieved 2782 unique records. Thirty articles (3 animal studies, 27 patient studies) were included in this systematic review. Methodological quality was rated as 'strong', 'moderate', and 'weak' in four, 16 and 10 of the included studies, respectively. Animal studies: Animal studies showed that RT had similar effects on bone density, micro-architecture, and strength as receiving a negative control (no treatment), whereas adding BPs to RT restored bone quality and strength to those of healthy bone. Correlations between changes in bone mineral density, bone quality and strength were not reported. Patient studies: Radiotherapy - Studies reporting on radiological response rates following RT used a wide range of definitions. Response rates ranged from 25 to 80%. Studies reporting on bone density after RT showed the same trend: bone density increased after RT. It was unclear whether multi fraction RT had a positive effect on bone density increase compared to single fraction RT. Pathological fracture rates after primary RT ranged from 0 to about 15%. Whereas some studies reported more pathological fractures after single fraction RT than after multi fraction RT, others did not confirm this effect. Only one study assessed both bone density and fracture rate and demonstrated that the density change of patients with a pathological fracture was lower than those of patients without a pathological fracture. Radiotherapy combined with bisphosphonates - One study reported on response rate and showed that the response rate after RT was significantly higher in patients receiving both RT and BPs compared to those receiving only RT. Bone density increased after treatment with RT and BPs, which was significant from about 3 months onwards. Studies comparing RT with RT + BPs found similar fracture rates in both treatment groups. One study assessed both radiological response and fracture rate, but did not report correlations between both outcome measures. Radiotherapy combined with RANKL inhibitors - None of the included studies addressed the effect of RT combined with RANKL inhibitors on b ne density, bone micro-architecture, bone strength or related outcome parameters. DISCUSSION: In clinical practice, patients are often treated with a combination of local RT and systemic treatments (e.g. chemotherapy or hormonal therapy, BPs and RANKL inhibitors). In this systematic review we only focused on BPs and RANKL inhibitors as treatments additional to RT, as these treatments intend to improve the bone mass. In contrast, other anticancer treatments are primarily used to attack tumor tissue and decrease lesion size. There was a lot of variation between studies in terms of defining and quantifying radiological response and bone density. The use of different methods and definitions complicated comparison of results between studies and might have resulted in the inability to identify changes in bone quality and fracture rate after radiotherapy. Therefore, it would be beneficial if such outcome measures would be standardized for use in future studies. All studies on bone density after RT showed the same trend: bone density increased after treatment with RT. However, as these studies lacked a control group (no treatment), it cannot be concluded that the increase in bone density was due to the RT. In addition, co-medication, including BPs, was allowed in most patient studies. As BPs are known to increase bone density, the observed increase in bone density could also be caused by the BPs. It was unclear whether multi fraction RT resulted in less pathological fractures than single fraction RT. However, most studies reporting on pathological fractures were not designed to measure fracture rates. To be able to assess the actual effect of RT on fracture risk, studies should be designed with fracture rate as the primary outcome measure. In addition, all factors affecting the fracture risk, such as lesion size and pre-existing impending fractures, should be taken into account in the study design. From clinical experience it is believed that RT strengthens bones due to re-calcification. No correlations between changes in bone density, bone micro-architecture, and bone strength were reported in the animal studies and barely in the patient studies. Without correlating these outcome measures, no conclusions can be drawn on whether it is the process of re-calcification that leads to improved bone strength or not. To understand the role that RT possibly has in stabilizing metastatic bone lesions, future studies should, therefore, determine both bone quality and bone strength or fracture rate within the same animal or patient. Despite the clinical experience that radiotherapy is an effective treatment for bone metastases, based on this review it was concluded that there was no sufficient evidence that radiotherapy had a positive effect on bone quality and fracture risk. In addition, animal studies showed that the addition of BPs to RT restored bone quality and bone strength to that of healthy bone, whereas this is not yet proven in patients. Furthermore, there were neither animal nor patient studies addressing the effect of RANKL inhibitors as an adjunct to RT on bone quality and bone strength. SIGNIFICANCE: Preventing pathological fractures and possible accompanying neurological problems is very important in patients suffering from bone metastases. This systematic review thoroughly analyses the currently available studies on the potentially stabilizing effect of RT, and RT combined with BPs or RANKL inhibitor in bone metastases originating from solid bone metastases and, therefore, aids in the clinical treatment decision making process.

38 Goodwin CR, Sankey EW, Liu A, Elder BD, Kosztowski T, Lo SF, et al. **A systematic review of clinical outcomes for patients diagnosed with skin cancer spinal metastases**. Journal of Neurosurgery Spine 2016;24(5):837-49.

**Abstract:** OBJECT Surgical procedures and/or adjuvant therapies are effective modalities for the treatment of symptomatic spinal metastases. However, clinical results specific to the skin cancer spinal metastasis cohort are generally lacking. The purpose of this study was to systematically review the literature for treatments, clinical outcomes, and survival following the diagnosis of a skin cancer spinal metastasis and evaluate prognostic factors in the context of spinal skin cancer metastases stratified by tumor subtype. METHODS The authors performed a literature review using PubMed, Embase, CINAHL, and Web of Science to identify articles since 1950 that reported survival, clinical outcomes, and/or prognostic factors for the skin cancer patient population with spinal metastases. The methodological quality of reviews was assessed using the PRISMA (Preferred Reporting Items for Systematic Reviews and Meta-Analyses) tool. RESULTS Sixty-five studies met the preset criteria and were included in the analysis. Of these studies, a total of 25, 40, 25, and 12 studies included patients who underwent some form of surgery, radiotherapy, chemotherapy, or observation alone, respectively. Sixty-three of the 65 included studies were retrospective in nature (Class of Evidence [CoE] IV), and the 2 prospective studies were CoE II. Based on the studies analyzed, the median overall survival for a patient with a spinal metastasis from a primary skin malignancy is 4.0 months; survival by tumor subtype is 12.5 months for patients with basal cell carcinoma (BCC), 4.0 months for those with melanoma, 4.0 months for those with squamous cell carcinoma, 3.0 months for those with pilomatrix carcinoma, and 1.5 months for those with Merkel cell carcinoma (p < 0.0001). The overall percentage of known continued disease progression after spine metastasis diagnosis was 40.1% (n = 244/608, range 25.0%-88.9%), the rate of known recurrence of the primary skin cancer lesion was 3.5% (n = 21/608, range 0.2%-100.0%), and the rate of known spine metastasis recurrence despite treatment for all skin malignancies was 2.8% (n = 17/608, range 0.0%-33.3%). Age greater than 65 years, sacral spinal involvement, presence of a neurological deficit, and nonambulatory status were associated with decreased survival in patients diagnosed with a primary skin cancer spinal metastasis. All other clinical or prognostic parameters were of low or insufficient strength. CONCLUSIONS Patients diagnosed with a primary skin cancer metastasis to the spine have poor overall survival with the exception of those with BCC. The median duration of survival for patients who received surgical intervention alone, medical management (chemotherapy and/or radiation) alone, or the combination of therapies was similar across interventions. Age, spinal region, and neurological status may be associated with poor survival following surgery.

39 Engelhardt J, Vignes JR. **Anterior cervical intradural arachnoid cyst, a rare cause of spinal cord compression: a case report with video systematic literature review**. Eur Spine J 2016;25 Suppl 1:19-26.

**Abstract:** PURPOSE: Mostly seen at the thoracic level, arachnoid cysts are a very rare cause of cervical spinal cord compression. Generally treated by laminectomy and cyst fenestration, this approach does not allow removing the cyst in its entirety without manipulating the weakened spinal cord. The aim of this report is to present the case of a cervical intradural arachnoid cyst surgically removed by an anterior approach with corporectomy.

METHODS: Here is the case of an 18-year-old amateur boxer presenting with a voluminous cervical intradural anterior arachnoid cyst, extending from C2 to C5. Symptoms were cervical pain, quadriparesis, and clumsiness of both arms which had appeared just after a traffic accident. An anterior approach was chosen, through a C5 corporectomy.

RESULTS: The patient totally recovered from his sensitive symptoms at discharge and from his motor symptoms 6 weeks later. Early as well as 3-years post-operatively, MRI confirmed expansion of the spinal cord without any centro-medullar signal. The patient remained asymptomatic 3 years after surgery. Since the first report in 1974, 16 cases of symptomatic cervical intradural arachnoid cysts were treated via a posterior approach, one by MRI-guided biopsy, and one was re-operated on through an anterior approach. For 14 patients, their conditions had improved, while one died of pneumonia, one presented a condition worsened, and one had a stable neurological status.

CONCLUSION: Using an anterior approach is a safe procedure that allows resection of a cervical arachnoid cyst without any manipulation of the weakened spinal cord, while giving the best possible view.

40 Chaudhry B, Siddique I. **The surgical management of metastatic spinal cord compression: A proposed cost-utility analysis**. International Journal of Surgery 2016;36 (Supplement 1):S112.

**Abstract:** Aim: Metastatic spinal cord compression (MSCC) is an oncological complication with potentially detrimental affects on a patient's quality of life. It's surgical management is thought to provide the largest unit gain in quality of life wheb compared to other methods of intervention. This is a proposal for a prospective cost-utility analysis following the development and analysis of a surrogate model through the review of literature. Method: The average cost of spinal decompression surgery was sought through adjustment of the patient-level costing data for implant costs. Implant data was recorded through x-ray interpretation; noting quantities of individual components used. The true implant cost for each respective case was calculated using individual component prices. Subsequently, a surrogate cost-utility analysis model was developed through the use of literature in order to work out the cost per QALY. Result: n=62; mean adjusted cost = 16,083.78; the surrogate model provided a cost-effectiveness ratio of 28,217.16/QALY; the hypothetical model provided a cost-effectiveness ratio of 29,895.50/QALY. Conclusion: Our study provided a surrogate cost-utility value below the 30,000 threshold employed by NICE. However, the proposed cost-utility analysis should encompass the completion of the EQ-5D questionnaire pre- and post-operatively in order to find true cost per QALY gained.

41 Bakar D, Tanenbaum JE, Phan K, Alentado VJ, Steinmetz MP, Benzel EC, et al. **Decompression surgery for spinal metastases: a systematic review**. Neurosurg Focus 2016;41(2):E2.

**Abstract:** OBJECTIVE The aim of this study was to systematically review the literature on reported outcomes following decompression surgery for spinal metastases. METHODS The authors conducted MEDLINE, Scopus, and Web of Science database searches for studies reporting clinical outcomes and complications associated with decompression surgery for metastatic spinal tumors. Both retrospective and prospective studies were included. After meeting inclusion criteria, articles were categorized based on the following reported outcomes: survival, ambulation, surgical technique, neurological function, primary tumor histology, and miscellaneous outcomes. RESULTS Of the 4148 articles retrieved from databases, 36 met inclusion criteria. Of those included, 8 were prospective studies and 28 were retrospective studies. The year of publication ranged from 1992 to 2015. Study size ranged from 21 to 711 patients. Three studies found that good preoperative Karnofsky Performance Status (KPS >= 80%) was a significant predictor of survival. No study reported a significant effect of time-to-surgery following the onset of spinal cord compression symptoms on survival. Three studies reported improvement in neurological function following surgery. The most commonly cited complication was wound infection or dehiscence (22 studies). Eight studies reported that preoperative ambulatory or preoperative motor status was a significant predictor of postoperative ambulatory status. A wide variety of surgical techniques were reported: posterior decompression and stabilization, posterior decompression without stabilization, and posterior decompression with total or subtotal tumor resection. Although a wide range of functional scales were used to assess neurological outcomes, four studies used the American Spinal Injury Association (ASIA) Impairment Scale to assess neurological function. Four studies reported the effects of radiation therapy and local disease control for spinal metastases. Two studies reported that the type of treatment was not significantly associated with the rate of local control. The most commonly reported primary tumor types included lung cancer, prostate cancer, breast cancer, renal cancer, and gastrointestinal cancer. CONCLUSIONS This study reports a systematic review of the literature on decompression surgery for spinal metastases. The results of this study can help educate surgeons on the previously published predictors of outcomes following decompression surgery for metastatic spinal disease. However, the authors also identify significant gaps in the literature and the need for future studies investigating the optimal practice with regard to decompression surgery for spinal metastases.

42 Wang Z, Qiao D, Lu Y, Curtis D, Wen X, Yao Y, et al. **Systematic literature review and network meta-analysis comparing bone-targeted agents for the prevention of skeletal-related events in cancer patients with bone metastasis**. Oncologist 2015;20(4):440-9.

**Abstract:** BACKGROUND: Complications from skeletal-related events (SREs) constitute a challenge in the care of cancer patients with bone metastasis (BM).

OBJECTIVES: This study evaluated the comparative effectiveness of pamidronate, ibandronate, zoledronate, and denosumab in reducing the morbidity of SREs in cancer patients with BM.

METHODS: Medline (1948 to January 2014), Embase (1980 to January 2014), the Cochrane Library (2014 issue 1), and Web of Science with Conference Proceedings (1970 to January 2014) were searched. Only randomized controlled trials assessing denosumab, bisphosphonates, or placebo in cancer patients with BM were included. The primary outcomes were SREs and SREs by type. The network meta-analysis (NMA) was performed with a random-effects Bayesian model.

RESULTS: The NMA included 14 trials with 10,192 patients. Denosumab was superior to placebo in reducing the risk of SREs (odds ratio [OR]: 0.49; 95% confidence interval [CI]: 0.31-0.75), followed by zoledronate (OR: 0.57; 95% CI: 0.41-0.77) and pamidronate (OR: 0.55; 95% CI: 0.41-0.72). Ibandronate compared with placebo could not reduce the risk of SREs. Denosumab was superior to placebo in reducing the risk of pathologic fractures (OR: 0.50; 95% CI: 0.32-0.79), followed by zoledronate (OR: 0.61; 95% CI: 0.43-0.86). Denosumab was superior to placebo in reducing the risk of radiation (OR: 0.51; 95% CI: 0.35-0.75), followed by pamidronate (OR: 0.67; 95% CI: 0.52-0.86) and zoledronate (OR: 0.70; 95% CI: 0.52-0.96).

CONCLUSION: This NMA showed that denosumab, zoledronate, and pamidronate were generally effective in preventing SREs in cancer patients with BM. Denosumab and zoledronate were also associated with reductions in the risk of pathologic fractures and radiation compared with placebo. Denosumab was shown to be the most effective of the bone-targeted agents.

43 Tunio M, Asiri MA, Hadab AA, Bayoumi Y. **Comparative efficacy, tolerability, and survival outcomes of various radiopharmaceuticals in castration-resistant prostate cancer with bone metastasis: A meta-analysis of randomized controlled trials**. Drug Des Devel Ther 2015;9:5291-9.

**Abstract:** Background: A meta-analysis was conducted to assess the impact of radiopharmaceuticals (RPs) in castration-resistant prostate cancer (CRPC) on pain control, symptomatic skeletal events (SSEs), toxicity profile, quality of life (QoL), and overall survival (OS). Materials and methods: The PubMed/MEDLINE, CANCERLIT, EMBASE, Cochrane Library database, and other search engines were searched to identify randomized controlled trials (RCTs) comparing RPs with control (placebo or radiation therapy) in metastatic CRPC. Data were extracted and assessed for the risk of bias (Cochrane's risk of bias tool). Pooled data were expressed as odds ratio (OR), with 95% confidence intervals (CIs; Mantel-Haenszel fixed-effects model). Results: Eight RCTs with a total patient population of 1,877 patients were identified. The use of RP was associated with significant reduction in pain intensity and SSE (OR: 0.63, 95% CI: 0.51-0.78, I<sup>2</sup>=27%, P,0.0001), improved QoL (OR: 0.71, 95% CI: 0.55-0.91, I<sup>2</sup>=65%, three trials, 1,178 patients, P=0.006), and a minimal improved OS (OR: 0.84, 95% CI: 0.64-1.04, I<sup>2</sup>=47%, seven trials, 1,845 patients, P=0.11). A subgroup analysis suggested an improved OS with radium-223 (OR: 0.68, 95% CI: 0.51-0.90, one trial, 921 patients) and strontium-89 (OR: 0.21, 95% CI: 0.05-0.91, one trial, 49 patients). Strontium-89 (five trials) was associated with increased rates of grade 3 and 4 thrombocytopenia (OR: 4.26, 95% CI: 2.22-8.18, P=0.01), leucopenia (OR: 7.98, 95% CI: 1.82-34.95, P=0.02), pain flare (OR: 6.82, 95% CI: 3.42-13.55, P=0.04), and emesis (OR: 3.61, 95% CI: 1.76-7.40, P=0.02). Conclusion: The use of RPs was associated with significant reduction in SSEs and improved QoL, while the radium-223-related OS benefit warrants further large, RCTs in docetaxel naive metastatic CRPC patients. Copyright © 2015, Tunio et al.

44 Tarantino R, Donnarumma P, Nigro L, Delfini R. **Surgery in extensive vertebral hemangioma: case report, literature review and a new algorithm proposal**. Neurosurg Rev 2015;38(3):585-92; discussion 92.

**Abstract:** Hemangiomas are benign dysplasias or vascular tumors consisting of vascular spaces lined with endothelium. Nowadays, radiotherapy for vertebral hemangiomas (VHs) is widely accepted as primary treatment for painful lesions. Nevertheless, the role of surgery is still unclear. The purpose of this study is to propose a novel algorithm of treatment about VHs. This is a case report of an extensive VH and a review of the literature. A case of vertebral fracture during radiotherapy at a total dose of 30 Gy given in 10 fractions (treatment time 2 weeks) using a linear accelerator at 15 MV high-energy photons for extensive VH is reported. Using PubMed database, a review of the literature is done. The authors have no study funding sources. The authors have no conflicting financial interests. In the literature, good results in terms of pain and neurological deficits are reported. No cases of vertebral fractures are described. However, there is no consensus regarding the treatment for VHs. Radiotherapy is widely utilized in VHs determining pain. Surgery for VHs determining neurological deficit is also widely accepted. Perhaps, regarding the width of the lesion, no indications are given. We consider it important to make an evaluation before initiating the treatment for the risk of pathologic vertebral fracture, since in radiotherapy, there is no convention regarding structural changes determined in VHs. We propose a new algorithm of treatment. We recommend radiotherapy only for small lesions in which vertebral stability is not concerned. Kyphoplasty can be proposed for asymptomatic patients in which VHs are small and in patients affected by VHs determining pain without spinal canal invasion in which the VH is small. In patients affected by pain without spinal canal invasion but in which the VH is wide or presented with spinal canal invasion and in patients affected by neurological deficits, we propose surgery.

45 Talamo G, Dimaio C, Abbi KKS, Pandey MK, Malysz J, Creer MH, et al. **Current role of radiation therapy for multiple myeloma**. Front Oncol 2015;5 (FEB) (no pagination)(40).

**Abstract:** Background: Radiation therapy (RT) is a treatment modality traditionally used in patients with multiple myeloma (MM), but little is known regarding the role and effectiveness of RT in the era of novel agents, i.e., immunomodulatory drugs and proteasome inhibitors. Methods: We retrospectively reviewed data from 449 consecutive MM patients seen at our institute in 2010-2012 to assess indications for RT as well as its effectiveness. Pain response was scored similarly to RTOG 0631 and used the Numerical Rating Pain Scale. Results: Among 442 evaluable patients, 149 (34%) patients and 262 sites received RT. The most common indication for RT was palliation of bone pain (n = 109, 42%), followed by prevention/treatment of pathological fractures (n = 73, 28%), spinal cord compression (n = 26, 10%), and involvement of vital organs/extramedullary disease (n = 25, 10%). Of the 55 patients evaluable for pain relief, complete and partial responses were obtained in 76.4 and 7.2%, respectively. Prior RT did not significantly decrease the median number of peripheral blood stem cells collected for autologous transplant, even when prior RT was given to both the spine and pelvis. Inadequacy of stem cell collection for autologous stem cell transplant (ASCT) was not significantly different and it occurred in 9 and 15% of patients receiving no RT and spine/pelvic RT, respectively. None of the three cases of therapy-induced acute myelogenous leukemia/MDS occurred in the RT group. Conclusion: Despite the introduction of novel effective agents in the treatment of MM, RT remains a major therapeutic component for the management in 34% of patients, and it effectively provides pain relief while not interfering with successful peripheral blood stem cell collection for ASCT. Copyright © 2015 Talamo, Dimaio, Abbi, Pandey, Malysz, Creer, Zhu, Mir and Varlotto.

46 Sebaaly A, Ghostine B, Kreichati G, Mallet JF, Glorion C, Moussa R, et al. **Aneurysmal Bone Cyst of the Cervical Spine in Children: A Review and a Focus on Available Treatment Options**. Journal of Pediatric Orthopaedics 2015;35(7):693-702.

**Abstract:** Objective: To present a series of pediatric cervical spine (CS) aneurysmal bone cysts (ABC), to review the literature, and to propose a treatment algorithm. Material: We present a series of 4 cases of ABC and review the literature using PubMed, EMBASE, and Google scholar. Results: Only 51 cases are documented. The mean age at diagnosis is 11.5 years, and there is a small female predominance (F:M ratio=1.6). Most of ABC occurs in the upper CS (41%), are located in the posterior component (75%), and extends in 40% of the vertebral body. A single treatment modality was used in 56.9%, whereas combination of surgery with other treatment modalities was used in the rest. Of the total number of cases, 56.8% were managed with marginal resection, and instrumentation was used in 80%. Mean follow-up was 72.5 months, with the majority of patients disease free. Pain is the most common symptom present at the latest follow-up. Conclusions: ABC of the spine is a pediatric tumor occurring rarely in the CS. Treatment options vary from simple curettage to total resection with or without instrumentation. Recurrence after surgery is highest after curettage alone. The main indications for surgery are rapid progression, despite intracystic injection, and/or the presence of neurological signs or symptoms. Level of Evidence: Level IV. Copyright © 2015 Wolters Kluwer Health, Inc. All rights reserved.

47 Qu S, Meng HL, Liang ZG, Zhu XD, Li L, Chen LX, et al. **Comparison of Short-Course Radiotherapy Versus Long-Course Radiotherapy for Treatment of Metastatic Spinal Cord Compression: A Systematic Review and Meta-Analysis**. Medicine 2015;94(43):e1843.

**Abstract:** In this study, we evaluate the efficacy of short-course radiotherapy (SCRT) versus long-course radiotherapy (LCRT) in the treatment of metastatic spinal cord compression (MSCC).PubMed, EMBASE, and Web of Science were searched up to April 2015. Relevant data were extracted based on inclusion and exclusion criteria. Methodological quality of randomized controlled trial (RCT) was evaluated using modified Jadad scale; non-RCT was evaluated using Newcastle-Ottawa Scale. Meta-analysis was performed using RevMan 5.3 software.Fourteen studies with 2239 patients were included. Results of meta-analysis showed that there were no significant differences between SCRT and long-course radiotherapy LCRT in 6-month overall survival rate (risk ratio [RR] = 0.97, 95% confidence interval [CI] 0.88, 1.07, P = 0.55), 1-year overall survival rate (RR = 0.94, 95% CI 0.85, 1.04, P = 0.22), motor function improvement (RR = 0.96, 95% CI 0.81, 1.13, P = 0.63), no change on motor function (RR = 0.98, 95% CI (0.88, 1.09), P = 0.74], and deterioration on motor function (RR = 0.96, 95% CI 0.71, 1.31, P = 0.78). Compared with SCRT, LCRT significantly increased 6-month local control rate (RR = 0.87, 95% CI 0.80, 0.95, P = 0.002), 1-year local control rate (RR = 0.83, 95% CI 0.71, 0.97, P = 0.02), and 2-year local control rate (RR = 0.83, 95% CI 0.79, 0.87, P < 0.00001).Both LCRT and SCRT provided similar survival rates and functional outcome, but LCRT showed better local control rates than SCRT. However, considering low cost and good patient's compliance, SCRT may be a better choice.

48 Pulenzas N, Cheon P, Wong E, Thavarajah N, Dennis K, Lutz S, et al. **A definition of "uncomplicated bone metastases" based on previous bone metastases radiation trials comparing single-fraction and multi-fraction radiation therapy**. Support Care Cancer 2015;1):S41-S2.

**Abstract:** Introduction: The most recent systematic review of randomized trials in patients with bone metastases has shown equal efficacy of single fraction (SF) and multiple fraction (MF) palliative radiation therapy in pain relief. It is important to determine the patient population to which the evidence applies. Objectives: This study aims to examine the eligibility criteria of the studies included in the systematic review to define characteristics of "uncomplicated" bone metastases. Methods: Inclusion and exclusion criteria of 21 studies included in the systematic review were compared. Common eligibility criteria were documented in hopes of defining the specific features of a common patient population representative of those in the studies. Results: More than half of the studies included patients with cytological or histological evidence of malignancy. Patients with impending and/or existing pathological fracture, spinal cord compression or cauda equina compression were excluded in most studies. Most studies also excluded patients receiving retreatment to the same site. Conclusions: "Uncomplicated" bone metastases can be defined as: presence of painful bone metastases unassociated with impending or existing pathologic fracture or existing spinal cord or cauda equina compression. Therefore, MF and SF have equal efficacy in patients with such presentations of bone metastases.

49 Puerta P, Guillen A, Mora J, Sunol M, Candela S, Ferrer E. **Isolated skull metastasis of ewing's sarcoma in a child**. Childs Nerv Syst 2015;31 (10):1952.

**Abstract:** Objective: Ewings sarcoma (ES) was described as a "diffuse hemangioendothelioma of bone". It affects long bones and pelvis. The predominant sites of metastases include lung, bone and bone marrow. Metastasis of ES to the central nervous system (CNS) is uncommon. We present an extremely rare case of skull metastasis of ES. Methods: We present a child affected of a metastatic ES of the skull and we describe our management based on a literature review through Pubmed Medline. Results: A 10-year-old male underwent resection of an ES in the left 5th rib 15 months previously, followed by chemotherapy and radiotherapy. He had a painless, progressive swelling over his right parietal area. CT showed an isodense parietal tumour which was homogeneously enhanced by contrast medium. It was partly extracranial and partly intracranial, with bone destruction. Gross total removal of the tumour was performed and the infiltrated dura was excised. We performed a duraplasty and a titanium mesh cranioplasty. The histology was identical to the specimens from the left rib tumour. The diagnosis was skull metastasis of ES. Adjuvant treatment was performed. Conclusion: ES is the second most common malignant bone tumour. It usually occurs in patients younger than 20 years of age and it's more frequent in males than females. Primary ES most often originates in long bone shafts, pelvic bones, ribs and vertebrae. This tumour frequently develops metastases. The principal sites of metastases are lung, bone and the bone marrow. Meningeal invasion and spinal cord compression are the best known forms of CNS involvement. The frequency of skull metastases of ES in children is unknown but, to our knowledge, there are only three cases previously reported. The multimodal treatment for ES is considered to be the optimal treatment method. Solitary skull metastasis should be removed totally, followed by systemic chemotherapy.

50 Nguyen NT, Hotte S, Dayes I. **Long-term Survival in a Patient with Metastatic Spinal Cord Compression from a Prostate Cancer with Ultra-high PSA: Case Report and Review of the Literature**. Cureus 2015;7(1):e242.

**Abstract:** A 77-year-old man presented to the hospital for non-ambulation of 48 hours prior to admission. He was found to have a metastatic spinal cord compression (MSCC), a PSA exceeding 27,000, and biopsy-confirmed prostate cancer. After palliative radiation (RT) to the spine and medical treatment, the patient recovered his functions fully and survived for more than 7.5 years, far beyond what would be expected based on current published literature. A systematic review of the literature of MSCC in patients with prostate cancer was carried out. Prognostic factors of ambulation after RT included pre-treatment neurological status, duration of neurological deficits, and severity of the neurological impairment. Positive predictive factors of local control included single level of metastasis, time of development of motor deficits of more than 14 days, no prior androgen-deprivation therapy (ADT), age under 65, and longer course of RT (10 fractions of 2 Gy). Absence of prior ADT, pre-treatment ambulation, a single site of metastasis, and haemoglobin of less than 12g/L were positive predictors for survival.

51 Li C, Shi JY, Yang ZR. **Spinal epidural lipoma: Report of a case and review of the literature**. Neurosurg Q 2015;25(2):211-5.

**Abstract:** Spinal epidural true lipoma is exceedingly rare. It can mimic the symptoms of disk herniation and sometimes is difficult to distinguish it from spinal epidural lipomatosis or angiolipoma. We report a case of a 43-year-old male patient presenting with low back pain and neurological deficits of right lower extremity, who was diagnosed and surgically treated. A search using Medline database is conducted and 6 other patients in the literature are found. Common symptoms included sciatica, motor weakness, and sensation loss. Most cases involved the lumbar region. Only 1 case was in the cervical cord (C5-C6). Conservative treatments failed in all cases. All cases performed mass extirpation through laminectomy or laminae fenestration. Prognoses were good in general. Spinal epidural lipoma is rare but should not be neglected. It can worsen the situation when accompanied with trauma. We suggest that surgeries should be carried out in symptomatic patients. More research attention should be paid in the etiology and histology of this disease in the future. Copyright © 2013 Wolters Kluwer Health, Inc.

52 Lee SH, Grant R, Kennedy C, Kilbride L. **Positioning and spinal bracing for pain relief in metastatic spinal cord compression in adults**. Cochrane Database of Systematic Reviews 2015;(9):CD007609.

**Abstract:** BACKGROUND: This is an updated version of the original Cochrane review published in Issue 3 (Lee 2012) on patient positioning (mobilisation) and bracing for pain relief and spinal stability in adults with metastatic spinal cord compression.Many patients with metastatic spinal cord compression (MSCC) have spinal instability, but their clinician has determined that due to their advanced disease they are unsuitable for surgical internal fixation. Mobilising may be hazardous in the presence of spinal instability as further vertebral collapse can occur. Current guidance on positioning (whether a patient should be managed with bed rest or allowed to mobilise) and whether spinal bracing is helpful, is contradictory.

OBJECTIVES: To investigate the correct positioning and examine the effects of spinal bracing to relieve pain or to prevent further vertebral collapse in patients with MSCC.

SEARCH METHODS: For this update, we searched for relevant studies from February 2012 to 31 March 2015. We searched the Cochrane Central Register of Controlled Trials (CENTRAL), MEDLINE and MEDLINE In Process, EMBASE, AMED, CINAHL, TRIP, SIGN, NICE, UK Clinical Research Network, National Guideline Clearinghouse and PEDro database. We also searched the metaRegister of Controlled Trials (mRCT), ClinicalTrials.gov, UK Clinical Trials Gateway (UKCTG), WHO International Clinical Trials Registry Platform (ICTRP) and Australia New Zealand Clinical Trials Registry (ANZCTR).For the original version, we searched the Cochrane Central Register of Controlled Trials (CENTRAL), MEDLINE, EMBASE, CINAHL, CANCERLIT, NICE, SIGN, AMED, TRIP, National Guideline Clearinghouse, and PEDro database, in February 2012.

SELECTION CRITERIA: We selected randomised controlled trials (RCTs) of adults with MSCC of interventions on positioning (mobilisation) and bracing.

DATA COLLECTION AND ANALYSIS: Two review authors independently assessed each possible study for inclusion and quality.

MAIN RESULTS: For the original version of the review, we screened 1611 potentially relevant studies. No studies met the inclusion criteria. Many papers identified the importance of mobilisation, but no RCTs of bed rest versus mobilisation have been undertaken. We identified no RCTs of bracing in MSCC.For this update, we identified 347 potential titles. We screened 300 titles and abstracts after removal of duplicates. We did not identify any additional studies for inclusion.

AUTHORS' CONCLUSIONS: Since publication of the original version of this review, no new studies were found and our conclusions remain unchanged.There is a lack of evidence-based guidance around how to correctly position and when to mobilise patients with MSCC or if spinal bracing is an effective technique for reducing pain or improving quality of life. RCTs are required in this important area.

53 Kiely PD, Quinn JC, Du JY, Lebl DR. **Posterior surgical treatment of cervical spondylotic myelopathy: review article**. HSS J 2015;11(1):36-42.

**Abstract:** BACKGROUND: Cervical spondylosis is now recognised as the leading cause of myelopathy and spinal cord dysfunction worldwide. Chronic spinal cord compression results in chronic inflammation, cellular apoptosis, and microvacular insufficiency, which are thought to the biologic basis for cervical spondylotic myelopathy (CSM).

QUESTIONS/PURPOSES: Our purpose was to address the key principles of CSM, including natural history and presentation, pathogenesis, optimal surgical approach, results and complication rates of posterior surgical approaches for CSM so that the rationale for addressing CSM by a posterior approach can be fully understood.

METHODS: We conducted a systematic search of PubMed/MEDLINE and the Cochrane Collaboration Library for literature published through February 2014 to identify articles that evaluated CSM and its management. Reasons for exclusion included patients with ossification of the posterior longitudinal ligament (OPLL), patients with degenerative disc disease without CSM, and patients with spine tumor, trauma and infection. Meeting abstracts/proceedings, white articles and editorials were additionally excluded.

RESULTS: The search strategy yielded 1,292 articles, which was reduced to 52 articles, after our exclusion criteria were introduced. CSM is considered to be a surgical disorder due to its progressive nature. There is currently no consensus in the literature whether multilevel spondylotic compression is best treated via an anterior or posterior surgical approach.

CONCLUSION: Multilevel CSM may be safely and effectively treated using a posterior approach, either by laminoplasty or with a laminectomy and fusion technique.

54 Kelly ML, Benzel EC. **Surgery Versus Radiation Therapy Alone in Treating Spinal Metastasis: A Perspective**. World Neurosurg 2015;83(6):1020-1.

55 He W, Chen F, Dalm B, Kirby PA, Greenlee JDW. **Metastatic involvement of the pituitary gland: a systematic review with pooled individual patient data analysis**. Pituitary 2015;18(1):159-68.

**Abstract:** Purpose: To report a rare case of pituitary metastasis (PM) from hepatocellular carcinoma (HCC) and help better understand the incidence of PM and its most common presenting symptoms through a pooled individual patient data analysis. Methods: Literature regarding PM was systematically reviewed with a pooled individual patient data analysis conducted. Pooled individual data analysis result is also compared with the result in a most recent systematic review. Results: Our results demonstrate that the incidence of PM among all intracranial metastases is 0.87 % (95 % CI 0.56, 1.18); it is 1.9 % (95 % CI 1.46, 2.34) among all autopsied cancer cases; it is 11.56 % (95 % CI 7.08, 16.04) among all breast cancer patients who had hypophysectomies and 12.83 % (95 % CI 10.5, 15.16) among all autopsied breast cancer patients. The fixed effect model showed that the incidence of PM in breast cancer patients group is significantly higher (p < 0.001) with an odds ratio of 6.71 (95 % CI 4.24, 10.61). Breast and lung cancer are the most common primary cancer of PM with a percentage of 37.2 and 24.2 respectively. The next most common primary sites are prostate and kidney respectively, although the percentages for each are only about 5. Diabetes insipidus (DI) remains the most common symptom among all reported PM cases with a pooled incidence of 42.34 % (95 % CI 36.15, 48.53). Although not significant (chi<sup>2</sup> = 2.846, df = 1, p = 0.061), it is less common in the most recent reported cases which has a pooled incidence of 32.76 % (95 % CI 20.31, 45.21). DI is extremely rare in the reported PM cases from HCC (none of the eight cases presented with DI). The symptoms of anterior hypopituitarism (23.68 vs 39.66 %, p = 0.015), visual deterioration (27.89 vs 41.38 %, p = 0.039), cranial nerve palsies (21.58 vs 41.38 %, p = 0.003) and headaches (15.79 vs 32.76 %, p = 0.005) were reported significantly higher than previously described in the literature. Conclusions: Pituitary metastasis is rare in patients with cancer, and the pituitary gland is an uncommonly involved location in patients with intracranial metastases. With advanced diagnostic imaging techniques and increased awareness about the manifestation of sellar lesions, the incidence of cranial nerve palsies and anterior pituitarism are higher than reported. This information may allow earlier diagnosis of PM. Copyright © 2014, Springer Science+Business Media New York.

56 Garg RK, Malhotra HS, Gupta R. **Spinal cord involvement in tuberculous meningitis**. Spinal Cord 2015;53(9):649-57.

**Abstract:** Objectives: To summarize the incidence and spectrum of spinal cord-related complications in patients of tuberculous meningitis. Setting: Reports from multiple countries were included. Methods: An extensive review of the literature, published in English, was carried out using Scopus, PubMed and Google Scholar databases. Results: Tuberculous meningitis frequently affects the spinal cord and nerve roots. Initial evidence of spinal cord involvement came from post-mortem examination. Subsequent advancement in neuroimaging like conventional lumbar myelography, computed tomographic myelography and gadolinium-enhanced magnetic resonance-myelography have contributed immensely. Spinal involvement manifests in several forms, like tuberculous radiculomyelitis, spinal tuberculoma, myelitis, syringomyelia, vertebral tuberculosis and very rarely spinal tuberculous abscess. Frequently, tuberculous spinal arachnoiditis develops paradoxically. Infrequently, spinal cord involvement may even be asymptomatic. Spinal cord and spinal nerve involvement is demonstrated by diffuse enhancement of cord parenchyma, nerve roots and meninges on contrast-enhanced magnetic resonance imaging. High cerebrospinal fluid protein content is often a risk factor for arachnoiditis. The most important differential diagnosis of tuberculous arachnoiditis is meningeal carcinomatosis. Anti-tuberculosis therapy is the main stay of treatment for tuberculous meningitis. Higher doses of corticosteroids have been found effective. Surgery should be considered only when pathological confirmation is needed or there is significant spinal cord compression. The outcome in these patients has been unpredictable. Some reports observed excellent recovery and some reported unfavorable outcomes after surgical decompression and debridement. Conclusions: Tuberculous meningitis is frequently associated with disabling spinal cord and radicular complications. Available treatment options are far from satisfactory. Copyright © 2015 International Spinal Cord Society All rights reserved.

57 da Silva GT, Bergmann A, Santos Thuler LC. **Prognostic factors in patients with metastatic spinal cord compression secondary to lung cancer: a systematic review of the literature**. Eur Spine J 2015;24(10):2107-13.

**Abstract:** PURPOSE: The Metastatic spinal cord compression (MSCC) secondary to lung cancer (LC) has worse prognosis when compared to MSCC related to other solid tumors. The purpose of this study is to identify the survival time and the prognostic factors in the MSCC secondary to LC.

METHODS: A systematic review of the literature has been carried out. Studies published between January 2005 and March 2015 were identified through the electronic database PubMed and LILACS. Two independent reviewers selected the articles.

RESULTS: 7 studies were identified, which met the inclusion criteria, involving 1010 patients. The survival in 6 and 12 months ranged between 18 and 61%, and between 3.8 and 32%, respectively. The median survival ranged between 2.8 and 9 months. The variables related to the survival improvement were: female, performance status 1 or 2, pre-radiotherapy and postoperative ambulatory status, absence of bone metastases and visceral metastases, interval from cancer diagnosis to spinal metastases or radiotherapy of MSCC>15 months, slower (>7 days) development of motor deficit, and the neurological status at the postoperative.

CONCLUSIONS: The prognosis of the MSCC secondary to LC was poor. Considering the small number of studies identified, further research is needed to identify prognostic factors that are independent of the MSCC secondary to LC.

58 Cheon PM, Wong E, Thavarajah N, Dennis K, Lutz S, Zeng L, et al. **A definition of "uncomplicated bone metastases" based on previous bone metastases radiation trials comparing single-fraction and multi-fraction radiation therapy**. Journal of Bone Oncology 2015;4(1):13-7.

**Abstract:** The most recent systematic review of randomized trials in patients with bone metastases has shown equal efficacy of single fraction (SF) and multiple fraction (MF) palliative radiation therapy in pain relief. It is important to determine the patient population to which the evidence applies. This study aims to examine the eligibility criteria of the studies included in the systematic review to define characteristics of "uncomplicated" bone metastases. Inclusion and exclusion criteria of 21 studies included in the systematic review were compared. Common eligibility criteria were documented in hopes of defining the specific features of a common patient population representative of those in the studies. More than half of the studies included patients with cytological or histological evidence of malignancy. Patients with impending and/or existing pathological fracture, spinal cord compression or cauda equina compression were excluded in most studies. Most studies also excluded patients receiving retreatment to the same site. "Uncomplicated" bone metastases can be defined as: presence of painful bone metastases unassociated with impending or existing pathologic fracture or existing spinal cord or cauda equina compression. Therefore, MF and SF have equal efficacy in patients with such bone metastases.

59 Chen B, Xiao S, Tong X, Xu S, Lin X. **Comparison of the Therapeutic Efficacy of Surgery with or without Adjuvant Radiotherapy versus Radiotherapy Alone for Metastatic Spinal Cord Compression: A Meta-Analysis**. World Neurosurg 2015;83(6):1066-73.

**Abstract:** BACKGROUND: Spinal metastases are 20 times more common than primary spinal tumors and often cause metastatic spinal cord compression (MSCC). Clinical manifestations (e.g., pain and neurologic dysfunction) adversely affect patients' quality of life. Radiotherapy (RT), chemotherapy, and surgery are the major therapeutic strategies for MSCC. There is some evidence that combining surgery with adjuvant RT may be a better option.

METHODS: This meta-analysis compared the therapeutic efficacy of surgery (with or without adjuvant RT) with RT alone in treatment of MSCC. Comparative studies of surgery (with or without adjuvant RT) versus RT alone for the treatment of MSCC were retrieved from the MEDLINE, EMBASE, and Cochrane Library databases. Primary (1-year survival) and secondary (motor function and complications) outcomes were compared by meta-analysis.

RESULTS: Of the 26 studies originally identified, 20 were excluded (not original research, lack of relevance, no group comparison, or lack of comparable data). Compared with RT alone, surgery (with or without adjuvant RT) was associated with improvement of ambulation (odds ratio = 1.74, 95% confidence interval = 1.35-2.25, P < 0.05), pain relief (odds ratio = 3.61, 95% confidence interval = 2.75-4.74, P < 0.05), and 1-year survival (odds ratio = 1.92; 95% confidence interval = 1.37-2.71, P < 0.01). No differences in regaining walking ability and substantially longer hospital stays were observed. Surgery showed better therapeutic efficacy than RT alone with regard to quality of life and life expectancy, without additional complications.

CONCLUSIONS: Further studies are needed to investigate the effects of these interventions on quality of life and to identify the best therapeutic strategy for patients with MSCC.

60 Broder MS, Gutierrez B, Cherepanov D, Linhares Y. **Burden of skeletal-related events in prostate cancer: unmet need in pain improvement**. Support Care Cancer 2015;23(1):237-47.

**Abstract:** PURPOSE: Up to 75% of patients with prostate cancer experience metastatic bone disease, which leads to an increased risk for skeletal-related events (SREs) including pathological bone fracture, spinal cord compression, and hypercalcemia of malignancy. Our objective was to systematically review the literature on the impact of SREs on quality of life (QOL), morbidity, and survival with a primary focus on the impact of SREs on pain in prostate cancer patients.

METHODS: We searched PubMed, limiting to peer-reviewed English-language human studies published in 2000-2010. The search was based on the US Food and Drug Administration and European Medicines Agency definition of an SRE, which includes pathologic fracture, spinal cord compression (SCC), hypercalcemia of malignancy, and radiotherapy or surgery to bone resulting from severe bone pain.

RESULTS: A total of 209 articles were screened, of which 173 were excluded, and 36 were included in this review. Patients with SREs had more pain and worse survival compared with no SREs. Pathologic bone fractures worsened QOL and were associated with shorter survival. Radiation therapy of SCC alleviated pain and improved morbidity. SCC was associated with decreases in patient survival. Radiation therapy and surgery to bone improved pain.

CONCLUSIONS: Specific SREs are associated with worse outcomes, including increased pain, poorer QOL, morbidity, and survival. Treatment of SREs is associated with improved pain, although there remains a need for more effective treatment of SREs in prostate cancer patients.

61 Blakaj DM, Guiou M, Weicker M, Mendel E. **The Evolving Treatment Paradigm for Metastatic Spine Disease**. World Neurosurg 2015;84(1):6-8.

62 Benvenutti-Regato M, De la Garza-Ramos R, Caro-Osorio E. **Thoracic epidural spinal angiolipoma with coexisting lumbar spinal stenosis: Case report and review of the literature**. Int J Spine Surg 2015;9:67.

**Abstract:** BACKGROUND: Spinal angiolipomas (SALs) are uncommon benign lesions that may present insidiously with back pain or acutely with weakness due to tumor bleeding/thrombosis. Given their rarity, these lesions are often overlooked in the differential diagnosis of epidural masses. The purpose of this article is to report the case of an epidural SAL and to conduct a literature review on the topic.

METHODS: A case report and review of the literature using the PubMed/Medline databases. All case reports and case series were reviewed up to June 2015.

RESULTS: A 65-year old female presented with neurogenic claudication and magnetic resonance imaging (MRI) revealed lumbar spinal stenosis. Following decompressive surgery, she experienced symptom resolution, but three months postoperatively she presented to the emergency department with acute paraparesis. A thoracic MRI revealed a lesion located between T8 and T10 causing severe spinal cord compression. Following emergent laminectomy and en bloc resection, the patient regained function and the lesion was diagnosed as SAL. Our literature review revealed 178 reported cases, with a female and thoracic predominance. The majority of patients underwent surgical treatment, achieving a gross total resection in most cases. Similarly, complete symptom resolution was the most common outcome.

CONCLUSION: Spinal angiolipomas are uncommon spinal tumors. However, they may be treated as any other space-occupying lesion, and surgical resection allows for complete symptom recovery in most patients.

63 Anonymous. **Erratum : Direct decompressive surgery followed by radiotherapy versus radiotherapy alone for metastatic epidural spinal cord compression: A meta-analysis (Spine (2014) 39 (E587-E592))**. Spine (Phila Pa 1976) 2015;40(9):E562.

## Skjelettmetastaser

1 van den Blink QU, Garcez K, Henson CC, Davidson SE, Higham CE. **Pharmacological interventions for the prevention of insufficiency fractures and avascular necrosis associated with pelvic radiotherapy in adults**. Cochrane Database of Systematic Reviews 2018;4:CD010604.

**Abstract:** BACKGROUND: Pelvic radiotherapy is a treatment delivered to an estimated 150,000 to 300,000 people annually across high-income countries. Fractures due to normal stresses on weakened bone due to radiotherapy are termed insufficiency fractures. Pelvic radiotherapy-related interruption of the blood supply to the hip is termed avascular necrosis and is another recognised complication. The reported incidences of insufficiency fractures are 2.7% to 89% and risk of developing avascular necrosis is 0.5%. These complications lead to significant morbidity in terms of pain, immobility and consequently risk of infections, pressure sores and mortality.

OBJECTIVES: To assess the effects of pharmacological interventions for preventing insufficiency fractures and avascular necrosis in adults over 18 years of age undergoing pelvic radiotherapy.

SEARCH METHODS: We performed electronic literature searches in the Cochrane Central Register of Controlled Trials (CENTRAL), MEDLINE, Embase and DARE to 19 April 2017. We also searched trial registries. Further relevant studies were identified through handsearching of citation lists of included studies.

SELECTION CRITERIA: Randomised controlled trials (RCTs) or non RCTs with concurrent comparison groups including quasi-RCTs, cluster RCTs, prospective cohort studies and case series of 30 or more participants were screened. We included studies assessing the effect of pharmacological interventions in adults over 18 years of age undergoing radical pelvic radiotherapy as part of anticancer treatment for a primary pelvic malignancy. We excluded studies involving radiotherapy for bone metastases. We assessed use of pharmacological interventions at any stage before or during pelvic radiotherapy. Interventions included calcium or vitamin D (or both) supplementation, bisphosphonates, selective oestrogen receptor modulators, hormone replacement therapy (oestrogen or testosterone), denosumab and calcitonin.

DATA COLLECTION AND ANALYSIS: Two review authors independently assessed trial quality and extracted data. We contacted study authors to obtain missing data. Data were to be pooled using the random-effects model if study comparisons were similar, otherwise results were to be reported narratively.

MAIN RESULTS: We included two RCTs (1167 participants). The first RCT compared zoledronic acid with placebo in 96 men undergoing pelvic radiotherapy for non-metastatic prostate cancer.The second RCT had four treatment arms, two of which evaluated zoledronic acid plus adjuvant androgen suppression compared with androgen suppression only in 1071 men undergoing pelvic radiotherapy for non-metastatic prostate cancer.Both studies were at a moderate to high risk of bias and all evidence was judged to be of very low certainty.The studies provided no evidence on the primary outcomes of the review and provided limited data in relation to secondary outcomes, such that meta-analyses were not possible. Both studies focused on interventions to improve bone health in relation to androgen deprivation rather than radiation-related insufficiency fractures and avascular necrosis. Few fractures were described in each study and those described were not specific to insufficiency fractures secondary to radiotherapy. Both studies reported that zoledronic acid in addition to androgen deprivation and pelvic radiotherapy led to improvements in BMD; however, the changes in BMD were measured and reported differently. There was no available evidence regarding adverse effects.

AUTHORS' CONCLUSIONS: The evidence relating to interventions to prevent insufficiency fractures and avascular necrosis associated with pelvic radiotherapy in adults is of very low certainty. This review highlights the need for prospective clinical trials using interventions prior to and during radiotherapy to prevent radiation-related bone morbidity, insufficiency fractures and avascular necrosis. Future trials could involve prospective assessment of bone health including BMD and bone turnover markers prior to pelvic radiotherapy. The interventions for investigation could begin as radiotherapy commences and remain ongoing for 12 to 24 months. Bone turnover markers and BMD could be used as surrogate markers for bone health in addition to radiographic imaging to report on presence of insufficiency fractures and development of avascular necrosis. Clinical assessments and patient reported outcomes would help to identify any associated adverse effects of treatment and quality of life outcomes.

2 Teyssonneau D, Gross-Goupil M, Domblides C, Haaser T, Pointillart V, Daste A, et al. **Treatment of spinal metastases in renal cell carcinoma: A critical review**. Critical Reviews in Oncology-Hematology 2018;125:19-29.

**Abstract:** Kidney cancer is the 9th most common cancer in men and the 14th most common in women worldwide. Renal cell carcinoma (RCC) constitutes 90% of all malignancies of the kidney. RCC, is known to be highly vascular and relatively radioresistant. Bone metastases are one of the most common metastatic sites and occur in around 30% of RCCs. They significantly impact the quality of life of patients causing pain and pathological fractures. Spinal metastases represent a particular case with regard to symptoms and treatment. Indeed, neurological pain is often added to the nociceptive pain caused by metastases. More importantly, neurological impairment can be seen, caused by spinal cord or nerve root compression (MSCC). Due to close contact with the spinal cord, the treatment of spinal bone metastases is challenging and requires a multidisciplinary approach. Specific treatment is currently focused on 4 main avenues which are surgery, radiotherapy, interventional radiology and systemic treatment. In June 2017 we carried out an extensive search on PubMed, Web of Science, and Cochrane Library to review the various treatment options and to establish a treatment strategy. This article presents the result of our critical review of the literature, given our expertise in the field.

3 Smith BW, Joseph JR, Saadeh YS, La Marca F, Szerlip NJ, Schermerhorn TC, et al. **Radiosurgery for Treatment of Renal Cell Metastases to Spine: A Systematic Review of the Literature**. World Neurosurg 2018;109:e502-e9.

**Abstract:** BACKGROUND: The incidence of renal cell carcinoma (RCC) continues to increase, and the spine is the most common site for bony metastasis. Radiation therapy is one treatment for spinal RCC metastasis. Stereotactic body radiotherapy (SBRT) is a newer treatment that reportedly has benefits over conventional external beam radiotherapy. This study systematically reviewed the current literature on SBRT for metastatic RCC to spine.

METHODS: A search of PubMed, Embase, and Scopus databases was conducted in accordance with PRISMA (Preferred Reporting Items for Systematic Reviews and Meta-Analyses) guidelines. Clinical articles evaluating SBRT for RCC metastases were identified. After inclusion and exclusion criteria were applied, the search resulted in 9 articles. Data including pain outcomes, local control, survival outcomes, vertebral compression fracture (VCF), and toxicity were extracted and evaluated.

RESULTS: The studies analyzed showed an improvement in pain in 41%-95% of patients. Local control rates after SBRT ranged 71.2%-85.7% at 1 year, a significant improvement when compared with conventional external beam radiotherapy. The rate of VCF after treatment with SBRT ranged 16%-27.5%, with single-fraction therapy being a risk factor for increased incidence. Overall toxicity rates ranged 23%-38.5%, with only 3 cases of grade 3 toxicity (nausea) and no cases of radiation myelitis.

CONCLUSIONS: Use of SBRT for spinal metastasis from RCC resulted in significant local control and pain outcomes. There is a risk of VCF with SBRT; however, treatment seems to be well tolerated with few serious side effects. There is continued need for long-term prospective studies investigating the optimal role of SBRT in the treatment algorithm of RCC spinal metastases.

4 Rich SE, Chow R, Raman S, Liang Zeng K, Lutz S, Lam H, et al. **Update of the systematic review of palliative radiation therapy fractionation for bone metastases**. Radiother Oncol 2018;126(3):547-57.

**Abstract:** PURPOSE: Radiation therapy is an effective modality for pain management of symptomatic bone metastases. We update the previous meta-analyses of randomized trials comparing single fraction to multiple fractions of radiation therapy in patients with uncomplicated bone metastases.

METHODS: A literature search was conducted in Ovid Medline, Embase, and Cochrane Central Register. Ten new randomized trials were identified since 2010, five with adequate and appropriate data for inclusion, resulting in a total of 29 trials that were analyzed. Forest plots based on each study's odds ratios were computed using a random effects model and the Mantel-Haenszel statistic.

RESULTS: In intention-to-treat analysis, the overall response rate was similar in patients for single fraction treatments (61%; 1867/3059) and those for multiple fraction treatments (62%; 1890/3040). Similarly, complete response rates were nearly identical in both groups (23% vs 24%, respectively). Re-treatment was significantly more frequent in the single fraction treatment arm, with 20% receiving additional treatment to the same site versus 8% in the multiple fraction treatment arm (p<0.01). No significant difference was seen in the risk of pathological fracture at the treatment site, rate of spinal cord compression at the index site, or in the rate of acute toxicity.

CONCLUSION: Single fraction and multiple fraction radiation treatment regimens continue to demonstrate similar outcomes in pain control and toxicities, but re-treatment is more common for single fraction treatment patients.

5 Pin Y, Paix A, Le Fevre C, Antoni D, Blondet C, Noel G. **A systematic review of palliative bone radiotherapy based on pain relief and retreatment rates**. Critical Reviews in Oncology-Hematology 2018;123:132-7.

**Abstract:** Palliative radiotherapy has been shown to have effects on Quality of Life during painful bone metastasis. This review aimed to determine equivalence in pain relief (PR) and retreatment rate (RR) using both single and multi-fraction irradiations, based on evaluation of the trial's quality. We performed a systematic review since ICRU 50 Report (1993) to June 2017, then evaluated trials for reproducibility and good methodology criteria. We found five studies that were reproducible in both dose and volume prescription. One study used three-dimensional (3D) treatment planning. Equivalence between single and multi-fraction schedules was demonstrated for PR after 3 months, but a 2-3 time RR appeared after single-fraction schedules, notably in the first year after treatment (primarily during the first four months). Reserving long course therapy for well-preserved patients would allow for better long-term efficacy with lower RR, while altered patients would suffer less from single-fraction treatments. It appears that life expectancy might not be used as a criterion for this choice.

6 Petersen LJ, Strandberg J, Stenholt L, Johansen MB, Zacho HD. **Reporting and handling of indeterminate bone scan results in the staging of prostate cancer: A systematic review**. Diagnostics 2018;8 (1) (no pagination)(9).

**Abstract:** Bone scintigraphy is key in imaging skeletal metastases in newly diagnosed prostate cancer. Unfortunately, a notable proportion of scans are not readily classified as positive or negative but deemed indeterminate. The extent of reporting of indeterminate bone scans and how such scans are handled in clinical trials are not known. A systematic review was conducted using electronic databases up to October 2016. The main outcome of interest was the reporting of indeterminate bone scans, analyses of how such scans were managed, and exploratory analyses of the association of study characteristics and the reporting of indeterminate bone scan results. Seventy-four eligible clinical trials were identified. The trials were mostly retrospective (85%), observational (95%), large trials (median 195 patients) from five continents published over four decades. The majority of studies had university affiliation (72%), and an author with imaging background (685). Forty-five studies (61%) reported an indeterminate option for the bone scan and 23 studies reported the proportion of indeterminate scans (median 11.4%). Most trials (44/45, 98%) reported how to handle indeterminate scans. Most trials (n = 39) used add-on supplementary imaging, follow-up bone scans, or both. Exploratory analyses showed a significant association of reporting of indeterminate results and number of patients in the study (p = 0.024) but failed to reach statistical significance with other variables tested. Indeterminate bone scan for staging of prostate cancer was insufficiently reported in clinical trials. In the case of indeterminate scans, most studies provided adequate measures to obtain the final status of the patients. Copyright © 2018 by the authors. Licensee MDPI, Basel, Switzerland.

7 Parker C, Heidenreich A, Nilsson S, Shore N. **Current approaches to incorporation of radium-223 in clinical practice**. Prostate Cancer Prostatic Dis 2018;21(1):37-47.

**Abstract:** Background: Treatment options for metastatic castration-resistant prostate cancer (mCRPC) have expanded in recent years and include cytotoxic agents (e.g., docetaxel and cabazitaxel), immunotherapy (e.g., sipuleucel-T), oral hormonal therapies targeting the androgen receptor axis (e.g., enzalutamide and abiraterone), and targeted alpha therapy (e.g., radium-223 dichloride (radium-223)). Although treatment guidelines have been updated to reflect the availability of new agents, it is not easy to apply them in daily clinical practice because recommendations vary depending on patient comorbidities and disease characteristics. Furthermore, therapeutic accessibility, clinical judgment, and experience affect the selection of treatment options. Methods: In this review, we provide practical guidance for the integration of radium-223 into the management of patients with mCRPC based on our collective clinical experience, as well as the available clinical trial data. Results: Radium-223 is a targeted alpha therapy; as a bone-seeking calcium mimetic, it accumulates in hydroxyapatite areas surrounding tumor lesions and selectively binds to the areas of increased bone turnover. Radium-223 prolongs overall survival and delays time to the first symptomatic skeletal events in men with mCRPC, and is indicated for the treatment of patients with CRPC, symptomatic bone metastases, and no known visceral metastases. We review its clinical efficacy and safety, practical guidance on identifying the appropriate patient, and recommendations for how best to educate and inform prospective patients regarding their treatment decision making. In addition, we review recent evidence for sequential and combination therapies with radium-223, provide our experiences with these treatment approaches, and discuss their implications for the future treatment of patients with mCRPC. Conclusions: Based on our clinical experience, radium-223 should be considered relatively early in the treatment course in patients with mCRPC with bone metastases. Coordination of care among multidisciplinary team members, patients, and caregivers is essential for optimizing safe and effective treatment with all CRPC therapies. Copyright © 2017 The Author(s).

8 Paniagua-Collado M, Cauli O. **Non-pharmacological interventions in patients with spinal cord compression: a systematic review**. J Neurooncol 2018;136(3):423-34.

**Abstract:** Spinal cord compression is a complex and challenging condition that greatly affects the quality of life. Non-pharmacological techniques have only been studied to a very lesser extent; although they are evidence to be beneficial. We performed Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) analysis of the scientific literature in several databases (Medline, Cochrane, Scopus, Cuiden, Pubmed, Lilacs and Embase); using the following keywords: spinal cord compression, spine compression, mobilization, positioning, brace and bracing. Eleven studies met the inclusion criteria and were finally included in the systematic review. 3 of them were related to metastatic spinal cord compression, 5 to spinal cord compression due to other causes and the last 3 of them regarded the health professional's knowledge in oncology patients. In all cases, it seems possible to manage spinal cord compression by using external mobilization and braces and that this treatment is beneficial to patients. Positioning plays a massive role in the disease and can improve or worsen the condition when used improperly; the supine position is overused and can have a negative impact both physically and psychologically. Non-pharmacological interventions could be useful for pain management, cardiovascular alterations and patients' well-being. One randomized clinical trial demonstrated that massage therapy, using either broad compression massage or light contact touch massage improved pain control. There is an urgent need of randomized clinical trials with these interventions in order to achieve an improved care of these patients.

9 Nuhn P, De Bono JS, Fizazi K, Freedland SJ, Grilli M, Kantoff PW, et al. **Update on Systemic Prostate Cancer Therapies: Management of Metastatic Castration-resistant Prostate Cancer in the Era of Precision Oncology**. Eur Urol 2018;16:16.

**Abstract:** CONTEXT: Introduction of novel agents for the management of advanced prostate cancer provides a range of treatment options with notable benefits for men with metastatic castration-resistant prostate cancer (mCRPC). At the same time, understanding of optimal patient selection, effective sequential use, and development of resistance patterns remains incomplete.

OBJECTIVE: To review current systemic therapies and recent advances in drug development for mCRPC and strategies to aid in patient selection and optimal sequencing.

EVIDENCE ACQUISITION: A literature review of PubMed/Medline, Cochrane Library, Current Contents Medicine, Web of Science, Clinical Trial.Gov, WHO-ICTRP (January 2004-November 2017), and the proceedings of major international meetings (2015/2016/2017) was performed in November 2017.

EVIDENCE SYNTHESIS: In the last few years, several new options for treatment of mCRPC have shown a survival benefit in phase III trials besides docetaxel:abiraterone, enzalutamide, cabazitaxel, radium-223, and sipuleucel-T. Radium-223 and denosumab have increased options in management of bone metastases. Currently, novel agents such as next-generation androgen receptor (AR) axis-targeting treatments, immunotherapeutics, or therapies targeting other oncogenic and genomic pathways, particularly poly(adenosine diphosphate-ribose) polymerase (PARP) inhibitors and PD-1 inhibitors, are under clinical investigation. With increasing treatment options for mCRPC, information on how to personalize management and how to select and sequence existing therapies is beginning to emerge, as are predictive biomarkers (homologous repair mutations, mismatch repair mutations, AR splice variant 7). Finally, early use of active agents in the castration-sensitive state will likely also change the clinical management of the disease when it becomes castrate resistant.

CONCLUSIONS: The emergence of new drugs for mCRPC has improved treatment options dramatically. Currently, systemic treatment options for mCRPC include hormonal therapy, chemotherapy, immunotherapy, and radionuclide therapy as well as bone-modifying agents and palliative or supportive measures. Further, new genetically targeted agents (PARP inhibitors and PD-1 inhibitors) are on the horizon for certain subsets of biomarker-selected patients. The best strategies for patient selection and optimal sequential use to achieve the longest cumulative survival improvement and to prevent early resistance remain unclear.

PATIENT SUMMARY: The current literature and proceedings from relevant congresses related to available systemic agents for the treatment of metastatic castration-resistant prostate cancer, including novel genetically targeted therapies, including poly(adenosine diphosphate-ribose) polymerase inhibitors and PD-1 inhibitors, were reviewed. Current therapies and ongoing developments are discussed.

10 Nieder C, Langendijk JA, Guckenberger M, Grosu AL. **Second re-irradiation: a narrative review of the available clinical data**. Acta Oncol 2018;57(3):305-10.

**Abstract:** Background: Considerable controversy exists about the safety and efficacy of second re-irradiations (three courses of radiotherapy to overlapping volumes). Therefore, all published clinical studies were reviewed. Material and methods: Contemporary and historical articles were identified. Outcomes such as survival, local control, symptom improvement and side effects were extracted. Contemporary results were grouped by anatomical location of the re-irradiated region in the body. Results: Most data were derived from central nervous system tumors, pelvic tumors and bone metastases. We could include nine contemporary, retrospective studies with 2-25 patients each. Nearly, all patients were treated with palliative intent. Most of the prescribed re-irradiation regimens were highly individualized and thus difficult to compare. Symptomatic responses were recorded in most patients. In palliatively treated patients with pelvic and bony target volumes, high-grade toxicity was uncommon. Conclusions: Despite of issues related to study size, length of follow-up and calculation of lifetime cumulative equivalent dose, the available data provide an initial framework for future studies and discussion of dose constraints. Selected dose-fractionation regimens may result in a satisfactory therapeutic ratio even after two previous courses of radiotherapy, if these were well tolerated. Copyright © 2017 Acta Oncologica Foundation.

11 Myrehaug S, Soliman H, Tseng C, Heyn C, Sahgal A. **Re-irradiation of Vertebral Body Metastases: Treatment in the Radiosurgery Era**. Clin Oncol (R Coll Radiol) 2018;30(2):85-92.

**Abstract:** Vertebral bodies remain one of the most common sites of metastases. In cases where surgical intervention is not indicated or appropriate, conventional external radiation therapy (cEBRT) has been the standard treatment modality. Unfortunately, cEBRT is typically limited, with low complete response and poor local control rates. Disappointing results with re-irradiation using cEBRT highlight the need for innovative salvage therapeutic strategies, such as stereotactic body radiotherapy. A detailed description of this complex treatment strategy is outlined, as is a systematic review of current literature. Although data are limited to single institution series, re-irradiation has consistently been found to be effective with respect to local control (1 year rates range from 66 to 90%) and pain response. Importantly, the treatment is shown to be safe, with the crude rate of radiation myelopathy <1% and a rate of vertebral compression fracture of 12%. As further research and technologic advances continue to refine therapy, stereotactic body radiotherapy is now a recommended option for the treatment of previously irradiated vertebral body metastases.

12 Majmundar N, Shao B, Assina R. **Lung adenocarcinoma presenting as intramedullary spinal cord metastasis: Case report and review of literature**. Journal of Clinical Neuroscience 2018.

**Abstract:** Intramedullary spinal cord metastasis (IMSCM) is a rare entity which lacks well-defined treatment guidelines, yet sees rising incidence. We report a case of a 67-year-old man who presented with severe neck pain and numbness in his right fourth and fifth digits, and was found to have a C5-7 IMSCM of previously unknown lung adenocarcinoma. He underwent gross total resection of the IMSCM, afatinib, and radiation treatment. He had full reversal of his pain and sensory deficit, and remained ambulatory without any focal neurological deficit. Additionally, we conducted a literature review of original case series of IMSCM published between 1983 and 2016, representing 138 unique cases, and discuss various treatments with a focus on surgical resection and general treatment of stage IV lung adenocarcinoma. 18.75% of cases of IMSCM were an initial presentation of underlying malignancy. Rapidly progressive pain and weakness was the most common presentation, often compromising ambulatory status. Median survival ranged from 3.8 to 11.6 months after treatment in patients who were deceased at time of publication. Treatments included corticosteroids, chemotherapy, various radiotherapies, and surgical resection. Surgical resection was found to greatly improve symptoms and preserve ambulatory status, and was associated with increased survival time up to double that of non-surgical treatments. Most authors recommended surgical resection only in symptomatic patients with reversible deficits, to palliate symptoms and preserve ambulation. IMSCM can herald an underlying malignancy, and surgical resection can preserve ambulatory status and palliate symptoms as well increase survival time in a subset of patients. Copyright © 2018 Elsevier Ltd

13 Liu YH, Hu YC, Yang XG, Lun DX, Wang F, Yang L, et al. **Prognostic Factors of Ambulatory Status for Patients with Metastatic Spinal Cord Compression: A Systematic Review and Meta-Analysis**. World Neurosurg 2018;04:04.

**Abstract:** BACKGROUND: This study aimed to identify prognostic factors for functional outcome of metastatic spinal cord compression (MSCC).

METHODS: All full texts in English regarding the prognostic factors for functional outcome of MSCC, published between January 2007 and October 2017, were identified using the electronic databases PubMed, Embase, and the Cochrane Library. An exploratory meta-analysis was also conducted when appropriate data were available.

RESULTS: A total of 25 studies, involving 4897 patients, met the inclusion criteria. Overall, 69.7% of patients across all studies were able to walk postoperatively compared with 49.0% preoperatively. Moreover, 84.7% of the patients maintained ambulation after treatment. Motor function was significantly associated with ambulatory status before treatment, time of developing motor deficits, interval from symptom to surgery, and preoperative performance status.

CONCLUSIONS: Ambulatory status before treatment, interval from symptom to treatment, and time of developing motor deficits can be considered as the most significant prognostic factors for posttreatment ambulatory status. Spinal metastasis should have a higher priority, and immediate intervention should be started before the development of irreversible neurologic deficits. Moreover, short-course radiotherapy might be a good option for patients with a limited life span. Consequently, the identified prognostic factors can be regarded as a preoperative assessment tool to predict neurologic outcome and guide clinical treatment for individual patients with MSCC. However, the retrospective nature of this study with low-quality evidence must be taken into account when interpreting these results, and further research is needed to identify prognostic factors.

14 Li R, Ravizzini GC, Gorin MA, Maurer T, Eiber M, Cooperberg MR, et al. **The use of PET/CT in prostate cancer**. Prostate Cancer Prostatic Dis 2018;21(1):4-21.

**Abstract:** Background: Positron emission tomography/computed tomography (PET/CT) has recently emerged as a promising diagnostic imaging platform for prostate cancer. Several radiolabelled tracers have demonstrated efficacy for cancer detection in various clinical settings. In this review, we aim to illustrate the diverse use of PET/CT with different tracers for the detection of prostate cancer. Methods: We searched MEDLINE using the terms 'prostate cancer', 'PET', 'PET/CT' and 'PET/MR'). The current review was limited to <sup>18</sup>F-NaF PET/CT, choline-based PET/CT, fluciclovine PET/CT and PSMA-targeted PET/CT, as these modalities have been the most widely adopted. Results: NaF PET/CT has shown efficacy in detecting bone metastases with high sensitivity, but relatively low specificity. Currently, choline PET/CT has been the most extensively studied modality. Although having superior specificity, choline PET/CT suffers from low sensitivity, especially at low PSA levels. Nevertheless, choline PET/CT was found to significantly improve upon conventional imaging modalities (CIM) in the detection of metastatic lesions at biochemical recurrence (BCR). Newer methods using fluciclovine and PSMA-targeted radiotracers have preliminarily demonstrated great promise in primary and recurrent staging of prostate cancer. However, their superior efficacy awaits confirmation in larger series. Conclusions: PET/CT has emerged as a promising staging modality for both primary and recurrent prostate cancer. Newer tracers have increased detection accuracies for small, incipient metastatic foci. The clinical implications of these occult PET/CT detected disease foci require organized evaluation. Efforts should be aimed at defining their natural history as well as responsiveness and impact of metastasis-directed therapy. Copyright © 2017 The Author(s).

15 Laufer I, Lo SS, Chang EL, Sheehan J, Guckenberger M, Sohn MJ, et al. **Population Description and Clinical Response Assessment for Spinal Metastases: Part 2 of the SPIne Response Assessment in Neuro-Oncology (SPINO) Group Report**. Neuro-oncol 2018;24:24.

**Abstract:** Background: Approximately 40% of metastatic cancer patients will develop spinal metastases. The current report provides recommendations for standardization of metrics used for spinal oncology patient population description and outcome assessment beyond local control endpoints on behalf of the SPIne response assessment in Neuro-Oncology (SPINO) group.

Methods: SPINO group survey was conducted in order to determine the preferences for utilization of clinician-based and patient-reported outcome measures for description of patients with spinal metastases. Subsequently, ClinicalTrials.gov registry was searched for spinal oncology clinical trials and measures for patient description and outcome reporting were identified for each trial. These two searches were used to identify currently used descriptors and instruments. A literature search was performed focusing on the measures identified in the survey and clinical trial search in order to assess their validity in the metastatic spinal tumor patient population. References for this manuscript were identified through PubMed and Medline searches.

Results: Published literature, expert survey and ongoing clinical trials were used in to synthesize recommendations for instruments for reporting of spinal stability, epidural tumor extension, neurologic and functional status and symptom severity.

Conclusions: Accurate description of patient population and therapy effects requires a combination of clinician-based and patient reported outcome (PRO) measures. The current report provides international consensus recommendations for the systematic reporting of patient- and clinician-reported measures required to develop trials applicable to surgery for spinal metastases and post-operative spine SBRT.

16 La Torre G, Wong M, Eftychiou N, Singh N, Simpson J, Dizdarevic S. **Sodium iodide symporter (NIS) expression in solitary plasmacytoma mimicking a bone metastasis from thyroid cancer**. Nucl Med Commun 2018;39 (4):385-6.

**Abstract:** Purpose: Sodium iodide symporter (NIS) mediates uptake of iodide into follicular cells of the thyroid gland. Breast cancer is the only malignancy other than thyroid cancer to have been shown to functionally express NIS endogenously. However, we report a case of plasmacytoma/myeloma expressing NIS, which mimicked thyroid cancer metastasis. Methods: Case: 72-year-old patient underwent 131-iodine treatment for papillary thyroid carcinoma. Imaging and histology revealed a co-existing NIS-expressing solitary spinal plasmacytoma. We present the imaging findings and review the literature on NIS-expression in plasmacytoma/myeloma. Result: Post ablation 131-I WB-scan showed high grade uptake within thyroid bed and a focus of low to moderate uptake within the chest at the level of T8. MRI showed a suspected metastatic lesion with vertebral body collapse, anterior wedging of T8 and suspected bilateral pedicle fractures. Follow-up 131-I scan demonstrated minimal residual uptake in the thyroid bed, and a reduced, but persistent uptake within the spinal lesion for which a biopsy was suggested. Histology revealed a plasma cell neoplasm with no evidence of metastatic thyroid carcinoma. The lesion was further treated with radiotherapy. A post-vertebroplasty <sup>18</sup>F-FDG-PET/CT scan showed artefactual activity at T8/9 and no FDG avid disease. A review of the literature indicates a new promising strategy using oncolytic viruses expressing the human NIS for the targeted destruction of disseminated myeloma but no previous case of endogenous expression of NIS in plasmacytoma/myeloma has been identified. Conclusion: Myeloma/plasmacytoma cells may rarely express NIS and therefore be visualised and potentially treated by radioactive iodine, or radioviral therapy.

17 Kolbl O. **Radiation therapy of cutaneous malignant melanoma. [German]**. Onkologe 2018:1-5.

**Abstract:** Background: In the past melanoma was considered intrinsically resistant to radiotherapy. In the last two decades radiotherapy was shown to be effective in the treatment of primary and recurrent tumors as well as in metastatic situations. Material and methods: This review is based on a PubMed search of the medical subject heading terms "radiotherapy and melanoma". Results and conclusion: Radiotherapy does not play an important role in the definitive treatment of cutaneous melanoma. An exception is medically inoperable patients with lentigo maligna, where definitive radiotherapy offers a treatment option with good local control rates. Postoperative radiotherapy reduces the risk of recurrence in patients with positive margins and in patients with desmoplastic melanoma and closed margins. Radiotherapy of the nodal basis should be considered in high-risk patients (size and number of involved nodes, extranodal spread, lymph node relapse). Palliative radiotherapy can effectively reduce the symptoms in patients with bone metastases. Local radiosurgery should be preferred to whole brain radiotherapy. Radiotherapy may be simultaneously combined with ipilimumab but should be combined with BRAF inhibitors only sequentially. Copyright © 2018 Springer Medizin Verlag GmbH, ein Teil von Springer Nature

18 Karampinos DC, Ruschke S, Dieckmeyer M, Diefenbach M, Franz D, Gersing AS, et al. **Quantitative MRI and spectroscopy of bone marrow**. J Magn Reson Imaging 2018;47(2):332-53.

**Abstract:** Bone marrow is one of the largest organs in the human body, enclosing adipocytes, hematopoietic stem cells, which are responsible for blood cell production, and mesenchymal stem cells, which are responsible for the production of adipocytes and bone cells. Magnetic resonance imaging (MRI) is the ideal imaging modality to monitor bone marrow changes in healthy and pathological states, thanks to its inherent rich soft-tissue contrast. Quantitative bone marrow MRI and magnetic resonance spectroscopy (MRS) techniques have been also developed in order to quantify changes in bone marrow water-fat composition, cellularity and perfusion in different pathologies, and to assist in understanding the role of bone marrow in the pathophysiology of systemic diseases (e.g. osteoporosis). The present review summarizes a large selection of studies published until March 2017 in proton-based quantitative MRI and MRS of bone marrow. Some basic knowledge about bone marrow anatomy and physiology is first reviewed. The most important technical aspects of quantitative MR methods measuring bone marrow water-fat composition, fatty acid composition, perfusion, and diffusion are then described. Finally, previous MR studies are reviewed on the application of quantitative MR techniques in both healthy aging and diseased bone marrow affected by osteoporosis, fractures, metabolic diseases, multiple myeloma, and bone metastases. Level of Evidence: 3. Technical Efficacy: Stage 2. J. Magn. Reson. Imaging 2018;47:332-353. Copyright © 2017 The Authors Journal of Magnetic Resonance Imaging published by Wiley Periodicals, Inc. on behalf of International Society for Magnetic Resonance in Medicine.

19 Hadden NJ, McIntosh JRD, Jay S, Whittaker PJ. **Prognostic factors in patients with metastatic spinal cord compression secondary to melanoma: a systematic review**. Melanoma Res 2018;28(1):1-7.

**Abstract:** Melanoma is one of the most common primary tumours associated with metastatic spinal cord compression (MSCC). The aim of this review is to identify prognostic factors specifically for MSCC secondary to melanoma. A systematic search of literature was performed in MEDLINE, Embase and the Cochrane Library to identify studies reporting prognostic factors for patients with MSCC secondary to melanoma. Two studies, involving a total of 39 patients, fulfilled the inclusion criteria. The variables associated with increased survival were receiving postoperative radiotherapy, receiving chemotherapy, perioperative lactate dehydrogenase level less than or equal to 8.0micro kat/l, preoperative haemoglobin level more than 11.5mg/dl, an interval of 4 or more years between melanoma diagnosis and skeletal metastasis, absence of further skeletal metastases, absence of visceral metastases, Eastern Cooperative Oncology Group Performance Status of 2 or less, two or fewer involved vertebrae, being ambulatory preradiotherapy and an interval of more than 7 days between developing motor deficits and radiotherapy. The variables associated with good functional outcome were slow development of motor dysfunction, good performance status and being ambulatory before radiotherapy. The most important prognostic factors for survival are Eastern Cooperative Oncology Group Performance Status of 2 or less and absence of visceral metastases. There is a lack of studies looking specifically at prognostic factors for patients with MSCC secondary to melanoma, and the number of patients involved in the existing studies is small.

20 Galgano M, Fridley J, Oyelese A, Telfian A, Kosztowski T, Choi D, et al. **Surgical management of spinal metastases**. Expert Rev Anticancer Ther 2018;18(5):463-72.

**Abstract:** INTRODUCTION: Metastatic spinal disease is a source of significant morbidity in patients with cancer. Recent advancements in adjuvant oncologic therapy has led to increased survival for many patients who harbor neoplastic disease. As a result of this, the chance of developing metastatic spinal disease over the course of a cancer patient's lifespan has increased. Symptomatic metastatic spinal disease can cause significant morbidity including severe pain, neurologic deficit, and loss of ambulation. Current treatment of these patients typically involves the use of multiple modalities, including surgery, radiation, and chemotherapy. Areas covered: An extensive literature review was performed to support the author's opinion on the matter of surgical management of spinal metastatic disease. Pubmed was utilized as a primary search engine. Expert commentary: Despite advances in chemotherapy and radiation therapy, surgery remains a mainstay in many of these patients, particularly with those with either significant metastatic spinal epidural compression or spinal instability. This review discusses the surgical management of metastatic spinal disease including a framework for decision making and technical considerations when deciding to operate on these patients.

21 Foucher Y, Lorent M, Tessier P, Supiot S, Sebille V, Dantan E. **A mini-review of quality of life as an outcome in prostate cancer trials: Patient-centered approaches are needed to propose appropriate treatments on behalf of patients**. Health and Quality of Life Outcomes 2018;16 (1) (no pagination)(40).

**Abstract:** Background: Patients with prostate cancer (PC) may be ready to make trade-offs between their quantity and their quality of life. For instance, elderly patients may prefer the absence of treatment if it is associated with a low-risk of disease progression, compared to treatments aiming at preventing disease progression but with a substantial deterioration of their Health-Related Quality of Life (HRQoL). Therefore, it seems relevant to compare the treatments by considering both survival and HRQoL. In this mini-review, the aim was to question whether the potential trade-offs between survival and HRQoL are considered in high impact factor journals. Methods: The study was conducted from the PubMed database for recent papers published between May 01, 2013, and May 01, 2015. We also restricted our search to nine medical journals with 2013 impact factor > 15. Results: Among the 30 selected studies, only six collected individual HRQoL as a secondary endpoint by using the Functional Assessment of Cancer Therapy-Prostate (FACT-P) questionnaire. In four studies, the time to HRQoL change was analyzed, but its definitions varied. In two studies, the mean changes in HRQoL between the baseline and the 12- or 16-week follow-up were analyzed. None of the six studies reported in a single endpoint both the quantity and the quality of life. Conclusions: Our mini-review, which only focused on recent publications in journals with high-impact, suggests moving PC clinical research towards patient-centered outcomes-based studies. This may help physicians to propose the most appropriate treatment on behalf of patients. We recommend the use of indicators such as Quality-Adjusted Life-Years (QALYs) as principal endpoint in future clinical trials. Copyright © 2018 The Author(s).

22 Ferrer-Mileo L, Luque Blanco AI, Gonzalez-Barboteo J. **Efficacy of cryoablation to control cancer pain. A systematic review**. Pain pract 2018;07:07.

**Abstract:** CONTEXT: The use of opioids to control cancer pain could be insufficient. Interventional techniques such as a cryoablation have emerged as alternatives to opioids.

OBJECTIVES: To summarize the current scientific evidence on the use of cryoablation to control cancer pain.

METHODS: A systematic search of the Scopus, Pubmed, and Cochrane databases was performed. All articles published before December 31, 2015 whose title or abstract specified cancer pain control as endpoint were selected. Articles without abstract and all non-systematic reviews were excluded.

RESULTS: 22 articles were included: one randomized clinical trial (RCT); two non-RCTs; one ambispective study; 9 retrospective studies; two non-specified cohort studies; three case series and four case reports. 496 patients with 580 lesions were treated. Lung cancer was the most common primary tumour. 82.8% of the metastases were bone metastases, with or without soft tissue involvement. Cryoablation decreased mean pain scores by 62.5% at 24 hours post-cryoablation, by 70% at 3 months, and by 80.9% at 6 months. Cryoablation was associated with a 44.2% improvement in quality of life (QoL) after 4 weeks and a 59.6% at 8 weeks. The need for opioids decreased by 75% at 24 h and by 61.7% at 3 months. Cryoablation in combination with radiotherapy, vertebroplasty or bisphosphonates appears to be better than cryoablation alone. Complications were highly variable among the studies, but no fatal complications were reported.

CONCLUSIONS: Cryoablation is effective in controlling cancer pain without relevant side effects. However, more studies are needed to confirm these results. This article is protected by copyright. All rights reserved.

23 Farina E, Capuccini J, Macchia G, Caravatta L, Nguyen NP, Cammelli S, et al. **Short course accelerated radiation therapy (SHARON) in palliative treatment of advanced solid cancer in older patients: A pooled analysis**. Journal of Geriatric Oncology 2018.

**Abstract:** Objectives: To evaluate the efficacy and safety of a conformal Short Course Accelerated Radiation therapy (SHARON) for symptomatic palliation of locally advanced or metastatic cancers in older patients. Materials and Methods: This is a pooled analysis on patients aged >=. 80 years selected between subjects enrolled in 3 phase I-II studies on a short course palliative treatment of advanced or metastatic cancer. The primary endpoint was to evaluate the symptoms response rate produced by accelerated radiotherapy delivered in 4 total fractions in twice a day. Total dose ranged between 14 Gy and 20 Gy while dose/fraction between 3.5 and 5 Gy. Results: A total of 48 patients were included in this analysis. Twenty-six patients (54.2%) had advanced primary or metastatic head and neck tumors, 11 (22.9%) locally advanced or metastatic thoracic cancers, 11 (22.9%) complicated bone metastases. The majority of patients presented pain (60.4%). With a median follow-up time of 5.5 months, no G4 acute and late toxicities were recorded. The overall palliative response rate was 91.7% with a median duration of palliation of 4 months. Conclusion: Short course accelerated radiotherapy in locally advanced or metastatic cancers is effective in terms of symptom relief and well tolerated even in older patients. Copyright © 2018.

24 Denunzio C, Presicce F, Giacinti S, Bassanelli M, Tubaro A. **Castration-resistance prostate cancer: What is in the pipeline?** Minerva Urol Nefrol 2018;70(1):22-41.

**Abstract:** INTRODUCTION: To evaluate the available evidence on the standard diagnosis and management of men with metastatic castration resistant prostate cancer (mCRPC), and providing the timely update on new pharmacological treatments. EVIDENCEACQUISITION: Asystematic literature search from from January 2000 until March 2017 was performed by combining the following MESH terms: castrate resistant prostate cancer, abiraterone, enzalutamide, 223radium, sipuleucel-T, docetaxel, cabazitaxel, resistance mechanisms, resistance to androgen deprivation, androgen receptor (AR) mutations, amplifications, splice variants, and AR alterations. We followed the Preferred Reporting Items for Systematic Review and Meta-Analysis (PRISMA). EVIDENCESYNTHESIS: In the few last years the introduction of new treatment modalities as abiraterone or enzalutamide have significantly change our prospective in mCRPC management increasing patients survival and quality of life. The standard imaging modalities to define the presence of regional or distant metastasis or the different resistant mechanisms to the available treatments are still an issue of debate, however several studies are ongoing to define the standard of care and to reduce treatments' resistance. Data from ongoing phase IIItrials are awaited to introduce in clinical new effective treatments that can be used in patients resistant to abiraterone/enzalutamide or more probably in a different phase of the disease. CONCLUSIONS: Castration resistant prostate cancer is now the key issue in prostate cancer management and research. Our challenge in the near future will be to identify the right treatment or better the right combination and sequencing of treatments that should be used in patients with mCRPCor even with advanced prostate cancer. Copyright © 2017 EDIZIONI MINERVA INERVAINERVA MEDICA.

25 de Souza LL, Pontes FSC, Pontes HAR, Neto NC, de Carvalho WRS, Guimaraes DM. **Central mucoepidermoid carcinoma: An up-to-date analysis of 147 cases and review of prognostic factors**. Journal of Cranio-Maxillofacial Surgery 2018;46(1):162-7.

**Abstract:** Objective: To integrate the available data published on central mucoepidermoid carcinoma (CMC) into a comprehensive analysis of its clinical aspects, histology, treatment, and prognostic factors. Methods: An electronic search was undertaken in July 2017. Eligibility criteria for publications included having clinical, histological, treatment, and time of follow-up data to confirm the diagnosis. Results: \* 36 publications (147 CMCs) were included.\* The lesion showed a slightly higher prevalence among women than men.\* There was a high prevalence in the fifth to seventh decades of life.\* The most common symptom was swelling and the most commonly observed area was the mandible.\* Histologically, low-grade tumors were the most common.\* The treatment of choice was tumor resection.In addition, gender, histological grade, conservative treatment, and lymph node metastasis were significant independent prognostic factors. Conclusion: Male patients with histological grade III CMC of the jaw bone, who used conservative treatment as the main treatment, and presented with lymph node metastasis, were more likely to have a worse prognosis. Copyright © 2017 European Association for Cranio-Maxillo-Facial Surgery

26 Chan DL, Thompson R, Lam M, Pavlakis N, Hallet J, Law C, et al. **External Beam Radiotherapy in the Treatment of Gastroenteropancreatic Neuroendocrine Tumours: A Systematic Review**. Clin Oncol 2018;31:31.

**Abstract:** AIMS: External beam radiotherapy (EBRT) is infrequently used to treat gastroenteropancreatic neuroendocrine tumours (GEPNETS), with little published data to date. We carried out a systematic review to assess the activity of EBRT for GEPNETS.

MATERIALS AND METHODS: Major databases were searched for papers including at least five patients treated with contemporary EBRT techniques. Eligible studies underwent dual independent review. The primary end points were response rate for lesions treated with definitive intent and recurrence-free survival for primary lesions treated with neoadjuvant or adjuvant intent.

RESULTS: Of 11 included studies (all retrospective), seven investigated pancreatic neuroendocrine tumours (PNETs, 100 patients, 14% grade 3) and four studies investigated extra-pancreatic neuroendocrine tumours (84 patients, 14% grade 3). Trials investigating PNETs administered a median of 50.4 Gy via three-dimensional conformal radiotherapy and intensity-modulated radiotherapy. EBRT was given with neoadjuvant or adjuvant intent in 56 patients, with a recurrence rate of 15%. For the 44 patients not undergoing surgery, the radiological response rate was 46%. Grade 3 + toxicity rates were 11% (acute) and 4% (late). Twelve patients with anorectal neuroendocrine carcinoma received 58 Gy to the primary tumour. Seventy-two patients were treated to sites of metastatic disease (34 bone, 27 brain, 11 soft tissue). Local and distant control were poorly reported. Overall survival ranged from 9 to 19 months. No studies in this group reported toxicity outcomes.

CONCLUSIONS: There are limited, retrospective data on the overall activity and safety of EBRT in GEPNETS. EBRT generally seems to be well tolerated in selected PNET patients with encouraging activity. Well-designed prospective studies in clearly defined populations are required to clarify the role of EBRT in neuroendocrine tumours.

27 Casadei R, Drago G, Di Pressa F, Donati D. **Humeral metastasis of renal cancer: Surgical options and a review of literature**. Orthopaedics and Traumatology: Surgery and Research 2018.

**Abstract:** Introduction: The humerus is the second most common long bone site of metastatic disease from renal cell carcinomas (RCC) after femur. Surgery has an important role in the treatment of these lesions due to renal cell tumor's resistance to chemotherapy and radiotherapy. Hypothesis: Prosthetic replacement is an effective and safe solution in treatment of renal humeral metastasis. Material and methods: Fifty-six patients affected by RCC bone metastases of the humerus that underwent a surgical reconstruction were reviewed. Thirty-five lesions were localized on proximal third, 12 on the shaft, 9 on distal third. Among proximal 29 were treated with resection and endoprosthetic replacement and 6 with plate and cement. Six diaphyseal lesions were stabilized with intramedullary nailing, 5 with plate and cement and 1 with an intercalary prosthesis. Regarding distal lesions, 7 elbow prostheses and 2 plates and cement were used. Results: The average age was 63 years. Metastasis was single in 55% of cases, and in 45% metachronous. A pathologic fracture (PF) occurred in 64% of cases. Only 9% of patients had a mechanical complication, 7% an infection and 5% neurological deficit. A local recurrence occurred in 14% of patients. An implant failure has been observed in 10 patients, 5 for mechanical complications, 2 for infections and 3 for local recurrence; of these 7 were treated with a prosthesis and 3 with plate and cement. The mean value of MSTS score was 64%, 63% and 59% respectively in patients with proximal, diaphyseal and distal humerus metastases. Discussion: Solitary and metachronous bone metastases have a longer survival. Disease-free interval > 2 years is another important prognostic factor. Reconstruction with a modular prosthesis is recommended in proximal and distal third. Instead in diaphyseal lesions a closed reduction and fixation with intramedullary locked nailing are preferred. When surgical indications are correctly followed, good oncologic and functional outcomes are obtained, leading to markedly improvement of patients' quality of life. Retrospective study: Level of evidence: IV. Copyright © 2018 Elsevier Masson SAS

28 Andronis L, Goranitis I, Bayliss S, Duarte R. **Cost-Effectiveness of Treatments for the Management of Bone Metastases: A Systematic Literature Review**. Pharmacoeconomics 2018;36(3):301-22.

**Abstract:** BACKGROUND: Metastatic cancers occur when cancer cells break away from the primary tumour. One of the most common sites of metastasis is the bone, with several therapeutic options currently available for managing bone metastases. In a resource-constrained environment, policy makers and practitioners need to know which options are cost effective.

OBJECTIVE: The aim of this systematic review was to review and appraise published economic evaluations on treatments for the management of bone metastases.

METHODS: We searched eight bibliographic databases (MEDLINE, MEDLINE in Process, EMBASE, CSDR, DARE, HTA, EED and CPCI) for relevant economic evaluations published from each database's inception date until March 2017. Study selection, quality assessment and data extraction were carried out according to published guidelines.

RESULTS: Twenty-four relevant economic analyses were identified. Seventeen of these studies focused on bone metastases resulting from a particular type of cancer, i.e. prostate (n = 8), breast (n = 7), lung (n = 1) or renal (n = 1), while seven report results for various primary tumours. Across types of cancer, evidence suggests that bisphosphonates result in lower morbidity and improved quality of life, for an additional cost, which is typically below conventional cost-effectiveness thresholds. While denosumab leads to health gains compared with zoledronic acid, it also results in substantial additional costs and is unlikely to represent value for money. The limited literature on the radiopharmaceutical strontium-89 (Sr89) and external beam radiotherapy (EBR) suggest that these treatments are cost effective compared with no treatment.

CONCLUSIONS: The reviewed evidence suggests that bisphosphonate treatments are cost-effective options for bone metastases, while denosumab is unlikely to represent value for money. Evidence on EBR and Sr89 is limited and less conclusive.

29 Zhang Z, Pu F, Shao Z. **The skeletal-related events of denosumab versus zoledronic acid in patients with bone metastases: A meta-analysis of randomized controlled trials**. Journal of Bone Oncology 2017;9:21-4.

**Abstract:** Objective The meta-analysis was used to evaluate the skeletal-related events (SREs) and efficacy of denosumab versus zoledronic acid (ZA) in patients with bone metastases. Methods The data of this meta-analysis study were searched from PUBMED, EMBASE, Cochrane Library, Web of Science with Conference Proceedings, Elsevier and China National Knowledge Infrastructure (CNKI) databases till August 2017. Two independent reviewers reviewed the reference lists of relevant articles. The fixed-effects model and random-effects model were used to summarize relative estimates and 95% confidence intervals (CIs) according to the heterogeneity of the included studies. Results Three randomized controlled trials (RCTs) including 4050 patients were identified in this meta-analysis study. The pooled analysis showed that denosumab could significantly reduce SREs, series SREs [Odds Ratio (OR) = 0.84; 95% CI, 0.74-0.95, I<sup>2</sup> = 0%, P = 0.008] in patients with bone metastases as compared with ZA. Similar results of spinal cord compression SRE and surgery to bone SRE were obtained with (OR = 0.84; 95% CI, 0.70-1.01, I<sup>2</sup> = 0%, P = 0.07) and (OR = 0.92; 95% CI, 0.78-1.08, I<sup>2</sup> = 0%, P = 0.28) separately, radiation to bone SRE (OR = 0.72; 95% CI, 0.46-1.10, I<sup>2</sup> = 11%, P = 0.13) and pathological fracture SRE (OR = 0.78; 95% CI, 0.35-1.73, I<sup>2</sup> = 25%, P = 0.54) showed similar results, there were no significant difference between denosumab and ZA in patients with bone metastases. Conclusion Denosumab was more effective than ZA in reducing the incidence of SRE in patients with bone metastases. Copyright © 2017 The Authors

30 Zacho HD, Karthigaseu NN, Fonager RF, Petersen LJ. **Treatment with bone-seeking radionuclides for painful bone metastases in patients with lung cancer: a systematic review**. BMJ support 2017;7(3):230-7.

**Abstract:** Treatment with bone-seeking radionuclides may provide palliation from pain originating from bone metastases. However, most studies have been conducted in patients with prostate cancer and patients with breast cancer. We aimed to perform a systematic review of the use of radionuclide treatment in lung cancer in accordance with the PRISMA guidelines. In the eligible trials, pain relief was reported in 75% of the patients included in the studies. The onset of pain relief was seen within 1-5 weeks after treatment, lasting up to 6 months. However, the methodology in the included trials was poor-only two randomised trials were eligible, and none of them compared radionuclide treatments with placebo or best standard of care. The remaining trials were case series with inherent problems of methodology reporting. Particularly challenging was the lack of reporting of baseline disease status and use of prior/concomitant analgaesics. Large randomised controlled trials are needed to clarify the efficacy of radionuclide treatment in lung cancer.

31 Yao A, Sarkiss CA, Ladner TR, Jenkins AL, 3rd. **Contemporary spinal oncology treatment paradigms and outcomes for metastatic tumors to the spine: A systematic review of breast, prostate, renal, and lung metastases**. J Clin Neurosci 2017;41:11-23.

**Abstract:** Metastatic spinal disease most frequently arises from carcinomas of the breast, lung, prostate, and kidney. Management of spinal metastases (SpM) is controversial in the literature. Recent studies advocate more aggressive surgical resection than older studies which called for radiation therapy alone, challenging previously held beliefs in conservative therapy. A literature search of the PubMed database was performed for spinal oncology outcome studies published in the English language between 2006 and 2016. Data concerning study characteristics, patient demographics, tumor origin and spinal location, treatment paradigm, and median survival were collected. The search retrieved 220 articles, 24 of which were eligible to be included. There were overall 3457 patients. Nine studies of 1723 patients discussed parameters affecting median survival time with comparison of different primary cancers. All studies found that primary cancer significantly predicted survival. Median survival time was highest for primary breast and renal cancers and lowest for prostate and lung cancers, respectively. Multiple spinal metastases, a cervical location of metastasis, and pathologic fracture each had no significant influence on survival. Survival in metastatic spinal tumors is largely driven by primary tumor type, and this should influence palliative management decisions. Surgery has been shown to greatly increase quality of life in patients who can tolerate the procedure, even in those previously treated with radiotherapy. Surgery for SpM can be used as first-line therapy for preservation of function and symptom relief. Future studies of management of SpM are warranted and primary tumor diagnosis should be studied to determine contribution to survival.

32 von Moos R, Costa L, Ripamonti CI, Niepel D, Santini D. **Improving quality of life in patients with advanced cancer: Targeting metastatic bone pain**. Eur J Cancer 2017;71:80-94.

**Abstract:** Metastatic bone disease in patients with advanced cancer is frequently associated with skeletal complications. These can be debilitating, causing pain, impaired functioning and decreased quality of life, as well as reduced survival. This review considers how the management of metastatic bone pain might be optimised, to limit the considerable burden it can impose on affected patients. Cancer-related pain is notoriously under-reported and under-treated, despite the availability of many therapeutic options. Non-opioid and opioid analgesics can be used; the latter are typically administered with radiotherapy, which forms the current standard of care for patients with metastatic bone pain. Surgery is appropriate for certain complicated cases of metastatic bone disease, and other options such as radiopharmaceuticals may provide additional relief. Treatments collectively referred to as bone-targeted agents (BTAs; bisphosphonates and denosumab) can offer further pain reduction. Initiation of therapy with BTAs is recommended for all patients with metastatic bone disease because these agents delay not only the onset of skeletal-related events but also the onset of bone pain. With evidence also emerging for pain control properties of new anticancer agents, the potential to individualise care for these patients is increased further. Optimisation of care depends on physicians' thorough appreciation of the complementary benefits that might be achieved with the various agents, as well as their limitations. Appropriate anti-tumour treatment combined with early initiation of BTAs and adequate analgesia plays a key role in the holistic approach to cancer pain management and may minimise the debilitating effects of metastatic bone pain. Copyright © 2016 Amgen Inc.

33 Varadarajan VV, Pace EK, Patel V, Sawhney R, Amdur RJ, Dziegielewski PT. **Follicular thyroid carcinoma metastasis to the facial skeleton: A systematic review**. BMC Cancer 2017;17 (1) (no pagination)(225).

**Abstract:** Background: Follicular thyroid carcinoma (FTC) metastasis to the facial skeleton is exceedingly rare. A case of FTC metastasizing to the mandible is presented and a systematic review of the literature describing thyroid metastasis to the facial skeleton is performed. Case presentation: A 73-year-old female presented with metastatic FTC to the mandible and underwent total thyroidectomy, segmental mandibulectomy, bone impacted fibular free flap reconstruction, and adjuvant radioactive iodine treatment. The PubMed database was searched for literature describing thyroid cancer with facial skeleton metastasis using the key words "thyroid," "cancer," "carcinoma," "metastasis," and "malignancy" with "oral cavity," "maxilla," "mandible," "sinus," "paranasal," and "orbit." Reports that only involved the soft tissues were excluded. Systematic review revealed 59 cases of well-differentiated thyroid cancer with facial skeleton metastasis: 35 mandibular metastases (21 = FTC), 6 maxilla metastases (2 = FTC), 9 orbital metastases (4 = FTC), and 11 paranasal sinus metastases (7 = FTC). Treatment included surgery, RAI, external beam radiotherapy (XRT), or a combination of these modalities. The one, two, and five-year survival rates were 100%, 79%, and 16%, respectively. Conclusion: Facial skeleton metastasis of FTC is a rare clinical challenge. Optimal treatment appears to include total thyroidectomy and resection of involved structures with or without adjuvant treatment. Copyright © 2017 The Author(s).

34 Van Poznak C, Somerfield MR, Barlow WE, Biermann JS, Bosserman LD, Clemons MJ, et al. **Role of Bone-Modifying Agents in Metastatic Breast Cancer: An American Society of Clinical Oncology-Cancer Care Ontario Focused Guideline Update**. J Clin Oncol 2017;35(35):3978-86.

**Abstract:** Purpose To update, in collaboration with Cancer Care Ontario (CCO), key recommendations of the American Society of Clinical Oncology (ASCO) guideline on the role of bone-modifying agents (BMAs) in metastatic breast cancer. This focused update addressed the new data on intervals between dosing and the role of BMAs in control of bone pain. Methods A joint ASCO-CCO Update Committee conducted targeted systematic literature reviews to identify relevant studies. Results The Update Committee reviewed three phase III noninferiority trials of dosing intervals, one systematic review and meta-analysis of studies of de-escalation of BMAs, and two randomized trials of BMAs in control of pain secondary to bone metastases. Recommendations Patients with breast cancer who have evidence of bone metastases should be treated with BMAs. Options include denosumab, 120 mg subcutaneously, every 4 weeks; pamidronate, 90 mg intravenously, every 3 to 4 weeks; or zoledronic acid, 4 mg intravenously every 12 weeks or every 3 to 4 weeks. The analgesic effects of BMAs are modest, and they should not be used alone for bone pain. The Update Committee recommends that the current standard of care for supportive care and pain management-analgesia, adjunct therapies, radiotherapy, surgery, systemic anticancer therapy, and referral to supportive care and pain management-be applied. Evidence is insufficient to support the use of one BMA over another. Additional information is available at www.asco.org/breast-cancer-guidelines and www.asco.org/guidelineswiki .

35 Van Der Velden JM, Gerlich AS, Wong E, Chow E, Intven M, Kasperts N, et al. **Impact of SBRT on pain and local control for bone metastases: A systematic review and meta-analysis**. Radiother Oncol 2017;123 (Supplement 1):S749.

**Abstract:** Purpose or Objective Pain due to bone metastases is the most common cancerrelated pain syndrome. Besides analgesics, conventional radiotherapy has been the cornerstone in the management of bone metastases. However, control of pain after conventional radiotherapy is modest, approximately 60%. Advances in radiotherapy technique enable the delivery of potentially ablative radiation doses, while respecting healthy tissue constraints under the heading of stereotactic body radiotherapy (SBRT). We conducted a systematic review and meta-analysis to quantify pain response and local control after SBRT for bone metastases. Material and Methods Following the Preferred Reporting Items for Systematic reviews and Meta-Analyses (PRISMA) guideline, Embase, PubMed and Cochrane Libraries were searched with the (synonym) terms 'bone metastases' and 'stereotactic body radiotherapy'. Studies delivering SBRT in 1 - 6 fractions to patients with or without previous radiotherapy or surgery were included. Information from studies reported in more than one publication was collated, and the most complete or recent article was cited. Study variables, including pain response and local control rates, were extracted from the selected articles. Pain response was defined as a complete or partial (i.e., at least 2 points decrease in pain score) response. To qualify for inclusion in the meta-analysis, outcomes had to be reported on an individual patient or lesion level, follow up had to be recorded at least 45% of the study population, and the size of the study population had to be 10 or more. Pooled estimates using randomeffects models were calculated for pain response and local control rates. Results After screening of 2619 unique articles, 54 articles (3359 patients) were included in the systematic review. Twentysix articles (1627 patients/lesions) were included in the meta-analysis for pain response, and 36 articles (2875 lesions) in the meta-analysis for local control. After SBRT, pain response rate ranged from 62% to 98% (see forest plot), and local control rate ranged between 25% and 97% (see forest plot). Excluding the study with the lowest local control rate, which included patients with spinal lesions from hepatocellular carcinoma, the local control rates varied between 74% and 97%. Pooled pain response rate was 80% (95% confidence interval [CI] 72% - 87%) with high heterogeneity (I<sup>2</sup> = 77%). Pooled local control rate was 87% (95% CI 84% - 90%) with high heterogeneity (I<sup>2</sup> = 76%). Conclusion SBRT for bone metastases results in high pain control and high local control rates. This observation needs to be further confirmed within large randomized controlled trials. (Figure Presented).

36 Trodello C, Pepper JP, Wong M, Wysong A. **Cisplatin and Cetuximab Treatment for Metastatic Cutaneous Squamous Cell Carcinoma: A Systematic Review**. Dermatol Surg 2017;43(1):40-9.

**Abstract:** BACKGROUND Cutaneous squamous cell carcinoma (cSCC) is the second most common form of skin cancer and metastasizes in 2% to 5% of cases. OBJECTIVE Systematic evaluation of published cases of metastatic cSCC (mSCC) treated with cisplatin or cetuximab from 1989 to 2014. MATERIALS AND METHODS A literature search was performed to identify cases of mSCC treated with cisplatin or cetuximab. Patient demographics, tumor characteristics, response rates, and disease-free survivals were extracted. RESULTS A total of 60 cases of mSCC treated with cisplatin and 9 cases treated with cetuximab reported in the literature from 1989 to 2014 were included in the analysis. Patients treated with cetuximab obtained a complete response of 67%, an overall response of 78%, and a median disease-free survival of 25 (range 3-48) months. Patients treated with cisplatin obtained a complete response of 22%, an overall response of 45%, and a median disease-free survival of 14.6 (range 3-112) months. CONCLUSION Head-to-head prospective clinical studies between cetuximab and cisplatin are needed to determine which is more efficacious. In addition, prospective tumor registries and randomized controlled trials should be developed in order to establish the ideal systemic regimen in cSCC. Copyright © 2016 by the American Society for Dermatologic Surgery, Inc. Published by Wolters Kluwer Health, Inc. All rights reserved.

37 Seixas N, Belsuzarri TAB, Belsuzarri NCB, Pozetti M, Araujo JFM. **Cavernous sinus syndrome as the first manifestation of metastatic breast disease**. Surg Neurol Int 2017;8(1).

**Abstract:** Background: The cavernous sinus is a venous plexus crossed by vital neurovascular structures. Metastases to the region are uncommon and often associated with a headache, facial pain, or progressive neurological deficit in III, IV, and VI cranial nerves. The treatment options are surgery, including endoscopic approach, radiotherapy, radiosurgery, and chemotherapy. Case Description: We report the case of a 26-year-old female with cavernous sinus syndrome due to breast cancer metastasis, who was subjected to chemotherapy with complete neurological recovery. A literature review was performed using the databases Bireme, Pubmed, Cochrane, Lilacs and Medline with the keywords: cavernous sinus/metastasis/surgery/radiosurgery for multiple management options review. Conclusion: Cavernous sinus metastases are rare, and the cavernous sinus syndrome is rarely the first sign of cancer, especially in young patients. Because the syndrome has multiple causes, the history of rapid progression and atypical image findings can arise suggesting metastatic diseases. As in our case, the image was suggestive of meningioma, however, the clinical presentation and further investigations led us to suspect as a metastatic disease. The therapeutic decision considers clinical and functional status, the extent of primary and metastatic disease, radiological study, tumor histopathology, and biological behavior. Often associated with significant symptoms and disseminated systemic disease, nowadays radiosurgery is the first and less invasive strategy, offering low risk of new deficits, clinical improvement, and good local control. The prognosis depends on early treatment and disease staging because mortality is associated with progression of cancer. Copyright © 2017 Surgical Neurology International Published by Wolters Kluwer - Medknow.

38 Saeed H, Patel R, Thakkar J, Hamoodi L, Chen L, Villano JL. **Multimodality therapy improves survival in intramedullary spinal cord metastasis of lung primary**. Hematology/ Oncology and Stem Cell Therapy 2017;10(3):143-50.

**Abstract:** Background Most metastatic spinal cord lesions are located either in the intradural, extramedullary, or in the epidural compartments. Intramedullary spinal cord metastasis (ISCM) is a rare central nervous system spread of cancer. The aim of this report was to evaluate ISCM in the published literature. Methods A literature review of PubMed from 1960 to 2016 was undertaken for the publications having demographic, clinical, histological, and outcome data. Results A total of 59 relevant papers were identified, showing 128 cases of intramedullary metastasis from lung cancer. The incidence of lung cancer as the primary malignancy with intramedullary metastasis was 56%. The median time from diagnosis of primary to intramedullary metastasis was 6 months. Survival improved with multimodality therapy compared to monotherapy (4 months vs. 6.3 months) (hazard ratio = 0.501; 95% confidence interval, 0.293-0.857). Conclusion Lung cancer is the predominant cause of intramedullary involvement of the spinal cord. Overall prognosis is poor, although a multimodality approach was associated with improved survival. Copyright © 2017 King Faisal Specialist Hospital & Research Centre

39 Sadeghi-Naini M, Aarabi S, Shokraneh F, Janani L, Vaccaro AR, Rahimi-Movaghar V. **Vertebroplasty and Kyphoplasty for Metastatic Spinal Lesions: A Systematic Review**. Clin Spine Surg 2017;27:27.

**Abstract:** INTRODUCTION: The spine is the most common site of bone metastases. Vertebroplasty (VP) and kyphoplasty (KP) have been proposed as potential minimally invasive therapeutic options for metastatic spinal lesion (MSL) pain. However, the efficacy of VP and KP on MSL pain is currently unclear.

OBJECTIVE: The aim of this study was to assess the effects of VP and KP compared with each other, usual care, or other treatments on pain, disability, and quality of life following MSL.

METHODS: We included randomized controlled trials and prospective nonrandomized controlled clinical trials assessing VP or KP for the treatment of pain following MSL without cord compression. We searched MEDLINE, EMBASE, PubMed, and CENTRAL.

RESULTS: The literature search revealed 387 citations. Of these, 9 trials met all eligibility criteria and were included in the qualitative analysis. In total, there were 622 patients enrolled in the trials and of them 432 were in the surgical treatment group (92 received KP, 97 received VP, 134 received VP and chemotherapy, 68 received VP and radiotherapy, and 41 received Kiva implant) and 190 were in the nonsurgical treatment group (83 received chemotherapy, 46 received radiotherapy, and 61 received other treatment). Using the grading of recommendations assessment, development and evaluation approach, pain (low-quality evidence) and functional scores (very low-quality evidence) improved more with VP plus chemotherapy than with chemotherapy alone (pain: mean difference, -3.01; 95% confidence interval, -3.21 to -2.80; functional score: mean difference, 15.46; 95% confidence interval, 13.58-17.34). KP seemed to lead to significantly greater improvement in pain, disability, and health-related quality of life (HRQoL) compared with nonsurgical management. VP plus Iodine-125 seemed to lead to significantly greater improvement in pain and disability in comparison with VP alone. VP plus radiochemotherapy resulted in better pain relief and HRQoL postoperatively in comparison with routine radiochemotherapy. There was low-quality evidence to prove that surgical treatment significantly decreases pain, and improves functional score and HRQoL following MSL in comparison with nonsurgical management.

CONCLUSION: On the basis of the analysis of currently published trial data, it is unclear whether VP for MSL provides benefits over KP.

LEVEL OF EVIDENCE: Level 2.

40 Roque IFM, Martinez-Zapata MJ, Scott-Brown M, Alonso-Coello P. **WITHDRAWN: Radioisotopes for metastatic bone pain**. Cochrane Database of Systematic Reviews 2017;3:CD003347.

**Abstract:** BACKGROUND: This is an update of the review published in Issue 4, 2003. Bone metastasis cause severe pain as well as pathological fractures, hypercalcaemia and spinal cord compression. Treatment strategies currently available to relieve pain from bone metastases include analgesia, radiotherapy, surgery, chemotherapy, hormone therapy, radioisotopes and bisphosphonates.

OBJECTIVES: To determine efficacy and safety of radioisotopes in patients with bone metastases to improve metastatic pain, decrease number of complications due to bone metastases and improve patient survival.

SEARCH METHODS: We sought randomised controlled trials (RCTs) in MEDLINE, EMBASE, CENTRAL, and the PaPaS Trials Register up to October 2010.

SELECTION CRITERIA: Studies selected had metastatic bone pain as a major outcome after treatment with a radioisotope, compared with placebo or another radioisotope.

DATA COLLECTION AND ANALYSIS: We assessed the risk of bias of included studies by their sequence generation, allocation concealment, blinding of study participants, researchers and outcome assessors, and incomplete outcome data. Two review authors extracted data. We performed statistical analysis as an "available case" analysis, and calculated global estimates of effect using a random-effects model. We also performed an intention-to-treat (ITT) sensitivity analysis.

MAIN RESULTS: This update includes 15 studies (1146 analyzed participants): four (325 participants) already included and 11 new (821 participants). Only three studies had a low risk of bias. We observed a small benefit of radioisotopes for complete relief (risk ratio (RR) 2.10, 95% CI 1.32 to 3.35; Number needed to treat to benefit (NNT) = 5) and complete/partial relief (RR 1.72, 95% CI 1.13 to 2.63; NNT = 4) in the short and medium term (eight studies, 499 participants). There is no conclusive evidence to demonstrate that radioisotopes modify the use of analgesia with respect to placebo. Leucocytopenia and thrombocytopenia are secondary effects significantly associated with the administration of radioisotopes (RR 5.03; 95% CI 1.35 to 18.70; Number needed to treat to harm (NNH) = 13). Pain flares were not higher in the radioisotopes group (RR 0.74; 95% CI 0.27 to 2.06). There are scarce data of moderate quality when comparing Strontium-89 (<sup>89</sup>Sr) with Samarium-153 (<sup>153</sup>Sm), Rhenium-186 (<sup>186</sup>Re) and Phosphorus-32 (<sup>32</sup>P). We observed no significant differences between treatments. Similarly, we observed no differences when we compared different doses of <sup>153</sup>Sm (0.5 versus 1.0 mCi).

AUTHORS' CONCLUSIONS: This update adds new evidence on efficacy of radioisotopes versus placebo, <sup>89</sup>Sr compared with other radioisotopes, and dose-comparisons of <sup>153</sup>Sm and <sup>188</sup>Re. There is some evidence indicating that radioisotopes may provide complete reduction in pain over one to six months with no increase in analgesic use, but severe adverse effects (leucocytopenia and thrombocytopenia) are frequent.

41 Raman S, Ganesh V, Chan S, Chow R, Hoskin P, Lam H, et al. **A review of practice patterns and clinical guidelines in the palliative radiation treatment of uncomplicated bone metastases**. International Journal of Radiation Oncology Biology Physics 2017;99 (2 Supplement 1):E525-E6.

**Abstract:** Purpose/Objective(s): Single fraction radiation treatment (SFRT) is recommended for its equivalence to multiple fraction (MF) RT in the palliation of uncomplicated bone metastases (BM). However, adoption of SFRT has been slow. The purpose of this study is to summarize SFRT-related patterns of practice and clinical guidelines in the palliative RT of uncomplicated BM. Purpose/Objective(s): Literature searches for studies published following 2014 were conducted using several online repositories of grey literature, Ovid MEDLINE, Embase and Embase Classic, and the Cochrane Central Register of Controlled Trials databases. Results: A total of 11 studies regarding patterns of practice and 21 articles detailing clinical practice guidelines were included for final synthesis. The majority of organizations have released strongly graded recommendations for SFRT use in treatment of uncomplicated BM, based on evidence of non-inferiority to MFRT. However, there are key differences between guidelines, such as varying strengths of recommendation for SFRT use over MFRT; contraindication of vertebral sites for SFRT; and risk estimation of pathologic fractures after SFRT. There are also differences in the recommendation of palliative RT for BM under the Choosing Wisely campaign. Differences in guidelines may be influenced by committee composition and organization mandate. Differences in patterns of practice may be influenced by individual centre policies, payment modalities and consideration of patient factors such as age, prognosis, and performance status. Increased use of SFRT was reported in 5 out of 6 studies reporting temporal trends post-2010. Conclusion: Although there is some misalignment between authoritative groups, the majority of guidelines recommend use of SFRT for uncomplicated BM and others consider it to be a reasonable alternative to MFRT.

42 Purvis TE, Goodwin CR, Lubelski D, Laufer I, Sciubba DM. **Review of stereotactic radiosurgery for intradural spine tumors**. CNS Oncology 2017;6(2):131-8.

**Abstract:** Stereotactic radiosurgery (SRS) has become an increasingly popular treatment modality for spinal tumors due to its noninvasive and targeted approach. Whether SRS has the promise of relieving pretreatment symptoms and providing local tumor control for patients with intradural spine tumors is still debated. This review explores the current literature on SRS treatment for both metastatic and benign intradural tumors, with a focus on differential use for intramedullary and intradural extramedullary neoplasms. Although mortality rates from underlying malignant disease remain high, SRS may benefit patients with spinal metastatic lesions. Benign tumors have shown a promising response to SRS therapy with low rates of complications. Larger studies are necessary to determine the indications and outcome profile of SRS for intradural spinal neoplasms. Copyright © 2017 Future Medicine Ltd.

43 Pons-Tostivint EEPT, Kirova YYK, Lusque AAL, Campone MMC, Levy CCL, Delaloge SSD, et al. **Impact of loco-regional treatment (LRT) on overall-survival (OS) in patients with de novo metastatic breast cancer (MBC): Results of the French ESME multicenter national observational programme**. Cancer Research Conference: San Antonio Breast Cancer Symposium, SABCS 2017;78(4 Supplement 1).

**Abstract:** Background: Previous retrospective studies and meta-analysis suggest an improved overall survival (OS) brought by loco-regional treatment (LRT) of primary tumor in de novo metastatic breast cancer (MBC) patients (pts), while prospective trials have mixed results. Most of the previous studies recruited pts before 2005 and consequently did not include recent medical therapies and advances used in MBC. Patients and methods: The ESME database include individual data from MBC pts diagnosed between 2008 and 2014, who initiated their treatment in 1 of the 18 participating French comprehensive cancer centers. Our first aim was to study the impact of LRT, defined as surgery, radiotherapy or both, on OS in de novo MBC pts, defined as pts diagnosed with synchronous metastasis or within 90 days from diagnosis of primary tumor. OS was calculated from the date of diagnosis of metastatic stage and was estimated by the Kaplan Meier method. Univariate and multivariate analyses were performed using Logrank-test and Cox-model, respectively. Results: Of the total ESME cohort (16703 pts), 4507 (26.9%) were diagnosed with de novo MBC and 4276 fulfilled inclusion criteria for the present study. Median age was 60 years. 66.3% pts had T3-T4. 13.1% (n=495) had triple-negative (TN) BC, 24.4% (n=918) HER2+ BC and 62.5% (n=2536) HR+/HER2-BC. Sites of metastases were bone (69%), liver (30.9%), nodes (29.5%) and lung (25.7%). 77.4% had less than 3 sites involved by metastatic disease. Of 4276 pts, 1706 (39.9%) received a LRT. Among them, 444 (26%) and 535 (31.4%) had surgery or radiotherapy alone respectively, 727 (42.6%) had a combination of both. 99% of pts received a systemic treatment: hormone therapy for 60.3% and chemotherapy +/- targeted therapy for 72.8% of them. Compared with pts with no LRT, pts in the LRT group were younger (median age: 57 vs 61 years, p<0.0001), had smaller tumor (40.4% <= T2 vs 28.2%, p<0.0001) with more N0 status (26.5% vs 19.3%, p<0.0001), and different phenotypes: TN 12.1% vs 13.8%; HER2+ 26.4% vs 23.1%; HR+/HER2-61.5% vs 63.1% (p=0.0447). Metastatic disease in the LRT group was more likely to be limited to 1 or 2 sites (86.4% vs 71.4%), with more non-visceral sites (52.3% vs 36.5%). With a median follow-up of 45.3 m, median OS and initial PFS for the whole population were 45.2 m [95%CI: 43.3-47.1] and 13.8 m [95%CI: 13.2-14.4], respectively. Median OS for TN, HR+/HER2- and HER2+ pts were 19 m [95%CI:17-21], 47.4 m [95%CI: 45.2-50.4] and 53.3 m [95%CI: 48.9-60.2], respectively. By multivariate analysis, LRT was an independent prognostic factor for OS (HR=0.76; 95%CI: 0.64-0.89; p=0.001), together with age, histological subtype, number and patterns of metastatic sites. More advanced analyses will be presented in December. </del> Conclusion: As in older series, this work finds that de novo MBC pts treated after 2008 may derive a prolonged OS, extending up to 4 years for HR+ and HER2+ subgroups. Given the classical prescription biases in such retrospective works, this should be carefully interpreted but might help in better selecting those pts for whom such strategy would be beneficial.

44 Phadnis S, Grosshans D, Johnson J, Khatua S, Fuller G, Zaky W. **Diffuse leptomeningeal glioneuronal tumor: A distinctive entity without current standard treatment. Case report and literature review**. Pediatric Blood and Cancer 2017;64 (Supplement 1):S82.

**Abstract:** Background: Diffuse Leptomeningeal Glioneuronal Tumor (DLGT) is a rare neoplasm which was recently included in the revisedWHO 2016 classification of tumors of the central nervous system (CNS).We report here a case of recurrent disseminated DLGT, its clinical presentation, molecular results and management. Objectives: To describe the presentation of a rare CNS tumour, discuss the potential role of adjuvant therapy and literature review. Design/Method: A MEDLINE search was conducted for queries including "Diffuse Leptomeningeal Glioneuronal Tumor". Relevant papers were selected for the literature review. Results: An eight year-old male patient presented with bilateral leg pain that was progressively worsening to the point of inability to bear weight. Brain magnetic resonance images (MRI) showed a 2 cm enhancing intramedullary neoplasm within the thoracic cord at T7-T8. There was no evidence of spinal metastasis or intracranial disease and lumbar puncture was negative for malignant cells. The patient underwent excisional biopsies and was diagnosed as papillary ependymoma at an outside institution. No further treatment was given, over the subsequent 14 months follow up magnetic resonance imaging revealed 3 new spinal lesions. Excisional biopsies were repeated and pathology reviewed at our institution demonstrated DLGT in both the initial and second biopsies. Immunophenotyping was positive for S100 protein, vimentin and synaptophysin, with no expression of EMA, GFAP, CK, NSE, or chromogranin, and low level of Ki67 staining. Among the complex cytogenetic alterations identified was a t(1;19)(q10;p10) translocation which corresponds with the diagnosis of DLGT. Due to the aggressive behavior of the tumor, the patient received craniospinal radiation to 36Gy(RBE) plus 7.2 and 5.4 Gy(RBE) boosts to the low and mid spine respectively followed by 6 cycles of temozolomide maintenance chemotherapy. Patient has been clinically stable with resolution of his symptoms and has stable residual disease on serial surveillance MRI imaging; one year since last surgery. Conclusion: DLGT is a very rare type of glioneuronal tumor that has recently been classified in the WHO classification. A literature review of single case reports or small case series showed that although Diffuse Leptomeningeal Glioneuronal Tumors express low grade markers, clinically they behave aggressively as they disseminate and recur. Limited data is available on the use of adjuvant therapy in DLGT treatment. Additional data about disease course, relevant biomarkers, and treatment outcomes are needed for further understanding of these rare brain tumors. In our patient, the combination of surgical resection and adjuvant chemo-radiotherapy has maintained stable disease for a year post re-excision.

45 Patel KN, Yu H, Le M, Paidpally V, Harvill M, Critchfield J. **Vertebroplasty and kyphoplasty outcomes in spinal metastatic osseous lesions: A systematic review and meta-analysis**. J Vasc Interv Radiol 2017;28 (2):e24.

**Abstract:** Purpose: Vertebroplasty (VP) and kyphoplasty (KP) are percutaneous techniques that are widely used to relieve pain and restore stability in metastatic spinal disease with pathologic vertebral compression fractures. The purpose of this systematic re-view is to compare outcomes between VP and KP in terms of safety and efficacy in providing pain relief and improving patients' functional status. Materials: A PRISMA-compliant systematic review was performed using the electronic database PubMed from conception to 2016. Levels of evidence and grades of recommendation were established based on the Oxford Centre for Evidence-Based Medicine guidelines. MedCalc (16.2.1) was used for data entry and analysis. Compar-ison between the groups (VP and KP) in terms of cement leakage and complications was calculated using a chi-square test. Pain level was assessed using the visual analog scale (VAS), and the groups were compared using t-test. A P value less than 0.05 was considered statistically significant. Results: Ten published studies on KP and three published studies on VP for meta-static spine lesions met the inclusion criteria, representing 342 patients undergoing VP and KP at various levels of the spine with most common treated level being the thoracic spine. No significant difference in the cement leaks (P = 0.35) and incidence of perioperative complication (P = 0.77) was noted between the KP and VP groups. The KP group showed significant reduction in the VAS by postoperative day 1 to 3 (P = 0.0002) and by postoperative month 0.5 to 3 (P < 0.0001). Within the KP group, a significant decrease in Oswestry Disability Index score from baseline was observed by postoperative day 1 to 3 and by postoperative month 0.5 to 3. Conclusions: Our systematic review shows that KP is more effective in reducing pain as early as postoperative day 1 to 3. Furthermore, patients who underwent KP had significant improvement in their functional status from baseline by as early as postoperative day 1 to 3 with continued improved functional status lasting up to 1 year. Meanwhile, no difference in cement leaks or perioperative complication rate was observed between the KP and VP groups.

46 Park KR, Lee CG, Reddy S, Bruera E, Yennu S. **Palliative radiation therapy in the last 30 days of life: A systematic review**. International Journal of Radiation Oncology Biology Physics 2017;99 (2 Supplement 1):E495.

**Abstract:** Purpose/Objective(s): To investigate the utilization of palliative radiation therapy (RT), risk factors related to the use of RT, and symptom response of palliative RT during the last 30 days of life through systemic review of literature. Purpose/Objective(s): A systematic electronic literature search of available medical literature databases was performed for these categories: radiation therapy, terminally ill patients, and end-of-life. Only studies on patients receiving palliative RT in the last 30 days of life were included. A formal meta-analysis was not feasible because of the heterogeneity of published studies and the lack of minimal standards in reporting results. Results: A total of 18 studies were evaluated: 9 were population based studies and 9 were from single institutions. RT utilization rate was variable according to study cohort. For all cancer types, 5-10% of patients who died of cancer received palliative RT in the last 30 days of life. Of patients who received any palliative RT, 9-15.3% received this in the last 30 days of life. The most common indications for RT were metastatic bone, lung/mediastinal, brain, or spinal disease. The most commonly used RT fractionation was 30 Gy in 10 fractions (36-90%). Single fraction RT utilization ranged from 0-59%, with reported rates of 8-9.4% in the US and 19-59% in Canada. The proportions of patients receiving >10 fractions during the last 30 days of life was 17-17.8%, 11-12%, and 11% in studies from the US, Canada and Norway, respectively. In 2 studies that reported time spent on RT relative to remaining life span, 52% of patients who survived less than 1 month died during their treatment courses, and half spent greater than 60% of their remaining lifespan on therapy. ECOG performance status 3-4 was significantly associated with receiving RT in the last 30 days of life and shorter survival. Only 26% of patients who survived less than 1 month were reported to show symptom response following RT. Conclusion: Palliative RT is utilized in about 10% of patients near the end of life. Dose fractionation regimens are variable, as is utilization of single fraction regimens. Many patients spend a large proportion of their end of life actively receiving treatment, with a high rate of mortality during treatment. Careful consideration of the benefits of palliative RT in this patient population should be weighed and greater use of shorter or single fraction regimens rather than more protracted regimens may be beneficial, especially in patients with poor performance status.

47 Myrehaug S, Sahgal A, Hayashi M, Levivier M, Ma L, Martinez R, et al. **Reirradiation spine stereotactic body radiation therapy for spinal metastases: systematic review**. Journal of Neurosurgery Spine 2017;27(4):428-35.

**Abstract:** OBJECTIVE Spinal metastases that recur after conventional palliative radiotherapy have historically been difficult to manage due to concerns of spinal cord toxicity in the retreatment setting. Spine stereotactic body radiation therapy (SBRT), also known as stereotactic radiosurgery, is emerging as an effective and safe means of delivering ablative doses to these recurrent tumors. The authors performed a systematic review of the literature to determine the clinical efficacy and safety of spine SBRT specific to previously irradiated spinal metastases. METHODS A systematic literature review was conducted, which was specific to SBRT to the spine, using MEDLINE, Embase, Cochrane Evidence-Based Medicine Database, National Guideline Clearinghouse, and CMA Infobase, with further bibliographic review of appropriate articles. Research questions included: 1) Is retreatment spine SBRT efficacious with respect to local control and symptom control? 2) Is retreatment spine SBRT safe? RESULTS The initial literature search retrieved 2263 articles. Of these articles, 160 were potentially relevant, 105 were selected for in-depth review, and 9 studies met all inclusion criteria for analysis. All studies were single-institution series, including 4 retrospective, 3 retrospective series of prospective databases, 1 prospective, and 1 Phase I/II prospective study (low- or very low-quality data). The results indicated that spine SBRT is effective, with a median 1-year local control rate of 76% (range 66%-90%). Improvement in patients' pain scores post-SBRT ranged from 65% to 81%. Treatment delivery was safe, with crude rates of vertebral body fracture of 12% (range 0%-22%) and radiation-induced myelopathy of 1.2%. CONCLUSIONS This systematic literature review suggests that SBRT to previously irradiated spinal metastases is safe and effective with respect to both local control and pain relief. Although the evidence is limited to low-quality data, SBRT can be a recommended treatment option for reirradiation.

48 Macherey S, Monsef I, Jahn F, Jordan K, Yuen KK, Heidenreich A, et al. **Bisphosphonates for advanced prostate cancer**. Cochrane Database of Systematic Reviews 2017;2017 (12) (no pagination)(CD006250).

**Abstract:** Background: The prevalence and incidence of pain and skeletal complications of metastatic bone disease such as pathologic fractures, spinal cord compression and hypercalcemia is high and an important contributor to morbidity, poor performance status and decreased quality of life. Moreover, pathologic fractures are associated with increased risk of death in people with disseminated malignancies. Therefore, prevention of pain and fractures are important goals in men with prostate cancer at risk for skeletal complications. Objectives: To assess the effects of bisphosphonates in men with bone metastases from prostate cancer. Search methods: We identified studies by electronic search of bibliographic databases including the Cochrane Controlled Trials Register and MEDLINE on 13 July 2017 and trial registries. We handsearched the Proceedings of American Society of Clinical Oncology (to July 2017) and reference lists of all eligible trials identified. This is an update of a review last published in 2006. Selection criteria: We included randomized controlled studies comparing the effectiveness of bisphosphonates in men with bone metastases from prostate cancer. Data collection and analysis: Two review authors independently extracted data and assessed the quality of trials. We defined the proportion of participants with pain response as the primary end point; secondary outcomes were skeletal-related events, mortality, quality of life, adverse events, analgesic consumption and disease progression. We assessed the quality of the evidence for the main outcomes using the GRADE approach. Main results: We included 18 trials reporting on 4843 participants comparing the effect of bisphosphonate administration to control regimens. Primary outcome: there was no clear difference in the proportion of participants with pain response (RR 1.15, 95% CI 0.93 to 1.43; P = 0.20; I<sup>2</sup> = 0%; 3 trials; 876 participants; low quality evidence). In absolute terms, bisphosphonates resulted in a pain response in 40 more participants per 1000 (19 fewer to 114 more). Secondary outcomes: bisphosphonates probably reduced the incidence of skeletal-related events in participants with prostate cancer metastatic to bone (RR 0.87, 95% CI 0.81 to 0.94; P = 0.27; I<sup>2</sup> = 19%; 9 trials; 3153 participants; moderate quality evidence). In absolute terms, bisphosphonates resulted in 58 fewer SREs per 1000 (85 fewer to 27 fewer). We found no clinically relevant differences in mortality (RR 0.97, 95% CI 0.91 to 1.04; P = 0.43; I<sup>2</sup> = 1%; 9 trials; 2450 participants; moderate quality evidence). In absolute terms, bisphosphonates resulted in 16 fewer deaths per 1000 (47 fewer to 21 more). Outcome definition of quality of life and the measurement tools varied greatly across trials and we were unable to extract any quantitative data for meta-analysis. Bisphosphonates probably increased the number of participants affected by nausea (RR 1.19, 95% CI 1.00 to 1.41; P = 0.05; I<sup>2</sup> = 0%; 9 trials; 3008 participants; moderate quality evidence). In absolute terms, bisphosphonates resulted in seven more cases of nausea per 1000 (0 fewer to 14 more). Bisphosphonates probably increased the number of renal adverse events (RR 1.65, 95% CI 1.11 to 2.46; P = 0.01; I<sup>2</sup> = 0%; 7 trials; 1794 participants; moderate quality evidence). In absolute terms, bisphosphonates resulted in 22 more renal adverse events per 1000 (4 more to 50 more). We found no clear difference in the number of participants with osteonecrosis of the jaw between groups (RR 1.92, 95% CI 0.75 to 4.90; P = 0.17; I<sup>2</sup> = 0%; 5 trials; 1626 participants; very low quality evidence). In absolute terms, bisphosphonates resulted in seven more cases with osteonecrosis of the jaw per 1000 (2 fewer to 29 more). We observed no clinically relevant difference in the proportion of participants with decreased analgesic consumption (RR 1.19, 95% CI 0.87 to 1.63; P = 0.28; I<sup>2</sup> = 37%; 4 trials; 416 participants). Statistical analysis revealed that bisphosphonates probably reduce the number of participants with disease progression (RR 0.94, 95% CI 0.90 to 0.98; P = 0.006; I<sup>2</sup> = 0%; 7 trials; 2115 participants; moderate quality evidence). In absolute terms, bisphosphonates resulted in 36 fewer cases of disease progression per 1000 (71 fewer to 7 fewer). Findings of our predefined subgroup and sensitivity analyses were no different from those of the primary analyses. Authors' conclusions: Based on low quality evidence, there may be no clinically relevant difference in the proportion of men with pain response between bisphosphonates and control regimens in men with bone metastases from prostate cancer. Bisphosphonates probably decrease the number of skeletal-related events and disease progression. These benefits need to be weighed against the increased risk of renal impairment and nausea in men receiving bisphosphonates. Future studies should explicitly evaluate patient important outcomes such as quality of life and pain by using standardized and comparable assessment tools. Copyright © 2017 The Cochrane Collaboration. Published by John Wiley & Sons, Ltd.

49 Lutz S, Balboni T, Jones J, Lo S, Petit J, Rich SE, et al. **Palliative radiation therapy for bone metastases: Update of an ASTRO Evidence-Based Guideline**. Pract Radiat Oncol 2017;7(1):4-12.

**Abstract:** PURPOSE: The purpose is to provide an update the Bone Metastases Guideline published in 2011 based on evidence complemented by expert opinion. The update will discuss new high-quality literature for the 8 key questions from the original guideline and implications for practice.

METHODS AND MATERIALS: A systematic PubMed search from the last date included in the original Guideline yielded 414 relevant articles. Ultimately, 20 randomized controlled trials, 32 prospective nonrandomized studies, and 4 meta-analyses/pooled analyses were selected and abstracted into evidence tables. The authors synthesized the evidence and reached consensus on the included recommendations.

RESULTS: Available literature continues to support pain relief equivalency between single and multiple fraction regimens for bone metastases. High-quality data confirm single fraction radiation therapy may be delivered to spine lesions with acceptable late toxicity. One prospective, randomized trial confirms both peripheral and spine-based painful metastases can be successfully and safely palliated with retreatment for recurrence pain with adherence to published dosing constraints. Advanced radiation therapy techniques such as stereotactic body radiation therapy lack high-quality data, leading the panel to favor its use on a clinical trial or when results will be collected in a registry. The panel's conclusion remains that surgery, radionuclides, bisphosphonates, and kyphoplasty/vertebroplasty do not obviate the need for external beam radiation therapy.

CONCLUSION: Updated data analysis confirms that radiation therapy provides excellent palliation for painful bone metastases and that retreatment is safe and effective. Although adherence to evidence-based medicine is critical, thorough expert radiation oncology physician judgment and discretion regarding number of fractions and advanced techniques are also essential to optimize outcomes when considering the patient's overall health, life expectancy, comorbidities, tumor biology, anatomy, previous treatment including prior radiation at or near current site of treatment, tumor and normal tissue response history to local and systemic therapies, and other factors related to the patient, tumor characteristics, or treatment.

50 Luksanapruksa P, Buchowski JM, Hotchkiss W, Tongsai S, Wilartratsami S, Chotivichit A. **Prognostic factors in patients with spinal metastasis: a systematic review and meta-analysis**. Spine J 2017;17(5):689-708.

**Abstract:** BACKGROUND CONTEXT: Incidence of symptomatic spinal metastasis has increased owing to improvement in treatment of the disease. One of the key factors that influences decision-making is expected patient survival. To our knowledge, no systematic reviews or meta-analysis have been conducted that review independent prognostic factors in spinal metastases.

PURPOSE: This study aimed to determine independent prognostic factors that affect outcome in patients with metastatic spine disease.

STUDY DESIGN: This is a systematic literature review and meta-analysis of publications for prognostic factors in spinal metastatic disease.

PATIENT SAMPLE: Pooled patient results from cohort and observational studies.

OUTCOME MEASUREMENT: Meta-analysis for poor prognostic factors as determined by hazard ratio (HR) and 95% confidential interval (95% CI).

METHODS: We systematically searched relevant publications in PubMed and Embase. The following search terms were used: ("'spinal metastases'" OR "'vertebral metastases'" OR ""spinal metastasis" OR 'vertebral metastases') AND ('"prognostic factors"' OR "'survival'"). Inclusion criteria were prospective and retrospective cohort series that report HR and 95% CI of independent prognostic factors from multivariate analysis. Two reviewers independently assessed all papers. The quality of included papers was assessed by using Newcastle-Ottawa Scale for cohort studies and publication bias was assessed by using funnel plot, Begg test, and Egger test. The prognostic factors that were mentioned in at least three publications were pooled. Meta-analysis was performed using HR and 95% CI as the primary outcomes of interest. Heterogeneity was assessed using the I<sup>2</sup> method.

RESULTS: A total of 3,959 abstracts (1,382 from PubMed and 2,577 from Embase) were identified through database search and 40 publications were identified through review of cited publications. The reviewers selected a total of 51 studies for qualitative synthesis and 43 studies for meta-analysis. Seventeen poor prognostic factors were identified. These included presence of a neurologic deficit before surgery, non-ambulatory status before radiotherapy (RT), non-ambulatory status before surgery, presence of bone metastases, presence of multiple bone metastases (>2 sites), presence of multiple spinal metastases (>3 sites), development of motor deficit in <7 days before initiating RT, development of motor deficit in <14 days before initiating RT, time interval from cancer diagnosis to RT <15 months, Karnofsky Performance Score (KPS) 10-40, KPS 50-70, KPS<70, Eastern Cooperative Oncology Group (ECOG) grade 3-4, male gender, presence of visceral metastases, moderate growth tumor on Tomita score (TS) classification, and rapid growth tumor on TS classification.

CONCLUSIONS: Seventeen independent poor prognostic factors were identified in this study. These can be categorized into cancer-specific and nonspecific prognostic factors. A tumor-based prognostic scoring system that combines all specific and general factors may enhance the accuracy of survival prediction in patients with metastatic spine disease.

51 Lin N. **Spinal metastases: A comparison of stereotactic body radiotherapy (SBRT) and conventional radiotherapy**. J Med Radiat Sci 2017;64 (Supplement 1):89.

**Abstract:** Background: The primary treatment for spinal metastases is conventional palliative radiotherapy. However, due to the risk of myelopathy, the radiation dose is limited by the spinal cord, and reirradiation can present challenges. Hence, stereotactic body radiotherapy (SBRT) has emerged as an alternative treatment method. In particular, SBRT has the potential to escalate the biologically effective radiation dose without exceeding the spinal cord tolerance.1 Objectives: To compare SBRT and conventional radiotherapy treatment for spinal metastases. Methods: A literature review of studies that discussed radiotherapy for spinal metastases was conducted. It focused on three main criteria to determine technique superiority: clinical outcomes, toxicity and practical issues. Results: The main goals for treatment of spinal metastases are to increase local control, relieve pain, decrease the likelihood of spinal cord compression and improve quality of life. A randomised controlled trial (RCT) by Braam et al.2 comparing conventionally fractionated radiotherapy and SBRT is ongoing; however, there are no current RCT results available yet. However, single arm studies of SBRT have shown relatively high rates of local control with minimal toxicity.3,4,5 Conclusion: SBRT treatment of the spine has been shown to be effective and safe; however, careful patient selection is very important. Nevertheless, conventional radiotherapy still plays an integral role in the palliative management of patients with spinal metastases. RCTs comparing both modalities with long-term follow-up should be conducted.

52 Lim MY, Adam B, Arnav A, Mauricio FS, Chow E. **Use of corticosteroids for pain control in cancer patients with bone metastases: A comprehensive literature review**. Support Care Cancer 2017;25 (2 Supplement 1):S89.

**Abstract:** Introduction Despite a limited understanding of the exact mechanism, corticosteroids are commonly employed for pain control in patients with bone metastases. Objectives The aim of this review was to evaluate the efficacy of corticosteroid-mediated pain control in patients with bone metastases associated with solid cancers. Methods A literature search was conducted using OVID MEDLINE and Embase databases (from 1946 up to July 19, 2016). Studies involving patients with bone metastases receiving corticosteroids as the primary means of pain control were included. Screening and data extraction were conducted by paired reviewers, with consensus established by discussion, or a third adjudicator. Results A total of 12 studies were included. Rates of pain relief achieved with corticosteroid use varied from 30% to 70%, but generally reflected mod-erate pain control. Corticosteroid use significantly reduced the incidence of pain flare alongside radiotherapy, reportedly by almost half of baseline pain severity. Adverse events were not documented consistently across studies, though grade 2-3 hyperglycemia was noted in approximately 2% of patients by some studies. Conclusions Recent evidence suggests that short-term corticosteroid use may provide moderate pain and pain flare control with radiotherapy for patients with bone metastases. The risk of developing adverse effects should be carefully considered prior to therapy initiation on a case-by-case basis.

53 Lim FMY, Bobrowski A, Agarwal A, Silva MF. **Use of corticosteroids for pain control in cancer patients with bone metastases: a comprehensive literature review**. Curr 2017;11(2):78-87.

**Abstract:** PURPOSE OF REVIEW: Despite a limited understanding of the exact mechanism, corticosteroids are commonly employed for pain control in patients with bone metastases. The aim of this review was to evaluate the efficacy of corticosteroid-mediated pain control in patients with bone metastases associated with solid cancers.

RECENT FINDINGS: A literature search was conducted using OVID MEDLINE and Embase databases (from 1946 up to July 19, 2016). Studies involving patients with bone metastases receiving corticosteroids as the primary means of pain control were included. Screening and data extraction were conducted by paired reviewers, with consensus established by discussion, or a third adjudicator. A total of 12 studies were included. Rates of pain relief achieved with corticosteroid use varied from 30 to 70%, but generally reflected moderate pain control. Corticosteroid use significantly reduced the incidence of pain flare alongside radiotherapy, reportedly by almost half of baseline pain severity. Adverse events were not documented consistently across studies, though grade two to three hyperglycemia was noted in approximately 2% of patients by some studies.

SUMMARY: Recent evidence suggests that short-term corticosteroid use may provide moderate pain and pain flare control with radiotherapy for patients with bone metastases. The risk of developing adverse effects should be carefully considered prior to therapy initiation on a case-by-case basis.

54 Lieng H, Hayden A, Christie D, Davis B, Emmett L, Holt T, et al. **Patterns of practice for relapsed prostate cancer and development of the Faculty of Radiation Oncology Genito-urinary Group (FROGG) consensus guidelines**. J Med Imaging Radiat Oncol 2017;61 (Supplement 1):117.

**Abstract:** Purpose: With the increasing availability of ultrasensitive PSA assays and PSMA-PET scans, as well as recent results from randomised clinical trials, the management of relapsed prostate cancer is evolving.1-4 The aim of this study was to assess current patterns of practice and management of relapsed prostate cancer by radiation oncologists in Australia and New Zealand to help develop consensus guidelines based on the best available evidence. Methods and Materials: The Royal Australian and New Zealand College of Radiologists Faculty of Radiation Oncology Genito-urinary Group (FROGG) conducted an online survey consisting of five clinical scenarios: biochemical relapse post-prostatectomy (RP), prostate bed recurrence post-prostatectomy, local recurrence post-definitive radiotherapy (RT), isolated regional node recurrence and recurrence with oligometastatic bone disease. FROGG delegated a committee to seek expert opinion and critically review the literature in these areas. Results: Forty radiation oncologists across Australia and New Zealand responded to the survey. In the case of a rising PSA to 0.2 lg/L post-prostatectomy for pT3aN0, Gleason 8 margin negative cancer, 50% would first arrange a PSMA-PET, and 95% would proceed with salvage radiotherapy. Salvage radiotherapy was given with concurrent androgen deprivation therapy (ADT) in 45% of responses, and 40% of respondents included elective pelvic node irradiation (EPNI). For a solitary pelvic lymph node recurrence identified on PSMA post- RP with a PSA of 1.2 mug/L, 92% recommended RT, whereas 8% would treat with ADT alone. RT was to the involved node and elective pelvic nodes in 76% of responses, with 24% treating the involved node alone, commonly using SBRT. ADT was given in 71% of EPNI and 40% of cases treating the involved node only. For an asymptomatic solitary bone metastasis, 84% would recommend radiotherapy (most frequently treating with SBRT), and of these 45% would also give ADT. After reviewing the literature, the nominated FROGG committee and experts drafted guidelines on these scenarios, which were further developed during the 2017 FROGG workshop, and consensus reached on the majority of management scenarios. In some cases, such as isolated pelvic nodal recurrence, oligometastatic recurrence and intra-prostatic relapse post-radiotherapy, it was identified that high-level evidence was lacking and patients should be considered for clinical trials. Conclusion: Due to variations in clinical practice for common management scenarios of prostate cancer relapse, FROGG has developed evidence-based recommendations to help guide clinicians and inform practice. Management of oligometastatic disease recurrence was identified as a priority area for further clinical research.

55 Kumar A, Weber MH, Gokaslan Z, Wolinsky JP, Schmidt M, Rhines L, et al. **Metastatic Spinal Cord Compression and Steroid Treatment: A Systematic Review**. Clin Spine Surg 2017;30(4):156-63.

**Abstract:** STUDY DESIGN: Systematic review.

OBJECTIVES: We conducted a systematic review of the literature to answer the following questions regarding the use of steroid therapy in metastatic spinal cord compression (MSCC): 1. In cases of MSCC, what is the effect of steroid administration before definitive radiotherapy or surgery on ambulatory status, bowel and bladder function and survival? 2. What steroid dosing regimens are associated with the best outcomes concerning neurological symptoms and complication prevention in cases of MSCC?

SUMMARY OF BACKGROUND DATA: Currently, there is significant variation in the initial bolus dose, daily maintenance dose and duration of treatment when steroids are used as a bridge to definitive therapy for MSCC.

METHODS: A literature search following PRISMA guidelines was conducted in June 2016, using Medline via Ovid SP, Medline via PubMed, Embase, Biosis Previews and the Cochrane Library. Search terms used in each database varied slightly to optimize results. All generic steroid formulations were included along with spinal cord compression or myelopathy combined with metastatic or malignant tumors. Papers discussing acute traumatic causes of spinal cord compression were excluded, as were papers discussing cord compression from nonmetastatic tumors or epidural lipomatosis. Subjects were limited to adult humans undergoing definitive treatment with radiotherapy or surgery.

RESULTS: Of the 309 papers retrieved, 66 full text studies were reviewed and 6 papers were found to address the stated questions.

CONCLUSIONS: There is a paucity of high quality literature evaluating the use of steroids in MSCC. On the basis of the evidence available an initial 10 mg intravenous bolus of dexamethasone followed by 16 mg PO QD has been associated with fewer complications compared with 100 mg bolus and 96 mg QD. Weaning of steroids should occur rapidly after definitive treatment. Risk of gastric bleeding or perforation can be managed with the routine use of proton-pump inhibitors.

LEVEL OF EVIDENCE: Level IIIa.

56 Kroeze SGC, Fritz C, Hoyer M, Lo SS, Ricardi U, Sahgal A, et al. **Toxicity of concurrent stereotactic radiotherapy and targeted therapy or immunotherapy: A systematic review**. Cancer Treat Rev 2017;53:25-37.

**Abstract:** Background and purpose Both stereotactic radiotherapy (SRT) and immune- or targeted therapy play an increasingly important role in personalized treatment of metastatic disease. Concurrent application of both therapies is rapidly expanding in daily clinical practice. In this systematic review we summarize severe toxicity observed after concurrent treatment. Material and methods PubMed and EMBASE databases were searched for English literature published up to April 2016 using keywords "radiosurgery", "local ablative therapy", "gamma knife" and "stereotactic", combined with "bevacizumab", "cetuximab", "crizotinib", "erlotinib", "gefitinib", "ipilimumab", "lapatinib", "sorafenib", "sunitinib", "trastuzumab", "vemurafenib", "PLX4032", "panitumumab", "nivolumab", "pembrolizumab", "alectinib", "ceritinib", "dabrafenib", "trametinib", "BRAF", "TKI", "MEK", "PD1", "EGFR", "CTLA-4" or "ALK". Studies performing SRT during or within 30 days of targeted/immunotherapy, reporting severe (Grade 3) toxicity were included. Results Concurrent treatment is mostly well tolerated in cranial SRT, but high rates of severe toxicity were observed for the combination with BRAF-inhibitors. The relatively scarce literature on extra-cranial SRT shows a potential risk of increased toxicity when SRT is combined with EGFR-targeting tyrosine kinase inhibitors and bevacizumab, which was not observed for cranial SRT. Conclusions This review gives a best-possible overview of current knowledge and its limitations and underlines the need for a timely generation of stronger evidence in this rapidly expanding field. Copyright © 2016 The Author(s)

57 Kougioumtzopoulou A, Zygogianni A, Liakouli Z, Kypraiou E, Kouloulias V. **The role of radiotherapy in bone metastases: A critical review of current literature**. European Journal of Cancer Care 2017;26(6).

**Abstract:** Radiotherapy is considered the treatment of choice for painful bone metastases. However, novel modalities of radiotherapy have emerged in the concept of oligometastasic disease. In addition, the increase of overall survival of patients with bone metastatic disease in the last decades due to systemic treatments has issued the silent topic of re-irradiation. The aim of this manuscript was to present a current thorough search of relevant literature. Originally, 6,087 articles revealed from PubMed database related to radiotherapy and bone metastases. The first objective was to identify prospective randomised phase III studies dealing with bone metastases and which treated primary with radiotherapy. Abstracts and non-English citations were excluded. Twenty-three phase III clinical trials, 17 prospective studies and eight meta-analysis/systemic reviews matching with these criteria, were identified. Eleven randomised studies were comparing single dose fraction to multi-fraction schedules of radiotherapy. The overall response rates and complete response rates were not significant between the two arms. Re-irradiations rates were significantly higher for the single dose fraction arms. Stereotactic radiotherapy showed excellent tumour control rates more than 80%. All trials showed the equivalence of either single or multi-fractionated radiotherapy for metastatic bone lesions. Stereotactic irradiation is feasible and safe for oligometastatic disease. However, it seems that the single fraction of 8 Gy is superior to 4 Gy, in terms of efficacy.

58 Konar SK, Bir SC, Maiti TK, Nanda A. **A systematic review of overall survival in pediatric primary glioblastoma multiforme of the spinal cord**. J Neurosurg Pediatrics 2017;19(2):239-48.

**Abstract:** OBJECTIVE The incidence of primary spinal cord glioblastoma multiforme (GBM) in the pediatric age group is very rare. Only a few case series and case reports have been published in the literature; therefore, overall survival (OS) outcome and the as-yet poorly defined management options are not discussed in detail. The authors performed a cumulative survival analysis of all reported cases of pediatric spinal cord GBM to identify the predictive factors related to final survival outcome. METHODS A comprehensive search for relevant articles was performed on PubMed's electronic database MEDLINE for the period from 1950 to 2015 using the search words "malignant spinal cord tumor" and "spinal glioblastoma multiforme." This study was limited to patients younger than 18 years of age. Survival rates for children with various tumor locations and treatments were collected from the published articles and analyzed. RESULTS After an extensive literature search, 29 articles met the study inclusion criteria. From the detailed information in these articles, the authors found 53 children eligible for the survival analysis. The majority (45%) of the children were more than 12 years old. Thirty-four percent of the cases were between 7 and 12 years of age, and 21% were younger than 7 years. In the Kaplan-Meier survival analysis, children younger than 7 years of age had better survival (13 months) than the children older than 7 years (7-12 years: 10 months, > 12 years: 9 months; p = 0.01, log-rank test). Fifty-five percent of the children were female and 45% were male. A cervical tumor location (32%) was the most common, followed by thoracic (28.3%). Cervicothoracic (18.9%) and conus (18.8%) tumor locations shared the same percentage of cases. Cervical tumors had a worse outcome than tumors in other locations (p = 0.003, log-rank test). The most common presenting symptom was limb weakness (53%), followed by sensory disturbances (25%). Median OS was 10 months. The addition of adjuvant therapy (radiotherapy [RT] and/or chemotherapy [CT]) after surgery significantly improved OS (p = 0.01, log-rank test). Children who underwent gross-total resection and RT had better outcomes than those who underwent subtotal resection and RT (p = 0.04, log-rank test). Cerebrospinal fluid spread, hydrocephalus, brain metastasis, and spinal metastasis were not correlated with OS in primary spinal GBM. CONCLUSIONS Adjuvant therapy after surgery had a beneficial effect on overall outcome of spinal GBM in the pediatric age group. Gross-total resection followed by RT produced a better outcome than subtotal resection with RT. Further large-scale prospective study is required to establish the genetic and molecular factors related to OS in primary GBM of the spinal cord in pediatric patients.

59 Kim Y. **There is a role of surgery in non-CNS oligometastatic disease**. J Thorac Oncol 2017;12 (11 Supplement 2):S1662-S3.

**Abstract:** For certain extra-pulmonary malignancies, such as colorectal cancer or sarcomas, the existence of curable oligometastatic disease state has been well established. Oligometastasis is a state of stage IV disease associated with limited spread of disease at the time of diagnosis. This condition may reflect a more indolent phenotype than that associated with more widespread disease at presentation. Recently, it becomes clearer that the patients with Stage IV NSCLC are heterogenous and hence, some patients have high disease burden whereas others have isolated metastatic lesions. In the 8th TNM staging system, M-stage was reclassified into M1a, M1b, M1c, and the patients with M1b may represents the oligometastatic status of NSCLC. It has been demonstrated that the predominant pattern of failure in patients with oligometastasis treated with the first-line systemic chemotherapy was mainly a local failure, the fact which leads an idea that the local treatment may improve cure rates in such patients. The incidence of oligometastasis in NSCLC has been reported 7-26% of NSCLC,1,2 with the major sites of metastases being bone, brain, adrenal glands and liver. In general, the successful treatment of patients with oligometastasis requires the ability to eradicate the primary site, the ability to image all sites of metastatic disease, the ability to ablate all metastatic sites, and having effective systemic therapy to eradicate undetected micrometastatic disease. Recently, routine use of improved diagnostic imaging tools such as PET-CT or Brain MRI, can better detect latent metastases in patients who would otherwise have been thought to have a localized disease, and hence, the diagnosis of "true" oligometastatic disease may be increasing.3 Development of local treatment modalities such as minimally invasive surgery (MIS) or stereotactic radiotherapy (SABR) enabled effective local abrasion of the metastatic sites without major morbidities. Above all, rapid development of effective molecular target agents and immune check point agents in the treatment of NSCLC are encouraging to reconsider surgery for the treatment of oligometastatic NSCLC patients. Most evidence of treatment effect of local treatment for oligometastasis derives from the survival data from retrospective patients groups. For brain metastases, 5-year survival rates have been reported 6.6-35% and adrenal gland metastases showed similar results (5-year survival rates 12- 40%). In a well-designed propensity score matching study suggested an improvement in survival favoring local abrasive therapy, but definite conclusions on the efficacy of local therapy for the treatment of extra-cranial oligometastatic NSCLC could not be reached.4 A metaanalysis which included 49 studies, suggested overall median overall survival of 19 months after local ablative treatment (5.9-52 months).5 Most recent study by Gomez and colleagues demonstrated a progression free survival benefit favoring local consolidative therapy.6 Hopefully, ongoing prospective trials may provide more strong evidence of the effect of local ablative therapy for oligometastasis in near future. Despite many reports that support local treatment for oligometastasis, the lack of control data in almost all reports is a problematic issue. Since local treatment for the oligometastasis is only performed in selected patients with relatively indolent disease, there is often no actual denominator for the entire group of patients who developed metastasis.7 Thus, determining the survival advantage of ablative local treatment of oligometastasis compared to palliative systemic therapy is difficult because the majority of existing data are with a substantial degree of selection bias. In the other aspect, however, we have learned that the patient selection is critical for the application of local treatment on the oligometastasis. In general, local treatment is indicated in metastatic NSCLC patients with favorable prognostic factors including absence of mediastinal lymph node metastasis, small number of metastases, complete control of rimary lesion, meta-chronous metastasis, and good performance status of the patients. Although there are relatively large numbers of papers on the brain or adrenal metastases, the reports of extra-cranial or extraadrenal metastases are rare. In a meta-analysis, the 5 year overall survival rates of extra-cranial/extra-adrenal metastasis was 50% and the prognosis was mainly influenced by lymph node metastasis status. 8 First used in the literature in 2012,9 the concept of oligoprogressive disease has been rapidly adopted. It can be best described in patients with tumors harboring actionable mutations who are treated with molecular targeted therapies. Initially, the response rate is great but the duration of response is relatively short, with resistance to therapy generally emerging within a year of start of treatment as a result of various genetic mechanisms. Not uncommonly, disease progression during molecular targeted therapy occurs at a limited number of anatomic sites. Recently, several studies reported improved progression free survival and overall survival in either intra-cranial or extra-cranial oligopregressive diseases by applying local abrasive therapy on those acquired resistant oligoprogressive diseases and by resuming target agents.10 Furthermore, the combination of immune check point agents and SABR on primary tumor and/or metastatic sites may be promising for treating oligometastatic NSCLC, due to a possible abscopal effect. In conclusion, although current evidence of local treatment of oligometastases is limited in NSCLC, with aid of recent diagnostic tools by which more stringent patient selection is possible, local ablative treatment of metastatic lesions can lead improved survival of patients with oligometastasis in conjunction with molecular target agents or immune check point agents.

60 Khanna N, Pandey A, Bajpai J. **Metastatic ewing's sarcoma: Revisiting the 'Evidence on the Fence'**. Indian J Med Paediatr Oncol 2017;38(2):173-81.

**Abstract:** Metastatic Ewing's sarcoma is a challenging disease for oncology care providers with wide spectrum of disease at presentation, widely varying approach to the treatment and varied outcomes. The paucity of randomized evidence is a barrier in developing a consensus. This perspective provides the evidence 'for and against' the benefit of aggressive approach including local and systemic therapy in patients presenting with metastatic Ewing's sarcoma and provide general recommendations so as to help select patients who will benefit with definitive intent treatment and also, avoid aggressive approach in patients with dismal outcome. Copyright © 2017 Indian Journal of Medical and Paediatric Oncology Published by Wolters Kluwer - Medknow.

61 Khan SA. **Local therapy of limited disease in ABC: What is the evidence?** Cancer Research Conference: San Antonio Breast Cancer Symposium, SABCS 2017;78(4 Supplement 1).

**Abstract:** Surgery and radiotherapy have been used as adjunctive treatments for women with Stage IV breast cancer and a low volume of disease, for many years. This encompasses patients with intact or recurrent disease at the primary site, as well as those with oligometastatic distant disease. The evidence to support local therapy (LT) approaches in this group of patients is largely retrospective, although randomized trials are ongoing. For patients with an intact primary tumor, over 20 retrospective analyses suggest that women undergoing primary site LT (PSLT) experience longer survival than those whose primary tumor receives no LT, with one meta-analysis of these data reporting a hazard ratio (HR) of 0.69 (95%CI 0.63, 0.77). However, a concern about selection bias as the explanation for this apparent benefit has led to several randomized trials. Two of these were reported recently, with mixed results. The design and the results of the two completed trials were different. In Mumbai, India (NCT00193778), initial therapy consisted of chemotherapy followed by randomization to PSLT or not; results showed no overall survival difference, but local control was improved in the PSLT arm. In Turkey, MF07-01 randomized Stage IV patients to PSLT or not, followed by usual systemic therapy; results suggest an improvement in overall survival at 5 years for women in the PSLT arm. Two other randomized trials are ongoing, both designed with initial systemic therapy. In the meantime, existing data do not clearly support the use of PSLT as a means of improved survival, but the local control advantage was clear in both trials, and therefore PSLT may be offered to women whose primary tumors do not respond well to systemic therapy. For women with oligometastatic disease, the data supporting LT measures is again retrospective, and consists of small, highly selected series. However, interest in LT approaches spans back many decades, and studies suggest that various strategies of surgery, radiotherapy, and more recently stereotactic body radiotherapy (SBRT), are associated with prolonged survival. The distant sites that have been subjected to these approaches include isolated metastases in lung, liver, bone, and brain. For isolated lung lesions in particular, resection also allows a clear distinction between primary and metastatic disease, since a large fraction of solitary lung lesions may in fact be primary lung tumors. In the liver, small retrospective series of highly selected patients undergoing resection suggest that longer-than-expected median survival can be observed in patients with limited disease and a long disease-free interval. Minimally invasive ablation techniques are being used with similar intent. For osseous sites, retrospective analyses of high-dose radiotherapy with ablative intent reflect similar caveats and similar results to the data on lung and liver. An important ongoing trial (NCT02364557) is randomizing women with a controlled primary tumor site and <=2 metastatic lesions that are amenable to treatment with SBRT or surgery, to usual care or usual care with the addition LT to distant sites that must be separated by a distance of >5 cm. These ongoing studies will bring much-needed clarity to the role pf LT approaches to both the primary site and limited distant disease.

62 Jimenez-Fonseca P, Gomez Saez JM, Santamaria Sandi J, Capdevila J, Navarro Gonzalez E, Zafon Llopis C, et al. **Spanish consensus for the management of patients with anaplastic cell thyroid carcinoma**. Clinical and Translational Oncology 2017;19(1):12-20.

**Abstract:** Anaplastic thyroid cancer (ATC) is the most aggressive solid tumor and almost uniformly lethal in humans. The Boards of the Thyroid Cancer Group of the Spanish Society of Endocrinology and Nutrition and the Grupo Espanol de Enfermedades Huerfanas e Infrecuentes of the Spanish Society of Oncology requested that an independent task force draft a more comprehensive consensus statement regarding ATC. All relevant literature was reviewed, including serial PubMed searches together with additional articles. This is the first, comprehensive Spanish consensus statement for ATC and includes the characteristics, diagnosis, initial evaluation, treatment goals, recommendations and modalities for locoregional and advanced disease, palliative care options, surveillance, and long-term monitoring. Newer systemic therapies are being investigated, but more effective combinations are needed to improve patient outcomes. Though more aggressive radiotherapy has reduced locoregional recurrences, median overall survival has not improved in more than 50 years. Copyright © 2016, Federacion de Sociedades Espanolas de Oncologia (FESEO).

63 Jang S, Patel PN, Kimple RJ, McCulloch TM. **Clinical Outcomes and Prognostic Factors of Adenoid Cystic Carcinoma of the Head and Neck**. Anticancer Res 2017;37(6):3045-52.

**Abstract:** BACKGROUND: Adenoid cystic carcinoma (ACC) is a salivary gland malignancy with unpredictable growth and poorly understood prognostic factors.

PATIENTS AND METHODS: A database search of patients treated at a single Institution was used to identify patients with histologically-confirmed ACC. Patient, tumor, and treatment characteristics were examined via review of medical records.

RESULTS: Overall survival of 70 patients identified at 5, 10, and 15 years was 80.4%, 61.3%, and 29.4%, respectively. Disease recurrence was seen in 31.9%; of these, 72.7% developed distant metastasis. Older age, higher stage, skull base involvement, positive margins, and metastatic disease, but not local recurrence, predicted a worse overall survival. Higher stage and skull base disease were also associated with shorter disease-free survival. While lung metastasis was the most common, vertebral metastasis was associated with poorer survival.

CONCLUSION: Disease stage, positive margins, skull base involvement, perineural invasion, time to recurrence, and location of metastasis, but not nodal involvement, could serve as poor prognostic factors in ACC.

64 Husain ZA, Sahgal A, De Salles A, Funaro M, Glover J, Hayashi M, et al. **Stereotactic body radiotherapy for de novo spinal metastases: systematic review**. Journal of Neurosurgery Spine 2017;27(3):295-302.

**Abstract:** OBJECTIVE The aim of this systematic review was to provide an objective summary of the published literature pertaining to the use of stereotactic body radiation therapy (SBRT) specific to previously untreated spinal metastases. METHODS The authors performed a systematic review, using Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) guidelines, of the literature found in a search of Medline, PubMed, Embase, and the Cochrane Library up to March 2015. The search strategy was limited to publications in the English language. RESULTS A total of 14 full-text articles were included in the analysis. All studies were retrospective except for 2 studies, which were prospective. A total of 1024 treated spinal lesions were analyzed. The median follow-up time ranged from 9 to 49 months. A range of dose-fractionation schemes was used, the most common of which were 16-24 Gy/1 fraction (fx), 24 Gy/2 fx, 24-27 Gy/3 fx, and 30-35 Gy/5 fx. In studies that reported crude results regarding in-field local tumor control, 346 (85%) of 407 lesions remained controlled. For studies that reported actuarial values, the weighted average revealed a 90% 1-year local control rate. Only 3 studies reported data on complete pain response, and the weighted average of these results yielded a complete pain response rate of 54%. The most common toxicity was new or progressing vertebral compression fracture, which was observed in 9.4% of cases; 2 cases (0.2%) of neurologic injury were reported. CONCLUSION There is a paucity of prospective data specific to SBRT in patients with spinal metastases not otherwise irradiated. This systematic review found that SBRT is associated with favorable rates of local control (approximately 90% at 1 year) and complete pain response (approximately 50%), and low rates of serious adverse events were found. Practice guidelines are summarized based on these data and International Stereotactic Radiosurgery Society consensus.

65 Huo M, Sahgal A, Pryor D, Redmond K, Lo S, Foote M. **Stereotactic spine radiosurgery: Review of safety and efficacy with respect to dose and fractionation**. Surg Neurol Int 2017;8:30.

**Abstract:** BACKGROUND: Stereotactic body radiotherapy (SBRT) is an emerging treatment option for spinal metastases with demonstrated efficacy in the upfront, postoperative, and re-treatment settings, as well as for tumor histologies considered radioresistant. Uncertainty exists regarding the optimal dose and fractionation schedule, with single and multifraction regimens commonly utilized.

METHODS: A literature search of the PubMed and Medline databases was conducted to identify papers specific to spine SBRT and the effect of varying dose/fractionation regimens on outcomes. Bibliographies of relevant papers were searched for further references, and international spine SBRT experts were consulted.

RESULTS: Local control rates generally exceed 80% at 1 year, while high rates of pain control have been attained. There is insufficient evidence to suggest superiority of either single or multiple fraction regimens with respect to local control and pain control. Low rates of toxicity have been reported, assuming strict dose constraints are respected. Radiation myelopathy may be the most morbid toxicity, although the rates are low. The risk of vertebral compression fracture appears to be associated with higher doses per fraction such as those used in single-fraction regimens. The Spinal Instability Neoplastic Score should be considered when evaluating patients for spine SBRT, and prophylactic stabilisation may be warranted. Pain flare is a relatively common toxicity which may be mediated with prophylactic dexamethasone. Because of the treatment complexity and potentially serious toxicities, strict quality assurance should occur at the organizational, planning, dosimetric, and treatment delivery levels.

CONCLUSION: Both single and multifraction regimens are safe and efficacious in spine SBRT for spinal metastases. There may be advantages to hypofractionated treatment over single-fraction regimens with respect to toxicity. Ongoing investigation is underway to define optimal dose and fractionation schedules.

66 Hong JC, Ayala-Peacock DN, Lee J, Blackstock AW, Okunieff P, Sung M, et al. **Predicting for long-term survival in oligometastatic patients treated with ablative radiation therapy: A multi-institutional pooled analysis**. International Journal of Radiation Oncology Biology Physics 2017;99 (2 Supplement 1):S218.

**Abstract:** Purpose/Objective(s): Ablative radiotherapy is increasingly used for oligometastatic treatment. Clinical measures identifying patients most likely to benefit are lacking. This study was undertaken to identify prognostic criteria in oligometastatic patients undergoing ablative radiotherapy (SBRT). Purpose/Objective(s): Consecutive oligometastatic patients treated with SBRT were pooled, forming a multi-institutional cohort. Patient and disease characteristics associated with overall survival (OS) and progression-free survival (PFS) were assessed by the Cox proportional hazards method. Recursive partitioning analysis (RPA) identified prognostic risk strata for OS and PFS based on clinical factors. Clinical factors considered included age, primary tumor site, sex, interval to metastatic diagnosis, number of treated metastases, presence of non-bone metastasis, number of involved organs, and systemic therapy for metastasis. Results: Three hundred seventy-six consecutive oligometastatic patients were included. Among primary diseases included were non-small cell lung (18%), colorectal (19%), and breast cancer (15%). OS RPA identified five prognostic groups: class 1: all patients with breast, kidney, or prostate cancer (BKP) (3-year OS 74%, 95% CI 65-85%); class 2: patients without BKP with disease-free interval of 75+ months (3-year OS 85%, 95% CI 69-100%); class 3: patients without BKP, shorter disease-free interval, <= two metastases, and age < 62 (3-year OS 55%, 95% CI 48-63%); class 4: patients without BKP, shorter disease-free interval, >= three metastases, and age < 62 (3-year OS 35%, 95% CI 22-57%); class 5: all others (3-year OS 13%, 95% CI 5-33%). PFS was defined by primary disease; class 1: all patients with breast, kidney, or prostate cancer (3-year PFS 42%, 95% CI 32-56%); class 2: other primary diseases (3-year PFS 17%, 95% CI 13-23%). Conclusion: We identified clinical factors defining oligometastatic patients with favorable outcomes, who we hypothesize are most likely to benefit from metastasis-directed therapy.

67 Ganesh V, Chan S, Raman S, Chow R, Hoskin P, Lam H, et al. **A review of patterns of practice and clinical guidelines in the palliative radiation treatment of uncomplicated bone metastases**. Radiother Oncol 2017;124(1):38-44.

**Abstract:** BACKGROUND AND PURPOSE: Single fraction radiation treatment (SFRT) is recommended for its equivalence to multiple-fraction (MF) RT in the palliation of uncomplicated bone metastases (BM). However, adoption of SFRT has been slow.

MATERIALS AND METHODS: Literature searches for studies published following 2014 were conducted using online repositories of gray literature, Ovid MEDLINE, Embase and Embase Classic, and the Cochrane Central Register of Controlled Trials databases.

RESULTS: A total of 32 articles detailing patterns of practice and clinical practice guidelines were included for final synthesis. The majority of organizations have released high level recommendations for SFRT use in treatment of uncomplicated BM, based on evidence of non-inferiority to MFRT. There are key differences between guidelines, such as varying strengths of recommendation for SFRT use over MFRT; contraindication in vertebral sites for SFRT; and risk estimation of pathologic fractures after SFRT. Differences in guidelines may be influenced by committee composition and organization mandate. Differences in patterns of practice may be influenced by individual center policies, payment modalities and consideration of patient factors such as age, prognosis, and performance status.

CONCLUSION: Although there is some variation between groups, the majority of guidelines recommend use of SFRT and others consider it to be a reasonable alternative to MFRT.

68 Ganesh V, Chan S, Raman S, Chow R, Hoskin P, Lam H, et al. **A review of patterns of practice and clinical guidelines in the palliative radiation treatment of uncomplicated bone metastases**. Support Care Cancer 2017;25 (2 Supplement 1):S76.

**Abstract:** Introduction Single fraction radiation treatment (SFRT) is recommended for its equivalence to multiple fraction (MF)RT in the palliation of un-complicated bone metastases (BM). However, adoption of SFRT has been slow. Objectives To summarize SFRT-related patterns of practice and clinical guidelines in the palliative RT of uncomplicated BM. Methods Literature searches for studies published following 2014 were conducted using several online repositories of grey literature, Ovid MEDLINE, Embase, Embase Classic, and the Cochrane Central Register of Controlled Trials databases. Results A total of 11 studies regarding patterns of practice and 21 articles detailing clinical practice guidelines were included for final synthesis. The majority of organizations have released high level recommendations for SFRT use in treatment of uncomplicated BM, based on evidence of non-inferiority to MFRT. However, there are key differences between guidelines, such as varying strengths of recommenda-tion for SFRT use over MFRT; contraindication in vertebral sites for SFRT; and risk estimation of pathologic fractures after SFRT. There are differences in the recommendation of palliative RT for BM under the Choosing Wisely campaign. Differences in guidelines may be influenced by committee composition and organization mandate. Differences in patterns of practice may be influenced by individual centre policies, payment modalities and consideration of patient factors such as age, prognosis, and performance status. Increased use of SFRT was reported in 5 out of 6 studies reporting temporal trends post-2010. Conclusions Although there is some misalignment between authoritative groups, the majority of guidelines recommend use of SFRT and others consider it to be a reasonable alternative to MFRT.

69 Fontanella P, Benecchi L, Grasso A, Patel V, Albala D, Abbou C, et al. **Decision-making tools in prostate cancer: From risk grouping to nomograms**. Minerva Urol Nefrol 2017;69(6):556-66.

**Abstract:** INTRODUCTION: Prostate cancer (PCa) is the most common solid neoplasm and the second leading cause of cancer death in men. After the Partin tables were developed, a number of predictive and prognostic tools became available for risk stratification. These tools have allowed the urologist to better characterize this disease and lead to more confident treatment decisions for patients. The purpose of this study is to critically review the decision-making tools currently available to the urologist, from the moment when PCa is first diagnosed until patients experience metastatic progression and death. EVIDENCE ACQUISITION: A systematic and critical analysis through Medline, EMBASE, Scopus and Web of Science databases was carried out in February 2016 as per the Preferred Reporting Items for Systematic Reviews and Meta- Analyses (PRISMA) statement. The search was conducted using the following key words: "prostate cancer," "prediction tools," "nomograms." EVIDENCE SYNTHESIS: Seventy-two studies were identified in the literature search. We summarized the results into six sections: Tools for prediction of life expectancy (before treatment), Tools for prediction of pathological stage (before treatment), Tools for prediction of survival and cancer-specific mortality (before/after treatment), Tools for prediction of biochemical recurrence (before/after treatment), Tools for prediction of metastatic progression (after treatment) and in the last section biomarkers and genomics. CONCLUSIONS: The management of PCa patients requires a tailored approach to deliver a truly personalized treatment. The currently available tools are of great help in helping the urologist in the decision-making process. These tests perform very well in high-grade and low-grade disease, while for intermediate-grade disease further research is needed. Newly discovered markers, genomic tests, and advances in imaging acquisition through mpMRI will help in instilling confidence that the appropriate treatments are being offered to patients with prostate cancer. Copyright © 2017 EDIZIONI MINERVA MEDICA.

70 Errani C, Mavrogenis AF, Cevolani L, Spinelli S, Piccioli A, Maccauro G, et al. **Treatment for long bone metastases based on a systematic literature review**. European Journal of Orthopaedic Surgery and Traumatology 2017;27(2):205-11.

**Abstract:** Purpose: To provide treatment guidelines for patients with long bone metastatic disease based on a systematic review of the literature and to propose an algorithm to guide orthopedic surgeons in decision-making for these patients. Materials and methods: We performed a computerized literature search in MEDLINE, EMBASE and Scopus for studies on patients with long bone metastases. We used the key words "long bones", "metastasis" and "treatment" for published studies that evaluated any treatment for long bone metastases. The articles found were then studied to determine the accuracy of surgical treatments for long bone metastases in every anatomic location, regardless of cancer type, stage and grade of the oncologic disease. Guidelines inferred from this literature review were collected, and an algorithm was proposed. Results: There was no clear evidence to support excision of a long bone metastatic lesion at the same surgical setting with internal fixation or prosthetic reconstruction. However, en bloc resection of an isolated bone metastasis may have a beneficial effect on survival. The life expectancy of the patients should be considered for any surgical treatment. Internal fixation preferably with reconstruction nails is indicated for meta-diaphyseal lesions; their rate of mechanical failure and complications ranges from 2 to 22 %. Prosthetic reconstruction is indicated for extensive lytic lesions or pathologic fractures in a meta-epiphyseal locations; their rate of mechanical failure and complications ranges from 3.7 to 35 %. Most of the internal fixation-related complications occur more than 1 year after treatment, in contrast to prosthetic reconstruction-related complications that may occur earlier. Conclusions: Intramedullary nail fixation or prosthetic reconstruction should be chosen on the basis of the location of the lesion, the extent of bone destruction and the stability of the construct to outlast the expected life of the patient. Implant-related complication is similar but may occur earlier with prosthetic reconstructions. Copyright © 2016, Springer-Verlag France.

71 Derlin T, von Klot CA, Hueper K. **Re: Sungmin Woo, Chong Hyun Suh, Sang Youn Kim, Jeong Yeon Cho, Seung Hyup Kim. Diagnostic Performance of Magnetic Resonance Imaging for the Detection of Bone Metastasis in Prostate Cancer: A Systematic Review and Meta-analysis. Eur Urol. In press. http://dx.doi.org/10.1016/j.eururo.2017.03.042**. Eur Urol 2017;72(4):e98-e9.

72 Dekker SE, Wasman J, Yoo KK, Alonso F, Tarr RW, Bambakidis NC, et al. **Clival Metastasis of a Duodenal Adenocarcinoma: A Case Report and Literature Review**. World Neurosurg 2017;100:62-8.

**Abstract:** Background Clival metastases of adenocarcinomas are exceptionally rare tumors, especially when they arise from the small intestine. We present the first, to our knowledge, report of a metastasis of a duodenal adenocarcinoma to the clivus. We also present a systematic review detailing metastasis to the clivus. Methods Studies were identified using the search terms "clival metastasis," "skull base metastasis," and "clivus" in PubMed. We collected the following information: histopathology of the primary tumor, symptoms, history, treatment, and follow-up. Results A comprehensive review of the literature yielded 56 cases. Patients developed the first symptoms of clival metastasis at a mean age of 58 years. The most common primary neoplasms originated from the prostate, kidney, or liver. Most patients presented with an isolated sixth nerve palsy or diplopia. The time interval from diagnosis of the primary tumor to symptomatic presentation of clival metastasis ranged from 2 months to 33 years. Sixteen patients initially presented with symptoms of clival metastasis without a previously diagnosed primary tumor. Survival data were available for 35 patients, of which 63% died within a range of 2 days to 31 months after initial presentation. Conclusions Most primary neoplasms originated from the prostate, kidney, and liver, which differ from previous reports on skull base metastases. Abducens nerve palsy is often the first presentation of clival metastasis. Clival metastasis from duodenal carcinoma, although very rare, should be considered in the differential diagnosis of bony lesions of the clivus in a patient with a history of duodenal adenocarcinoma. Copyright © 2016 Elsevier Inc.

73 Chow R, Hoskin P, Hollenberg D, Lam M, Dennis K, Lutz S, et al. **Efficacy of single fraction conventional radiation therapy for painful uncomplicated bone metastases: a systematic review and meta-analysis**. Annals of palliative medicine 2017;6(2):125-42.

**Abstract:** BACKGROUND: Single fraction radiotherapy (SFRT) and multiple fraction radiotherapy (MFRT) are effective for painful uncomplicated bone metastases and have been shown to be of similar efficacy. The optimal conventional external beam SFRT dose for maximum pain relief remains uncertain. The aim of this systematic review was to comprehensively review and synthesize overall pain response rates by dose.

METHODS: A literature search was conducted in Ovid MEDLINE(R) (1946 to June 2016 week 3), Embase Classic & Embase (1947 to 2016 week 26) and Cochrane Central Register of Controlled Trials (May 2016) using keywords such as bone metastases, radiotherapy and single fraction (SF).

RESULTS: The 635 results from the search were screened, and ultimately 27 were included for quantitative synthesis. The review indicated that 10 and 6 Gy may produce superior overall response (OR) and complete response (CR) rates compared to 8 Gy, and 6 Gy may result in better partial response (PR) than 8 Gy. However, only a few studies documented doses other than 8 Gy. In trials that directly compared 8 Gy to 4 Gy or 6 Gy, 8 Gy was deemed statistically superior.

CONCLUSIONS: 8 Gy SFRT was the most commonly administered dose for palliation of bone metastases supporting its efficacy and safety. Future studies should explore the efficacy of 10 Gy while minimizing its side effects.

74 Chow R, Hoskin P, Chan S, Mesci A, Hollenberg D, Lam H, et al. **Efficacy of multiple fraction conventional radiation therapy for painful uncomplicated bone metastases: A systematic review**. Radiother Oncol 2017;122(3):323-31.

**Abstract:** BACKGROUND: Radiation therapy is effective for painful uncomplicated bone metastases, with multiple fraction radiation therapy (MFRT) administered frequently. The optimal dose for MFRT to yield maximum pain relief remains unclear. The aim of this systematic review was to determine pain response across MFRT doses.

METHODS: A literature search was conducted in Ovid MEDLINE(R) <1946 to July Week 3 2016>, Embase Classic & Embase <1947 to 2016Week 30> and Cochrane Central Register of Controlled Trials <June 2016>. Pain response rates and the side effects for MFRT doses were extracted.

RESULTS: From the 3719 articles identified from the search, 17 were included for quantitative synthesis. 22.5Gy/5 had the highest overall response (OR) rate, 30Gy/15 had better complete response (CR) rate and 20Gy/2 had better partial response (PR) rate. Only 4 of the 17 included studies directly compared MFRT doses with each other - one reported marginally-better OR for 24Gy/6 over 20Gy/2; another found 20Gy/10 to be slightly more efficacious than 30Gy/15 and 22.5Gy/5 for OR. Two randomized trials compared 20Gy/5 and 30Gy/10 - one favored 20Gy/5 while the other concluded 30Gy/10 to be the better option. The overall rate of GI toxicities, nausea, and vomiting did not differ greatly between MFRT doses.

CONCLUSION: No major difference exists between the schedules and toxic events studied in these trials. This is consistent with the wealth of randomized data which show no dose response for pain relief after radiotherapy for metastatic bone pain.

75 Chow R, Hoskin P, Chan S, Mesci A, Hollenberg D, Lam H, et al. **Efficacy of multiple fraction conventional radiation therapy for painful uncomplicated bone metastases: A systematic review**. Support Care Cancer 2017;25 (2 Supplement 1):S188.

**Abstract:** Introduction Radiation therapy is effective for painful uncomplicated bone metastases, with multiple fraction radiation therapy (MFRT) administered frequently. The optimal dose for MFRT to yield maximum pain relief remains unclear. Objectives The aim of this systematic review was to determine pain response across MFRT doses. Methods A literature search was conducted in Ovid MEDLINE (R) (1946 to July Week 3 2016), Embase Classic & Embase (1947 to 2016 Week 30) and Cochrane Central Register of Controlled Trials (June 2016). Pain response rates and the side effects for MFRT doses were extracted. Results From the 3,719 articles identified from the search, 17 were included for quantitative synthesis. 22.5Gy/5 had the highest overall response (OR) rate, 30Gy/15 had better complete response (CR) rate and 20Gy/2 had better partial response (PR) rate. Only 4 of the 17 included studies directly compared MFRT with each other-one reported marginally-better OR for 24Gy/6 over 20Gy/2; another found 20Gy/10 to be slightly more effica-cious than 30Gy/15 and 22.5Gy/5 for OR. Two randomized trials com-pared 20Gy/5 and 30Gy/10-one favoured 20Gy/5 while the other concluded 30Gy/10 to be the better option. The overall rate of GI toxicities, nausea and vomiting did not differ greatly between MFRT doses. Conclusions No major difference exists between the schedules and toxic events studies in these trials consistent with the wealth of randomized data which shows no dose response for pain relief after radiotherapy for metastatic bone pain.

76 Chan D, Thompson R, Lam M, Pavlakis N, Hallet J, Law C, et al. **External beam radiotherapy (EBRT) in the treatment of gastroenteropancreatic neuroendocrine tumors: A systematic review**. Neuroendocrinology 2017;105 (Supplement 1):327.

**Abstract:** Introduction: EBRT is infrequently used to treat GEPNETS. Aim(s): To systematically review the evidence for EBRT in this setting. Materials and methods: Major databases and conference abstracts underwent dual independent review. Eligible studies included >= 5 patients treated with contemporary EBRT techniques for GEPNETs. The primary endpoint was local control. Results: Of 11 included studies (all retrospective), 7 investigated pancreatic NETs (PNET, 100 patients, 14% G3, 42% with chemotherapy) and four studies investigated Gastroenteric NET (GE-NET, 84 patients, 14% G3). Trials investigating PNETs administered a median of 50.4Gy via 3D-CRT and IMRT. EBRT was given with neoadjuvant or adjuvant intent in 56 patients with recurrence rate 15%. The response rate for 44 patients not undergoing surgery, the radiological response rate was 46%. Grade 3+ toxicity rates were 11% (acute) and 4% (late). Median distant recurrence-free survival ranged from 12-24 months, and overall survival (OS) from 24-56 months. 12 patients with GE-NET received RT to the primary tumour (all anorectal NECs) and 72 to metastases (34 bone, 27 brain, 11 soft tissue). Only one study reported dose at median of 50Gy. Local and distant control were poorly reported. OS ranged from 9-19 months. No GE-NET studies reported toxicity outcomes. Conclusion: EBRT appears to be well tolerated in selected pNET patients with encouraging efficacy. Outcomes from EBRT in metastatic NETS are not well reported. More studies are required to better define the role of EBRT in NETs.

77 Carrwik C, Murakami H, Willander J, Robinson Y. **Potential harms of interventions for spinal metastatic disease**. Cochrane Database of Systematic Reviews 2017;2017 (9) (no pagination)(CD012724).

**Abstract:** This is a protocol for a Cochrane Review (Intervention). The objectives are as follows: The primary objective of this review is to compare the potential harms of treatment for spinal metastatic disease for the following treatments: 1. Surgical intervention. 2. Surgical intervention with radiation therapy. 3. Radiation therapy alone. Our secondary objectives are: 1. comparing the harms of different surgical methods; 2. comparing the harms between different radiation protocols. Copyright © 2017 The Cochrane Collaboration. Published by John Wiley & Sons, Ltd.

78 Bizzarri N, De Cian F, Di Domenico S, Parodi L, Palmeri A, Maramai M, et al. **Peritoneal carcinomatosis from primary malignant ovarian paraganglioma: A challenging management of an extremely rare case**. Int J Gynecol Cancer 2017;27 (Supplement 4):1442.

**Abstract:** Aims Paraganglioma is one of the rarest neoplasms involving the ovary, with only 7 previous reports. We present the case of a patient with peritoneal carcinomatosis from ovarian paraganglioma (OP) and a systematic review of the literature. Method Clinical information was retrieved from medical records and a systematic review was performed. Results A 33-year-old woman presented with a 12-month history of hypertension and weight loss. CT-scan showed bilateral complex ovarian masses, peritoneal carcinomatosis, para-aortic lymphoadenopathy and IVC-wall infiltration, no parenchymal organs involvement. Laparoscopic biopsy showed a Sertoli-Leydig ovarian tumor (SLOT). After 3-cycles of bleomycin+etoposide+cisplatin she had stable disease and underwent laparotomy with extensive debulking surgery also involving recto-sigmoidectomy with primary anastomosis (no macroscopic residual disease). Histology reported a solid cordonal neoplasm with neuroendocrine immunophenotype consistent with SLOT with neuroendocrine differentiation (FIGO-stage IIIC). Postoperative course was complicated by anastomosis dehiscence (re-operated) and pulmonary sepsis. 6-months after surgery a CT-scan showed recurrent disease in abdomen and chest. Subsequent clinico-pathological review reported the case as malignant OP with unusual features. Somatostatin-analogue was started. Following further disease-progression with bone metastases (treated with palliative radiotherapy) a trial with Sunitinib was started. Patient died 30-months after initial diagnosis. Of the 7 cases reported to date, one had peritoneal metastasis at presentation; as in our case, this was initially misdiagnosed as SLOT. Conclusion OP is extremely rare. Clinico-pathological correlation and wide immunohistochemical panel are important to avoid misdiagnosis. Due to its rarity, a standard treatment is not recommended, but cytoreductive surgery to no residual disease seems to be a favorable approach.

79 Anonymous. **Proceedings of the 2017 Spring Meeting of the Society of British Neurological Surgeons**. British Journal of Neurosurgery Conference 2017;31(2).

**Abstract:** The proceedings contain 121 papers. The topics discussed include: cellular inflammatory response to penetrating trauma caused by transplantation surgery in the brain; alcohol related traumatic brain injury in neuro-intensive care; 5-ALA immunofluoresence guided endoscopic resection of high grade gliomas; volumetric growth correlates with histological grade in meningioma; genomic analysis, surgical treatment and outcomes of lower-grade gliomas in a single institution; rhabdoid meningioma: a single unit experience of treatment for a rare and aggressive variant and review of the literature; single centre experience of surgical resection and orbital reconstruction in sphenoorbital meningiomas: a 11 year series; high intensity ultrasound to ablate sacral chordoma: preliminary data; do we achieve disease control with adjuvant stereotactic radiosurgery or radiotherapy in atypical meningiomas? a retrospective cohort analysis of 79 cases; shunt procedures in idiopathic intracranial hypertension, the role of obesity in shunt failure; outcomes of hemispherotomy in paediatric epilepsy surgery; changes in quality of life after single-level selective dorsal rhizotomy; management of childhood craniopharyngioma - staged individualised treatment; are the SINS and NOMS classifications useful in predicting the need for surgery in patients with metastatic vertebral body involvement?; and systematic review of en bloc resection in the management of Ewing's sarcoma of the mobile spine with respect to local control and disease free survival.

80 Anonymous. **Abstracts from the Symposium on Clinical Interventional Oncology, CIO 2017**. Journal of Vascular and Interventional Radiology Conference: Symposium on Clinical Interventional Oncology, CIO 2017;28(2).

**Abstract:** The proceedings contain 25 papers. The topics discussed include: the effect of catheter size on left innominate vein stenosis in breast cancer patients after totally implantable venous access ports; transradial versus transfemoral access in radioembolization for hepatocellular carcinoma with yttrium-90 microspheres; percutaneous ultrasound-guided biopsy of pulmonary lesions: a single-center experience; specialty-based industry reimbursements in oncologic medicine: a 3-year analysis of open payments; baseline data on the first 121 enrolled patients in the RESIN registry; tumor grade and primary treatment response following DEB-TACE for hepatocellular carcinoma based on liver explant; a 2017 immunotherapy update: current applications, assessing imaging response, and looking to the future; subacute infection of viabahn stent graft in the popliteal artery; preprocedure paravertebral block for amyotrophic lateral sclerosis patients undergoing percutaneous gastrostomy tube placement; vertebroplasty and kyphoplasty outcomes in spinal metastatic osseous lesions: a systematic review and meta-analysis; moxifloxacin prophylaxis for patients undergoing radioembolization with a history of biliary colonization; percutaneous single fiducial placement and concurrent biopsy in lung nodules treated with stereotactic radiosurgery; and image-guided biopsy of potential metastatic lesions in colon and pancreatic cancer: how often is management changed?.

81 Alibhai SMH, Zukotynski K, Walker-Dilks C, Emmenegger U, Finelli A, Morgan SC, et al. **Bone Health and Bone-targeted Therapies for Prostate Cancer: a Programme in Evidence-based Care - Cancer Care Ontario Clinical Practice Guideline**. Clin Oncol (R Coll Radiol) 2017;29(6):348-55.

**Abstract:** AIMS: To make recommendations with respect to bone health and bone-targeted therapies in men with prostate cancer.

MATERIALS AND METHODS: A systematic review was carried out by searching MEDLINE, EMBASE and the Cochrane Library from inception to January 2016. Systematic reviews and randomised-controlled trials were considered for inclusion if they involved therapies directed at improving bone health or outcomes such as skeletal-related events, pain and quality of life in patients with prostate cancer either with or without metastases to bone. Therapies included medications, supplements or lifestyle modifications alone or in combination and were compared with placebo, no treatment or other agents. Disease-targeted agents such as androgen receptor-targeted and chemotherapeutic agents were excluded. Recommendations were reviewed by internal and external review groups.

RESULTS: In men with prostate cancer receiving androgen deprivation therapy, baseline bone mineral density testing is encouraged. Denosumab should be considered for reducing the risk of fracture in men on androgen deprivation therapy with an increased fracture risk. Bisphosphonates were effective in improving bone mineral density, but the effect on fracture was inconclusive. No medication is recommended to prevent the development of first bone metastasis. Denosumab and zoledronic acid are recommended for preventing or delaying skeletal-related events in men with metastatic castration-resistant prostate cancer. Radium-223 is recommended for reducing symptomatic skeletal events and prolonging survival in men with symptomatic metastatic castration-resistant prostate cancer.

CONCLUSIONS: The recommendations represent a current standard of care that is feasible to implement, with outcomes valued by clinicians and patients.

82 Zustovich F, Pastorelli D. **Therapeutic management of bone metastasis in prostate cancer: an update**. Expert Rev Anticancer Ther 2016;16(11):1199-211.

**Abstract:** Introduction: Bone metastases affect the majority of patients with castration-resistant prostate cancer (CRPC), resulting in significant morbidity and mortality. This review describes the current therapies available for the management of CRPC patients with bone metastases. Areas covered: Studies on the use of currently available therapeutic approaches for palliating pain, delaying skeletal-related events (SREs) and prolonging survival in CRPC patients with bone metastases have been examined. PubMed database was searched in May 2016 starting with the following keywords: ('castration-resistant prostate cancer' OR 'CRPC') AND 'bone metastases', and approximately 270 results were retrieved. More specific searches were then performed on the epidemiology and molecular pathogenesis (in particular, 'vicious cycle' was used as a keyword), the management of pain, SREs and survival. The following keywords were also used individually: abiraterone, cabazitaxel, denosumab, docetaxel, enzalutamide, radium-223, sipuleucel-T, samarium-153, strontium-89, zoledronate. Randomized-controlled trials, observational studies, reviews, systematic reviews and meta-analyses were selected and articles were excluded if not in English. Expert commentary: Currently, clear recommendations on the optimal use of the agents available to treat mCRPC are lacking. Therefore, to ensure patients the best treatment, both their clinical characteristics and the features of each product have to be considered. Copyright © 2016 Informa UK Limited, trading as Taylor & Francis Group.

83 Zuckerman SL, Laufer I, Sahgal A, Yamada YJ, Schmidt MH, Chou D, et al. **When less is more: The indications for mis techniques and separation surgery in metastatic spine disease**. Spine (Phila Pa 1976) 2016;41(Supplement20):S246-S53.

**Abstract:** Objective. The aim of this study was to review the techniques, indications, and outcomes of minimally invasive surgery (MIS) and separation surgery with subsequent radiosurgery in the treatment of patients with metastatic spine disease. Summary of Background Data. The utilization of MIS techniques in patients with spine metastases is a growing area within spinal oncology. Separation surgery represents a novel paradigm where radiosurgery provides long-term control after tumor is surgically separated from the neural elements. Methods. PubMed, Embase, and CINAHL databases were systematically queried for literature reporting MIS techniques or separation surgery in patients with metastatic spine disease. PRISMA guidelines were followed. Results. Of the initial 983 articles found, 29 met inclusion criteria. Twenty-five articles discussed MIS techniques and were grouped according to the primary objective: percutaneous stabilization (8), tubular retractors (4), mini-open approach (8), and thoracoscopy/endoscopy (5). The remaining 4 studies reported separation surgery. Indications were similar across all studies and included patients with instability, refractory pain, or neurologic compromise. Intraoperative variables, outcomes, and complications were similar in MIS studies compared to traditional approaches, and some MIS studies showed a statistically significant improvement in outcomes. Studies of mini-open techniques had the strongest evidence for superiority. Conclusions. Low-quality evidence currently exists for MIS techniques and separation surgery in the treatment of metastatic spine disease. Given the early promising results, the next iteration of research should include higher-quality studies with sufficient power, and will be able to provide higher-level evidence on the outcomes of MIS approaches and separation surgery. Copyright © 2016 Wolters Kluwer Health, Inc. All rights reserved.

84 Zeng ZC, He J, Huang Y, Shi SM. **Treatment toxicity and efficacy in comparison conventional fractionation with hypofractionation for bone metastases from primary liver cancer**. International Journal of Radiation Oncology 2016;96 (2 Supplement 1):E521.

**Abstract:** Purpose/Objective(s): To assess and compare the toxicity and efficacy between conventional fractionation and hypofractionated schedules in patients with painful bone metastases from primary liver cancer, and to explore the indications for the different fractionation schedules. Materials/Methods: We did a prospective, randomized, controlled trial which was registered as ChiCTR-TRC-10000967 (Chinese Clinical Trial Register) in our department. Between January 2009 and December 2014, 200 patients were enrolled and randomly assigned (1:1) to receive either 2 Gy per fraction with 20 fractions for bone metastases without expansile soft-tissue masses and 30 fractions for bone metastases with expansile softtissue masses (A group), or 4 Gy per fraction with 7 fractions for bone metastases without expansile soft-tissue masses and 10 fractions for bone metastases with expansile soft-tissue masses (B group) by a central computer-generated allocation sequence using dynamic minimization to conceal assignment. All pain scores were recorded according to the Numerical rating scale. Results: Mean follow-up for all patients was 9.3 months. The overall response rate and complete response rate in the A group (96.0% and 41.0%) seem higher than those in the B group (92.0% and 37.0%), but do not have significant differences (P = 0.499). The fractions for the response to radiotherapy leading to pain relief were significantly more in the A group (6f) than in the B group (4f), P < 0.001. The median durations of overall pain relief for the A group were 5.0 and 4.2 months in the B group. Grade I and II acute upper gastrointestinal toxicity were 13.0% and 3% in the A group and of 19.0% and 8.0% in the B group. One patient in the B group was observed in Grade III acute upper gastrointestinal toxicity. These differences were not statistically significant. Mild acute lower gastrointestinal toxicities were recorded in both groups. Grade I and II acute lower gastrointestinal toxicity were 11.0% and 3% in the A group and of 18.0% and 5.0% in the B group. More fatigue was recorded in the B group (39.0%) than that in the A group (26.0%). The median overall survival for all patients was 7.2 months (95% CI, 5.60e8.80). No significant differences were observed in the overall survival between the A group with 7.4 months (95% CI, 5.94e8.86) and the B group with 6.7 months (95% CI, 3.99e9.81). On multivariate analyses, survival was significantly associated with well-controlled intrahepatic tumor, Karnofsky performance status (KPS), g-glutamyltranspeptidase levels, a-fetoprotein levels, and the treatment of Zoledronic acid, Child-Pugh classification, and the complete response to treatment. Conclusion: The time of the response to radiation therapy leading to pain relief was appeared later in the conventional fractionation schedule than the hypofractionated schedule, but the median duration of overall pain relief in the conventional fractionation schedule was longer.

85 Xu Y, Zhong W, Zhao J, Chen M, Li L, Wang M. **[Clinical Features of Intradural Extramedullary Spinal Cord Metastases in Primary Lung Cancer]**. Chinese Journal of Lung Cancer 2016;19(8):539-44.

**Abstract:** BACKGROUND: Intradural extramedullary spinal cord metastases in lung cancer is rare, and it leads to severe neurological damage. The aim of this study is to identify the clinical features of intradural extramedullary spinal cord metastases in primary lung cancer patients.

METHODS: The 8 cases of lung cancer with intradural extramedullary metastases, who were hospitalized in Peking Union Medical College Hospital (PUMCH) during May 2013 to May 2016, were enrolled in the retrospective study. Medical charts of the 8 patients were reviewed systematically.

RESULTS: Intradural extramedullary spinal cord metastases was diagnosed in 7 cases with non-small cell lung cancer (NSCLC) and 1 case with small cell lung cancer (SCLC). Cauda equina syndrome was the most common clinical manifestation. Malignant cells in cerebrospinal fluid were positive in all the 5 cases (100%) who underwent lumbar puncture. Contrast-enhanced magnetic resonance imaging (MRI) of spine manifested as diffuse abnormal enhancement of pial lining of spinal cordin 3 cases, intradural extramedullary nodules in 4 cases, and both of them in 1 case. Neurological symptoms were improved or stable in 4 cases who underwent targeted therapy and/or radiotherapy. The median overall survival was 5.8 months.

CONCLUSIONS: Intradural extramedullary spinal cord metastases can be diagnosed with caution according to its neurological symptoms and contrast-enhanced MRI presentation.Targeted therapy and/or radiotherapy may be effective for symptoms control.

86 Xu Y, Zhong W, Zhao J, Chen M, Li L, Wang M. **Clinical features of intradural extramedullary spinal cord metastases in primary lung cancer**. Ann Oncol 2016;27 (Supplement 9):ix152.

**Abstract:** Background: Intradural extramedullary spinal cord metastases in lung cancer is rare, and it leads to severe neurological damage. The purpose of this study was to identify the clinical features of intradural extramedullary spinal cord metastases in primary lung cancer patients. Methods: 8 cases of lung cancer with intradural extramedullary metastases, who were hospitalized in Peking Union Medical College Hospital (PUMCH) during May, 2013 to May, 2016, wereenrolled in the retrospective study. Medical charts of the 8 patients were reviewed systematically. Results: Intradural extramedullary spinal cord metastases was diagnosed in 7 cases with non-small cell lung cancer (NSCLC) and 1 case with small cell lung cancer (SCLC). Cauda equina syndrome was the most common clinical manifestation. Malignant cells in cerebrospinal fluid were positive in all the 5 cases (100%) who underwent lumbar puncture. Contrast-enhanced magnetic resonance imaging (MRI) of spine manifested as diffuse abnormal enhancement of pial lining of spinal cord in 3 cases, intradural extramedullary nodules in 4 cases, and both of themin 1 case. Neurological symptoms were improved or stable in 4 cases who underwent targeted therapy and/or radiotherapy. The median overall survival was 5.8 months (95%CI, 1.9-9.6m). Table: Clinical characteristics and treatment outcomes of patients with intradural extramedullary spinal metastasis Conclusions: Intradural extramedullary spinal cord metastases canbe diagnosed with caution according to its neurological symptoms and contrast-enhanced MRI presentation. Targeted therapy and/or radiotherapy may be effectivefor symptoms control.

87 Wolf A, Johnstone R, Siddiqi F. **Intradural Extramedullary Spinal Cord Metastasis of the Prostate: A Case Presentation and Review of the Literature**. Can J Neurol Sci 2016;43(4):588-92.

**Abstract:** Prostate cancer is associated with vertebral metastasis in up to 10% of patients; however, intradural spinal cord metastases (ISCM) are much less frequent. We present the clinical and histopathological findings of a patient with ISCM arising from prostate. A PubMed literature search for ISCM from the prostate yielded a total of nine additional cases. ISCM of the prostate occurs at a late stage of systemic disease and the prognosis is generally poor. Decompressive surgery followed by adjuvant radiation therapy may help reduce intractable pain and stabilize neurological symptoms, thereby improving quality of life.

88 Willeumier JJ, van der Linden YM, Dijkstra PD. **Lack of clinical evidence for postoperative radiotherapy after surgical fixation of impending or actual pathologic fractures in the long bones in patients with cancer; a systematic review**. Radiother Oncol 2016;121(1):138-42.

**Abstract:** Patients with disseminated cancer and bone metastases have a limited life expectancy and therefore any treatment should have a clear beneficial effect, outweighing all possible downsides. This systematic review aims to identify and evaluate available evidence regarding function, pain, quality of life, survival and complications of postoperative radiotherapy (RT) after surgical stabilization of impending or actual pathologic fractures of the long bones due to bone metastases. A literature search resulted in two articles reporting on 64 and 110 patients of whom 55% and 28% received postoperative RT, respectively. Both studies were retrospective cohort studies and postoperative RT had been administered depending on the surgeons' choice. The first study reported better outcomes regarding function, re-interventions and survival in patients receiving postoperative RT. The second study reported no significant difference regarding complications between the two groups. The quality of the evidence was very low due to the observational character of both studies, risk of indication bias, small study sizes, use of non-standardized outcome measures, and limited statistical analyses. The current available literature is insufficient to conclude whether postoperative RT after surgical stabilization should be standard care. It is important to realize this lack of clear evidence when calling upon RT as adjuvant palliative treatment.

89 Versteeg AL, Verlaan JJ, Sahgal A, Mendel E, Quraishi NA, Fourney DR, et al. **The spinal instability neoplastic score: Impact on oncologic decision-making**. Spine (Phila Pa 1976) 2016;41(Supplement20):S231-S7.

**Abstract:** Objective. To address the following questions in a systematic literature review: 1. How is spinal neoplastic instability defined or classified in the literature before and after the introduction of the Spinal Instability Neoplastic Score (SINS)? 2. How has SINS affected daily clinical practice? 3. Can SINS be used as a prognostic tool? Summary of Background Data. Spinal neoplastic-related instability was defined in 2010 and simultaneously SINS was introduced as a novel tool with criteria agreed upon by expert consensus to assess the degree of spinal stability. Methods. PubMed, Embase, and clinical trial databases were searched with the key words "spinal neoplasm," "spinal instability," "spinal instability neoplastic score," and synonyms. Studies describing spinal neoplastic-related instability were eligible for inclusion. Primary outcomes included studies describing and/or defining neoplastic-related instability, SINS, and studies using SINS as a prognostic factor. Results. The search identified 1414 articles, of which 51 met the inclusion criteria. No precise definition or validated assessment tool was used specific to spinal neoplastic-related instability prior to the introduction of SINS. Since the publication of SINS in 2010, the vast majority of the literature regarding spinal instability has used SINS to assess or describe instability. Twelve studies specifically investigated the prognostic value of SINS in patients who underwent radiotherapy or surgery. Conclusion. No consensus could be determined regarding the definition, assessment, or reporting of neoplastic-related instability before introduction of SINS. Defining spinal neoplasticrelated instability and the introduction of SINS have led to improved uniform reporting within the spinal neoplastic literature. Currently, the prognostic value of SINS is controversial. Copyright © 2016 Wolters Kluwer Health, Inc. All rights reserved.

90 Van Der Velden JM, Verkooijen HM, Versteeg AL, Gerlich AS, Verlaan JJ, Zhang L, et al. **Predicting pain response after conventional radiotherapy in 1018 patients with bone metastases**. Radiother Oncol 2016;119 (Supplement 1):S665-S6.

**Abstract:** Purpose or Objective: Many patients with advanced cancer develop bone metastases, with pain as a common, devastating consequence. Adequate treatment is important to maintain quality of life. Radiotherapy is the standard treatment for patients with painful bone metastases. Meta analyses of radiotherapy trials have consistently shown a pain response rate of approximately 60% implying that many patients are treated insufficiently. It would be worthwhile to identify patients who will not respond to radiotherapy as these patients might be candidates for other treatments. Furthermore, better understanding and identification of the patients who do not respond to radiation, might help in the development of innovative treatments as alternative or addition to standard (radiation) treatment options. We studied the relationship between patient and treatment characteristics and pain response in patients with metastatic bone disease, with the aim to construct a prediction model to guide individualized treatment decision-making. Material and Methods: We analyzed all prospectively collected data on pain response from a palliative radiotherapy clinic in an academic hospital. Patients were considered responders if they reported a decrease in pain score of at least 2 points with stable analgesic use within 3 months after treatment. A multivariable logistic regression model was developed with age, gender, primary tumor, Karnofsky performance status (KPS), painful localization, presence of visceral metastases, previous systemic treatment, analgesic use at baseline, and baseline pain score. For variable selection, we started with the full model and applied backward stepwise selection with a selection criterion of p < 0.20. Performance of the model was quantified using the c-statistic and corrected for optimism. A worst case scenario (assuming no response in patients who were lost to follow up) was added as sensitivity analysis. Results: A total of 1018 patients treated between January 1999 and November 2007 were included. Outcome was recorded in 588 (58%) patients, of which 394 (67%) reported a response. Primary tumor, KPS, baseline pain score, and analgesic use were predictive for response with a corrected c-statistic of 0.59 (Table). Assuming non-response in the 430 patients without follow up (worst case scenario), there was still an association between response and primary tumor, KPS, and baseline pain score. Conclusion: Primary tumor, performance status, baseline pain score, and analgesic use are associated with pain response in patients with bone metastases. However, combining these factors in a prediction model showed poor discrimination limiting its use in clinical practice. Response rates after radiotherapy are moderate, and its prediction is difficult, which shows the need for development of innovative treatments for patients with bone metastases.

91 Vale CL, Burdett S, Rydzewska LHM, Albiges L, Clarke NW, Fisher D, et al. **Addition of docetaxel or bisphosphonates to standard of care in men with localised or metastatic, hormone-sensitive prostate cancer: A systematic review and meta-analyses of aggregate data**. The Lancet Oncology 2016;17(2):243-56.

**Abstract:** Background: Results from large randomised controlled trials combining docetaxel or bisphosphonates with standard of care in hormone-sensitive prostate cancer have emerged. In order to investigate the effects of these therapies and to respond to emerging evidence, we aimed to systematically review all relevant trials using a framework for adaptive meta-analysis. Methods: For this systematic review and meta-analysis, we searched MEDLINE, Embase, LILACS, and the Cochrane Central Register of Controlled Trials, trial registers, conference proceedings, review articles, and reference lists of trial publications for all relevant randomised controlled trials (published, unpublished, and ongoing) comparing either standard of care with or without docetaxel or standard of care with or without bisphosphonates for men with high-risk localised or metastatic hormone-sensitive prostate cancer. For each trial, we extracted hazard ratios (HRs) of the effects of docetaxel or bisphosphonates on survival (time from randomisation until death from any cause) and failure-free survival (time from randomisation to biochemical or clinical failure or death from any cause) from published trial reports or presentations or obtained them directly from trial investigators. HRs were combined using the fixed-effect model (Mantel-Haenzsel). Findings: We identified five eligible randomised controlled trials of docetaxel in men with metastatic (M1) disease. Results from three (CHAARTED, GETUG-15, STAMPEDE) of these trials (2992 [93%] of 3206 men randomised) showed that the addition of docetaxel to standard of care improved survival. The HR of 0.77 (95% CI 0.68-0.87; p<0.0001) translates to an absolute improvement in 4-year survival of 9% (95% CI 5-14). Docetaxel in addition to standard of care also improved failure-free survival, with the HR of 0.64 (0.58-0.70; p<0.0001) translating into a reduction in absolute 4-year failure rates of 16% (95% CI 12-19). We identified 11 trials of docetaxel for men with locally advanced disease (M0). Survival results from three (GETUG-12, RTOG 0521, STAMPEDE) of these trials (2121 [53%] of 3978 men) showed no evidence of a benefit from the addition of docetaxel (HR 0.87 [95% CI 0.69-1.09]; p=0.218), whereas failure-free survival data from four (GETUG-12, RTOG 0521, STAMPEDE, TAX 3501) of these trials (2348 [59%] of 3978 men) showed that docetaxel improved failure-free survival (0.70 [0.61-0.81]; p<0.0001), which translates into a reduced absolute 4-year failure rate of 8% (5-10). We identified seven eligible randomised controlled trials of bisphosphonates for men with M1 disease. Survival results from three of these trials (2740 [88%] of 3109 men) showed that addition of bisphosphonates improved survival (0.88 [0.79-0.98]; p=0.025), which translates to 5% (1-8) absolute improvement, but this result was influenced by the positive result of one trial of sodium clodronate, and we found no evidence of a benefit from the addition of zoledronic acid (0.94 [0.83-1.07]; p=0.323), which translates to an absolute improvement in survival of 2% (-3 to 7). Of 17 trials of bisphosphonates for men with M0 disease, survival results from four trials (4079 [66%] of 6220 men) showed no evidence of benefit from the addition of bisphosphonates (1.03 [0.89-1.18]; p=0.724) or zoledronic acid (0.98 [0.82-1.16]; p=0.782). Failure-free survival definitions were too inconsistent for formal meta-analyses for the bisphosphonate trials. Interpretation: The addition of docetaxel to standard of care should be considered standard care for men with M1 hormone-sensitive prostate cancer who are starting treatment for the first time. More evidence on the effects of docetaxel on survival is needed in the M0 disease setting. No evidence exists to suggest that zoledronic acid improves survival in men with M1 or M0 disease, and any potential benefit is probably small. Funding: Medical Research Council UK. Copyright © 2016 Vale et al. Open Access article distributed under the terms of CC-BY.

92 Tilley D, Kerba M, Kostaras X, Fairchild A. **Development of provincial palliative radiotherapy guidelines**. Radiother Oncol 2016;120 (Supplement 1):S62.

**Abstract:** Purpose: Radiotherapy (RT) practice variability in the palliative setting is well-documented. Clinical practice guidelines inform standardized, evidence-based, beneficial practice, while simultaneously discouraging unnecessary or potentially harmful practices. The process of creating provincial palliative RT clinical practice guidelines is associated with multiple challenges. We describe the unique approach required in aligning multidisciplinary goals as compared to traditional tumour sitespecific guidelines. Methods and Materials: Radiation oncologists from the provincial Palliative Care Tumour Team, along with guideline specialists from the Guideline Resource Unit, formed the primary guideline working group tasked with updating the Palliative RT guidelines. Tumour site specific representatives (ex. Central Nervous System Tumour Team) were incorporated as needed, as well as experts in supportive care, on a guideline by guideline basis. For each guideline, a systematic literature review was conducted to identify relevant evidence. Recommendations were initially developed within the primary working group, then revised in collaboration with experts from other disciplines. Once working group consensus was reached, guideline recommendations were circulated to all radiation oncologists and Palliative Tumour Team members for input. After several rounds of feedback and modifications, provincial consensus was reached. Results: Initially, one RT guideline had been created for all provincial palliative RT recommendations. These guidelines have since been split into smaller, more functional palliative RT guidelines: 1) Brain Metastases; 2) Bone Metastases and Spinal Cord Compression; 3) Bleeding and Gastrointestinal Obstruction; and 4) Superior Vena Cava Obstruction, Dyspnea, and Hemoptysis. The majority of recommendations were either modified or new due to advancements in research or changes in consensus based approaches. In total, 70 recommendations were approved. Recommendations were supported by a range of evidence from high (level one evidence) to low quality (consensus opinion). Conclusions: By combining the newly updated palliative RT guidelines with an educational intervention, variations in practice may be mitigated. Using our model, similar efforts can be undertaken in other jurisdictions.

93 Tao R, Bishop AJ, Brownlee Z, Allen PK, Settle SH, Chang EL, et al. **Stereotactic Body Radiation Therapy for Spinal Metastases in the Postoperative Setting: A Secondary Analysis of Mature Phase 1-2 Trials**. Int J Radiat Oncol Biol Phys 2016;95(5):1405-13.

**Abstract:** PURPOSE: To evaluate the outcomes in patients treated on prospective phase 1-2 protocols with postoperative stereotactic body radiation therapy (SBRT) and identify the associated prognostic variables.

METHODS AND MATERIALS: Sixty-six patients with 69 tumors were treated with SBRT on prospective phase 1-2 studies for spinal metastases between 2002 and 2010. All patients underwent SBRT after spine surgery, which included laminectomy, vertebrectomy, or a combination of these techniques. Renal cell carcinoma was the most common histology represented (n=35, 53%) followed by sarcomas (n=13, 20%). Thirty-one patients (47%) were treated with prior conventional radiation to the spine (median dose 30 Gy). Patients were followed up with spinal magnetic resonance imaging (MRI) studies to determine the treated tumor control (TC). Pain and other symptom data were collected prospectively to determine treatment response and toxicity.

RESULTS: The median follow-up time was 30 months (range, 1-145 months) for all patients and 75 months for living patients (range, 6-145 months). The actuarial 1-year rate of TC was 85%, adjacent vertebral body control was 85%, and overall survival (OS) was 74% (median 29 months). On multivariate competing-risks analysis, sarcoma histology (subhazard ratio [SHR] = 2.38, 95% confidence interval [CI] 1.05-5.6, P=.04) and larger preoperative tumor volumes (SHR=1.01, 95% CI 1.0-1.01, P=.006) were significantly associated with worse TC. Karnofsky performance status was the only significant predictor for OS on multivariate analysis. There were no differences in TC between patients treated with different surgical techniques or different preoperative or postoperative Bilsky grades. There were no grade 3 or higher neurologic toxicities.

CONCLUSION: This study represents a large series of prospective data available on patients treated with SBRT in the postoperative setting. The combination of surgery with SBRT can offer patients with metastatic disease to the spine the chance of durable tumor control with minimal toxicity.

94 Simanek M, Koranda P. **SPECT/CT imaging in breast cancer - current status and challenges**. Biomedical Papers of the Medical Faculty of Palacky University in Olomouc, Czech Republic 2016;160(4):474-83.

**Abstract:** BACKGROUND: The increasing incidence of breast cancer worldwide raises the importance of improving imaging techniques for disease stratification after early lesion detection. SPECT/CT imaging is now widely available but its diagnostic potential is not fully utilized for more specific purposes including breast cancer patient stratification.

METHODS AND RESULTS: A Pubmed search for both original and review articles related to the value of SPECT/CT in breast cancer patients and comparison to other diagnostic methods. 62 articles were found using the key words SPECT/CT, Fusion Image and Breast Cancer. Development of a new generation of SPECT/CT systems and their introduction into practice has changed the old diagnostic algorithm. The increasing importance of SPECT/CT in the detection of bone metastases is confirmed. The diagnostic accuracy of new SPECT/CT instruments in the diagnostics of bone metastases is nearly comparable to PET/CT scans. SPECT/CT is more widely available and costs less than PET. It is able not only to identify a sentinel lymph nodes in atypical localizations but also to detect sentinel lymph nodes non visualized on previous planar scans. SPECT/CT offers precise anatomic localization of sentinel lymph nodes, thereby facilitating surgery. Knowledge of precise sentinel lymph node localization can also be applied in radiotherapy.

CONCLUSIONS: The role of hybrid SPECT/CT imaging in breast cancer patients is changing. It is a powerful modality for skeletal and nodal staging in breast cancer patients with important impact on therapy.

95 Shibata H, Kato S, Sekine I, Abe K, Araki N, Iguchi H, et al. **Diagnosis and treatment of bone metastasis: comprehensive guideline of the Japanese Society of Medical Oncology, Japanese Orthopedic Association, Japanese Urological Association, and Japanese Society for Radiation Oncology**. ESMO open 2016;1(2):e000037.

**Abstract:** Diagnosis and treatment of bone metastasis requires various types of measures, specialists and caregivers. To provide better diagnosis and treatment, a multidisciplinary team approach is required. The members of this multidisciplinary team include doctors of primary cancers, radiologists, pathologists, orthopaedists, radiotherapists, clinical oncologists, palliative caregivers, rehabilitation doctors, dentists, nurses, pharmacists, physical therapists, occupational therapists, medical social workers, etc. Medical evidence was extracted from published articles describing meta-analyses or randomised controlled trials concerning patients with bone metastases mainly from 2003 to 2013, and a guideline was developed according to the Medical Information Network Distribution Service Handbook for Clinical Practice Guideline Development 2014. Multidisciplinary team meetings are helpful in diagnosis and treatment. Clinical benefits such as physical or psychological palliation obtained using the multidisciplinary team approaches are apparent. We established a guideline describing each specialty field, to improve understanding of the different fields among the specialists, who can further provide appropriate treatment, and to improve patients' outcomes.

96 Raval A, Dan TD, Williams NL, Pridjian A, Den RB. **Radioisotopes in management of metastatic prostate cancer**. Indian J Urol 2016;32(4):277-81.

**Abstract:** INTRODUCTION: Metastatic prostate cancer continues to be a leading cause of morbidity and mortality in men with prostate cancer. Over the last decade, the treatment landscape for patients with castrate-resistant disease has drastically changed, with several novel agents demonstrating an improvement in overall survival in large, multi-institutional randomized trials. Traditional treatment with radioisotopes has largely been in the palliative setting. However, the first in class radiopharmaceutical radium-223 has emerged as the only bone-directed treatment option demonstrating an improvement in overall survival.

METHODS: Medline publications from 1990 to 2016 were searched and reviewed to assess the use of currently approved radioisotopes in the management of prostate cancer including emerging data regarding integration with novel systemic therapies. New positron emission tomography-based radiotracers for advanced molecular imaging of prostate cancer were also queried.

RESULTS: Radioisotopes play a crucial role in the diagnosis and treatment of prostate cancer in the definitive and metastatic setting. Molecular imaging of prostate cancer and theranostics are currently being investigated in the clinical arena.

CONCLUSIONS: The use of modern radioisotopes in selected patients with mCRPC is associated with improvements in overall survival, pain control, and quality of life.

97 Prieske K, Haeringer N, Grimm D, Trillsch F, Eulenburg C, Burandt E, et al. **Patterns of distant metastases in vulvar cancer**. Gynecol Oncol 2016;142(3):427-34.

**Abstract:** Objective Metastatic vulvar cancer is a rare disease. Information on metastatic patterns and corresponding prognosis or therapeutic approaches is scarce. We therefore analyzed pattern and course of metastatic disease in a large single center cohort. Methods All patients with primary squamous-cell cancer of the vulvar [n = 391, median age: 60 years (range 20-94)] treated at the Gynecological Cancer Center Hamburg-Eppendorf 1996-2013 were retrospectively evaluated for occurrence of distant metastasis. Furthermore, a systematic Medline database search was performed using the terms: 'vulvar cancer' AND 'metastasis', 'chemotherapy', 'patterns of recurrence', or 'prognosis'. Results Out of 391 patients with primary squamous cell vulvar cancer, 20 patients (5.1%) eventually presented with distant metastases. In these 20 patients, median time to first diagnosis of metastasis after primary diagnosis was 13.4 months (range 4-104). Often patients experienced one or more local recurrences before distant spread (12/20, 60.0%). Documented metastatic sites were lung (n = 9), liver (n = 7), bone (n = 5), skin (n = 4) and lymph-nodes (axillary/thoracic/paraaortic, n = 3). The majority of patients presented with unilocal metastases (13/20, 65.0%). In univariate analysis tumor diameter, invasion depth, nodal status and number of metastatic lymph-nodes were identified predictive for occurrence of distant metastases. 2-year-overall-survival-rate after metastases of all metastatic patients was 11.3%; median survival from first diagnosis of metastases was 5.6 months. Conclusion The occurrence of distant metastasis from vulvar cancer is a rare event with very limited prognosis. Further efforts, especially translational research will be crucial to identify prognostic markers as well as therapeutic targets to improve survival in these patients. Copyright © 2016 Elsevier Inc.

98 Pappa T, Alevizaki M. **Management of hereditary medullary thyroid carcinoma**. Endocrine 2016;53(1):7-17.

**Abstract:** Hereditary medullary thyroid carcinoma (MTC) represents up to one-third of MTC cases and includes multiple endocrine neoplasia syndrome type 2A (and its variant familial MTC) and 2B. The aim of this paper is to provide an overview of the disease focusing on the management of hereditary MTC patients, who have already developed tumor, as well as discuss the recommended approach for asymptomatic family members carrying the same mutation. A PubMed search was performed to review recent literature on diagnosis, genetic testing, and surgical and medical management of hereditary MTC. The wide use of genetic testing for RET mutations has markedly influenced the course of hereditary MTC. Prophylactic thyroidectomy of RET carriers at an early age eliminates the risk of developing MTC later in life. Pre-operative staging is a strong prognostic factor in patients, who have developed MTC. The use of recently approved tyrosine kinase inhibitors (vandetanib, cabozantinib) holds promising results for the treatment of unresectable, locally advanced, and progressive metastatic MTC. Genetic testing of the RET gene is a powerful tool in the diagnosis and prognosis of MTC. Ongoing research is expected to add novel treatment options for patients with advanced, progressive disease. Copyright © 2016, Springer Science+Business Media New York.

99 Ost P. **How to optimise the potential of SBRT**. Radiother Oncol 2016;119 (Supplement 1):S292-S3.

**Abstract:** Radiotherapy is a well-established treatment for painful vertebral metastases. Multiple prospective studies report pain response rates of 50 to 90%. Based on randomized studies, 8 Gy in a single fraction is the standard of care for painful uncomplicated bone metastases. Despite the lack of a dose response relationship for pain control, there is good rationale for dose escalation with the aim to improve upon existing rates of local tumour control and pain control. Stereotactic body radiotherapy is ideally suited to safely escalate the dose and improve tumour control. In order to optimize the potential of SBRT, adequate patient selection and specific technical considerations should be taken into account. PATIENT SELECTION Several considerations should be taken into account before delivering SBRT for vertebral metastases. A first consideration is the life expectancy of the patient, which should be evaluated with validated scoring systems (e.g. NRF score, Recursive partitioning analysis index, PRISM). Patients with a short life expectancy in need for palliative radiotherapy should be managed with short effective radiotherapy courses. In patients with longer life expectancy local control might be an important end point potentially requiring a higher radiotherapy dose. A second consideration is the characteristic of the vertebral metastasis and divides the metastases into uncomplicated or complicated. A systematic review suggested the following working definition for uncomplicated bone metastases: those unassociated with impending or existing pathologic fracture or existing spinal cord compression or cauda equina compression. Although this definition looks straightforward it is still variable to interpretation and might be incomplete. The Spinal Instability Neoplastic Score (SINS) might help us estimate the risk of vertebral fracture limiting SBRT to stable and potentially unstable metastases. Different definitions of spinal cord compression are available with the minimum evidence for cord compression being indentation of the thecal sac at the level of clinical features. Finally, other aspects such as, primary tumour type, other metastases, symptoms, practical considerations, current systemic treatment and previous radiotherapy' should be taken into TECHNICAL CONSIDERATIONS For treatment simulation several options are available for patient immobilization. Independent of the system used, the patient must be positioned in a stable position capable for reproducibility of positioning, allowing the patient to feel as comfortable as possible. A typical CT scan length should extend at least 10 cm superior and inferior beyond the treatment field borders (slice thickness of <=2.5 - 3 mm). CT contrast will help visualize the soft tissue and adjacent normal tissues. The International Spine Radiosurgery consortium developed a consensus guideline for target volume definition. MRI images are mandatory for delineation. Axial volumetric T1 and T2 sequences without gadolinium are a standard with <=3 mm slice thickness. Contouring of norm al tissue should be standardized for example: start contouring at 10 cm above the target volume to 10 cm below the target (RTOG 0631). Different fractionation schedules exist with variable total doses. None of the proposed schedules is proven to be superior to another. In case of single fraction, the doses vary between 16 and 24 Gy, with a strong trend for increasing pain relief with higher radiation doses, particularly with doses >= 16 Gy. In case of fractionated radiotherapy, doses vary between 7-10 Gy for a 3 fraction schedule and between 5-6 Gy for a 5 fraction schedule. Most centers prescribe the dose (Dpr) to a % volume of the PTV. A PTV dose coverage of <80% of the Dpr should be avoided (RTOG 0631). This Dpr. should be prescribed to the isocenter or periphery of target. To minimize the risk for toxicity it is advised to strictly adhere to the published dose-constraints keeping in mind that they are mostly unvalidated. Control and correction of the patient and tumor position should be done with vol metric or stereoscopic X-ray imaging at least before each treatment fraction. Extensive recommendations and guidelines for a stereotactic or high precision QA program, supplementing the QA program for linear accelerators can be found in literature and should be followed (e.g. AAPM TG 101 report). OUTCOME The International Bone Metastases Consensus Working Party developed guidelines for the assessment of endpoints of palliative radiotherapy of bone metastases. It is recommended to follow the proposed definitions of pain assessment and pain response. Toxicity should evaluated at follow up visits using standardized criteria such as the National Cancer Institute (NCI) Common Terminology Criteria for Adverse Events (CTCAE) v.4.0.

100 Olson RA, Tiwana M, Barnes M, Cai E, McGahan C, Roden K, et al. **Impact of Using Audit Data to Improve the Evidence-Based Use of Single-Fraction Radiation Therapy for Bone Metastases in British Columbia**. Int J Radiat Oncol Biol Phys 2016;94(1):40-7.

**Abstract:** PURPOSE: To assess the impact of a population-based intervention to increase the consistency and use of single-fraction radiation therapy (SFRT) for bone metastases.

METHODS AND MATERIALS: In 2012, an audit of radiation therapy prescriptions for bone metastases in British Columbia identified significant interphysician and -center (26%-73%) variation in the use of SFRT. Anonymous physician-level and identifiable regional cancer center SFRT use data were presented to all radiation oncologists, together with published guidelines, meta-analyses, and recommendations from practice leaders. The use of SFRT for bone metastases from 2007 through 2011 was compared with use of SFRT in 2013, to assess the impact of the audit and educational intervention. Multilevel logistic regression was used to assess the relationship between the usage of SFRT and the timing of the radiation while controlling for potentially confounding variables. Physician and center were included as group effects to account for the clustered structure of the data.

RESULTS: A total of 16,898 courses of RT were delivered from 2007 through 2011, and 3200 courses were delivered in 2013. The rates of SFRT use in 2007, 2008, 2009, 2010, 2011, and 2013 were 50.5%, 50.9%, 48.3%, 48.5%, 48.0%, and 59.7%, respectively (P<.001). Use of SFRT increased in each of 5 regional centers: A: 26% to 32%; B: 36% to 56%; C: 39% to 57%; D: 49% to 56%; and E: 73% to 85.0%. Use of SFRT was more consistent; 3 of 5 centers used SFRT for 56% to 57% of bone metastases RT courses. The regression analysis showed strong evidence that the usage of SFRT increased after the 2012 intervention (odds ratio 2.27, 95% confidence interval 2.06-2.50, P<.0001).

CONCLUSION: Assessed on a population basis, an audit-based intervention increased utilization of SFRT for bone metastases. The intervention reversed a trend to decreasing SFRT use, reduced costs, and improved patient convenience. This suggests that dissemination of programmatic quality indicators in oncology can lead to increased utilization of evidence-based practice.

101 Niedersuess-Beke D, Strasser-Weippl K. **Treatment of elderly patients with advanced urological cancer**. Memo - Magazine of European Medical Oncology 2016;9(1):20-9.

**Abstract:** The treatment of advanced urological cancers has evolved tremendously over the last decade. As the incidence of these cancers is increasing with age, uro-oncologists are increasingly faced with the challenge of choosing optimal therapeutic strategies for elderly patients. Comorbidities interfering with cancer treatment can be identified by geriatric assessment tools that should be applied in elderly cancer patients before starting therapy. Using these tools competing risks of morbidity and mortality can be evaluated. We provide a review on evidence based treatments in elderly prostate, bladder and renal cell carcinoma patients. Copyright © 2016, Springer-Verlag Wien.

102 Nieder C, Langendijk JA, Guckenberger M, Grosu AL. **Prospective randomized clinical studies involving reirradiation : Lessons learned**. Strahlenther Onkol 2016;192(10):679-86.

**Abstract:** BACKGROUND: Reirradiation is a potentially useful option for many patients with recurrent cancer. The purpose of this study was to review all recently published randomized trials in order to identify methodological strengths and weaknesses, comment on the results, clinical implications and open questions, and give advice for the planning of future trials.

MATERIALS AND METHODS: Systematic review of trials published between 2000 and 2015 (databases searched were PubMed, Scopus and Web of Science).

RESULTS: We reviewed 9 trials, most of which addressed reirradiation of head and neck tumours. The median number of patients was 69. Trial design, primary endpoint and statistical hypotheses varied widely. The results contribute mainly to decision making for reirradiation of nasopharynx cancer and bone metastases. The trials with relatively long median follow-up confirm that serious toxicity remains a concern after high cumulative total doses.

CONCLUSION: Multi-institutional collaboration is encouraged to complete sufficiently large trials. Despite a paucity of large randomized studies, reirradiation has been adopted in different clinical scenarios by many institutions. Typically, the patients have been assessed by multidisciplinary tumour boards and advanced technologies are used to create highly conformal dose distributions.

103 Neto T, Horta R, Balhau R, Coelho L, Silva P, Correia-Sa I, et al. **Resection and microvascular reconstruction of bisphosphonate-related osteonecrosis of the jaw: The role of microvascular reconstruction**. Head Neck 2016;38(8):1278-85.

**Abstract:** Background: Current treatment guidelines caution against osseous reconstruction using free flap tissue to treat bisphosphonate-related osteonecrosis of the jaw (BRONJ). The primary rationale for this stance is the theoretical risk of nonunion and recurrence of disease within the reconstruction. Emerging evidence suggests that these theoretical risks may be overestimated. We performed a literature review of this procedure for the treatment of advanced BRONJ. We also present a new case report of resection and microvascular reconstruction in a 58-year-old man with stage III BRONJ. Methods: A MEDLINE search was performed to gather all reports of maxillary and mandibular reconstruction using free tissue flap transfer for BRONJ. Inclusion criteria were confirmed stage II or III BRONJ, free tissue transfer and reconstruction, and reported complications. Articles were excluded if they contained only local flap reconstruction, wound closure without reconstruction, or osteoradionecrosis. Outcomes from our case report were added to the analysis. Results: We identified 10 articles that met criteria. Adding our case, we identified 40 cases of free flap reconstruction. The rate of nonunion was 5% (2 of 40). Fistulas formed in 4 cases (10%). BRONJ recurred in 2 cases (5%). Conclusion: Complication rates after free flap microvascular reconstruction in BRONJ seem acceptable. Nonunion is relatively rare and should not be the sole reason to recommend against free flap reconstruction. A randomized clinical trial would help clarify the role of this procedure in refractory BRONJ; however, we believe that segmental resection and microvascular reconstruction is a viable option in select cases of BRONJ. © 2016 Wiley Periodicals, Inc. Head Neck 38:1278-1285, 2016. Copyright © 2016 Wiley Periodicals, Inc.

104 Nakamura N. **Palliative radiotherapy for painful bone metastases**. Ann Oncol 2016;27 (Supplement 7):vii65.

**Abstract:** Radiotherapy is a highly successful modality to palliate pain due to bone metastases, with mild adverse effects and short treatment durations. According to previous metaanalyses, response rates and complete response rates were 59-73 and 23-34%, respectively. The median period until pain relief is 3-4 weeks, while the median period until a pain increase is 5-6 months. For uncomplicated painful bone metastases, which are defined as the presence of painful bone metastases that are not associated with impending or existing pathological fracture or existing spinal cord or cauda equine compressions, multiple randomized trials have shown that a single 8-Gy fraction regimen is equally effective as multiple fraction regimens, such as 20 Gy in 5 fractions or 30 Gy in 10 fractions. A single fraction regimen is equally effective not only in terms of response rates of pain relief but also in the period until a pain increase, incidence of spinal cord compression, incidence of pathological fracture, quality of life, as well as acute and late adverse effects. Therefore, a single fraction regimen is applicable not only for patients with a poor prognosis but also for those with a good prognosis. For patients with complicated bone metastases, multiple fraction regimens are recommended. Multiple fraction regimens are also recommended for patients with neuropathic pain. For patients who have recurrent or persistent pain after radiotherapy, reirradiation of the same sites is also effective. The response to the first irradiation is not a predictive factor of the response to reirradiation. Radiopharmaceuticals such as Strontium-89 are an important option for multifocal painful bone metastases, of which the number of anatomical sites is too high to reasonably be treated with external beam radiotherapy. Stereotactic body radiotherapy (SBRT) for spinal metastases should be used only within clinical trials.

105 Molina C, Goodwin CR, Abu-Bonsrah N, Elder BD, De la Garza Ramos R, Sciubba DM. **Posterior approaches for symptomatic metastatic spinal cord compression**. Neurosurg Focus 2016;41(2):E11.

**Abstract:** Surgical interventions for spinal metastasis are commonly performed for mechanical stabilization, pain relief, preservation of neurological function, and local tumor reduction. Although multiple surgical approaches can be used for the treatment of metastatic spinal lesions, posterior approaches are commonly performed. In this study, the role of posterior surgical procedures in the treatment of spinal metastases was reviewed, including posterior laminectomy with and without instrumentation for stabilization, transpedicular corpectomy, and costotransversectomy. A review of the literature from 1980 to 2015 was performed using Medline, as was a review of the bibliographies of articles meeting preset inclusion criteria, to identify studies on the role of these posterior approaches among adults with spinal metastasis. Thirty-four articles were ultimately analyzed, including 1 randomized controlled trial, 6 prospective cohort studies, and 27 retrospective case reports and/or series. Some of the reviewed articles had Level II evidence indicating that laminectomy with stabilization can be recommended for improvement in neurological outcome and reduction of pain in selected patients. However, the use of laminectomy alone should be carefully considered. Additionally, transpedicular corpectomy and costotransversectomy can be recommended with the expectation of improving neurological outcomes and reducing pain in properly selected patients with spinal metastases. With improvements in the treatment paradigms for patients with spinal metastasis, as well as survival, surgical therapy will continue to play an important role in the management of spinal metastasis. While this review presents a window into determining the utility of posterior approaches, future prospective studies will provide essential data to better define the roles of the various options now available to surgeons in treating spinal metastases.

106 Maurer T, Eiber M, Fanti S, Budaus L, Panebianco V. **Imaging for Prostate Cancer Recurrence**. European Urology Focus 2016;2(2):139-50.

**Abstract:** Context: Correct identification of metastatic sites in recurrent prostate cancer (PCa) is of crucial importance because it leads to further treatment decisions. Objective: To provide an overview on current imaging procedures and their performance in recurrent PCa. Evidence acquisition: Medline search via PubMed was performed with the keywords imaging, recurrent, and prostate cancer as well as more detailed searches including the keywords bone scan, bone scintigraphy, computed tomography, magnetic resonance imaging, positron emission tomography, PET, choline, FDG, prostate-specific membrane antigen, and PSMA, with emphasis on recent literature from 2010 to the present. Non-English published literature was excluded. Abstracts and full-text articles were reviewed and assessed for relevant content. Evidence synthesis: In diagnostic imaging and particularly with newer technologies like positron emission tomography (PET), a profound lack of prospectively designed studies in recurrent PCa has to be noted. In most studies histologic validation has only been performed in a subset of patient cohorts. Heterogeneity of included patient cohorts, lack of standardized assessment, as well as diverging end points, hamper systematic comparison of different image modalities. Thus evidence for currently used imaging in recurrent PCa is only presented descriptively. Conclusions: Computed tomography and magnetic resonance imaging (MRI) as well as bone scintigraphy still represent the standard imaging for recurrent PCa; however, particularly for detection of local recurrence, multiparametric MRI is a valuable imaging modality. PET using choline and particularly tracers against prostate-specific membrane antigen might improve visualization of metastatic lesions. These findings need to be validated in prospective trials. Patient summary: Imaging of recurrent prostate cancer (PCa) is important to guide further treatment. Computed tomography, magnetic resonance imaging, and bone scintigraphy represent the current standard. Positron emission tomography, especially with cancer-specific tracers, might improve imaging of recurrent PCa in the future. Standard imaging for recurrent prostate cancer includes computed tomography, scintigraphy, and magnetic resonance imaging (MRI). Multiparametric MRI can differentiate local recurrence from residual benign tissue. Positron emission tomography using choline, and particularly tracers against prostate-specific membrane antigen, might improve visualization of metastatic lesions. Validation in prospective trials is required. Copyright © 2016 European Association of Urology.

107 Marin S, Garde J, Salvador Coloma C, Juan O, Arribas L, Garcia Sanchez J, et al. **Oligometastatic non-small-cell lung cancer (NSCLC) and unresectable primary tumor: Updated retrospective analysis of safety and efficacy of the radical treatment for the primary tumor and the metastases**. J Thorac Oncol 2016;1):S120.

**Abstract:** Background: Non-small-cell lung cancer oligometastatic at diagnosis represents a therapeutic challenge. Nowadays we have limited evidence about the radical treatment benefit for the primary tumor and the metastases. Methods: Retrospective study of patients with NSCLC unresectable and oligometastatic (3 or less lesions, in a unique location), radical treated the primary tumor and the metastases. We have done a systematic review of the clinical histories from NSCLC advanced patients diagnosed between October 2011 and November 2015. The aim of our study is to analyze the safety and efficacy of this treatment strategy in terms of response rate, progression free survival (PFS) and overall survival (OS). Results: 34 patients met inclusion criteria. Median age 58 years, male (78.3%) and ECOG (0-1) 95.7%. Histology: adenocarcinoma (64.7%), squamous carcinoma (23.5%), sarcomatoid (5.8%) and other histology (5.8%). All patients have unresectable mediastinal lymph nodes. Oligometastase location brain metastases (64.7%), lung metastases (17.6%), bone metastases (8.8%), other location (5.8%). Chemotherapy: CDDP- pemetrexed (41.1%), CDDP-vinorelbine (35.29%), carboplatin- paclitaxel (8.8%), CDDP-gemcitabine (5.8%), CDDP-docetaxel (5.8%). Sequential thoracic radiotherapy (43.5%) and concomitant radiotherapy (52.2%). Metastase treatment: Radiosurgery (58.8%), external radiotherapy (23.5%), surgery (11.7%), radiofrequency (2.9%), none (2.9%). Toxicity G3 (29.4%). Response rate (68.9%), PFS 12 months (95%CI: 8.2-13.7), OS 19 months (CI: 15.6-21.3). Conclusions: The radical treatment in oligometastatic unresectable NSCLC patients is a safe therapeutic strategy. Despite the limited data of prospective and randomized studies, it could be contemplated as an effective therapeutic alternative in selected patients.

108 Linsenmeier C, Brown ML. **Defining the incidence and treatment of skull base metastases in breast cancer: Case report and selective literature review**. Strahlenther Onkol 2016;192 (11):857.

**Abstract:** Objective: Bone metastases are one of the most common sites of recurrent disease in breast cancer patients and typically arise in the vertebral spine or extremities. Skull base metastases (SBM) are relatively rare. Based on 2 recent cases of SBM, we evaluated the literature to better define the incidence and management of this presentation in breast cancer patients. Materials and Methods: We present two patients with a past history of breast cancer and SBM. One patient developed anosmia, the other complained about sinusitis and pain in the left maxillary sinus. After several courses of antibiotics and analgesics, imaging eventually demonstrated a suspicious mass in the skull base. A biopsy confirmed the histological diagnosis of breast cancer metastases. After staging with PET-CT, one patient presented with a suspicious ovarian lesion, which was operated on laparoscopically and confirmed a breast cancer metastasis. The other patient showed no evidence of further disease. Both patients with SBM were irradiated with a curative dose using a highly conformal technique. One patient remains free of recurrent disease after two years of follow up; the other patient is currently under treatment. A search of the PubMed database for "base of skull metastasis and breast cancer" was performed. The search was repeated with "and radiotherapy". Results: We identified 43 articles concerning SBM and breast cancer. By adding "and radiotherapy", 14 articles remained. According to the literature, SBM are rare and typically arise secondary to breast, lung or prostate cancer. Various treatment methods, including surgery, radiotherapy, systemic agents or a combination, have been used. Limited data is available regarding radiation dose, technique and outcome in breast cancer patients with SBM. Improvement in symptoms following radiotherapy has been documented. Conclusion: SBM secondary to breast cancer are rare. However, awareness of the skull base as a potential metastatic site in breast cancer is important, as early detection and treatment is crucial to improve patient outcome, and to alleviate and control disabling symptoms.

109 Lin J, Hng TM. **Treatment resistant papillary thyroid cancer**. Clin Endocrinol (Oxf) 2016;1):39-40.

**Abstract:** Synopsis: Investigations for TSH elevation revealed a mulitnodular goitre. Progress ultrasound suggested malignancy and a follicular neoplasm was confirmed on biopsy. A total thyroidectomy was followed by radioactive iodine (RAI) ablation. Histopathology revealed papillary thyroid cancer (insular variant) with extensive capsular and vascular invasion. Uptake in the T1 and L2 vertebrae was noted post therapy. Further RAI was administered but thyroglobulin remained elevated (1380 mcg/ L). Resection of metastatic T1 and L2 lesions were undertaken. A 3rd dose of RAI was administered and thyroglobulin levels measured 1089 mcg/L pre-treatment. Thyroglobulin levels continued to rise (2252 mcg/L prior to 4th RAI treatment), with new lung and recurrent bone metastases developing. Selected lesions were 18 FDG-PET positive. Due to a paucity treatment options, a 5th RAI dose was administered (total dose of 21.6 GBq). External beam radiotherapy was delivered to the T1 lesion. Discussion: RAI resistance occurs when there is (1) no uptake on post therapy scan, (2) progression of disease and (3) rising thyroglobulin1. Although the metastases appeared iodine avid in this case, anatomical and biochemical response was lacking. These lesions corresponded to FDGPET, reflecting a mixture of well and less well differentiated cell types. The optimum I131 dose to treat metastatic disease remains unclear. Higher doses are used when increased risk is perceived based on clinical and histopathological features2. This dose can range between 3.7 and 7.4Gbq2 but data addressing the optimal therapeutic and safe accumulative dose is lacking. Secondary malignancies have been associated with RAI therapy and are dose dependent3. A meta-analysis has shown a 1.19 relative risk of secondary malignancies in patients receiving treatment for TC4. Tyrosine kinase inhibitors are currently being investigated and used as treatment for iodine refractory TC. However, access to these drugs in Australia is limited and if available, occurs in the setting of clinical trials.

110 Laufer I, Zuckerman SL, Bird JE, Bilsky MH, Lazary A, Quraishi NA, et al. **Predicting Neurologic Recovery after Surgery in Patients with Deficits Secondary to MESCC: Systematic Review**. Spine (Phila Pa 1976) 2016;41 Suppl 20:S224-S30.

**Abstract:** STUDY DESIGN: Systematic literature review and expert survey OBJECTIVE.: The aim of this study was to determine factors associated with neurologic improvement in patients with neurologic deficits secondary to metastatic epidural spinal cord compression (MESCC). Clear understanding of these factors will guide surgical decision-making by helping to elucidate which patients are more likely to benefit from surgery and how surgeons can increase the probability of neurologic and functional restoration.

SUMMARY OF BACKGROUND DATA: Surgical spinal cord decompression has been shown to improve neurologic function in patients with symptomatic MESCC. However, prognostication of neurologic improvement after surgery remains challenging, owing to sparse data and complexity of these patients.

METHODS: PubMed and Embase databases were searched for relevant publications. PRISMA Statement guided publication selection and data reporting. GRADE guidelines were used for evidence quality evaluation and recommendation formulation.

RESULTS: Low-quality evidence supports the use of the duration and severity of neurologic deficit as predictors of neurological recovery in patients with MESCC. Low-quality evidence supports the use of thoracic level of compression and previous irradiation as adverse predictors of neurological recovery. Nearly all of the AOSpine Knowledge Forum Tumor members who responded to the survey agreed that ambulation with assistance represented a successful surgical result and that duration of ambulation loss and the severity of weakness should be considered when trying to predict whether surgery would result in restoration of ambulation.

CONCLUSIONS: Review of literature and expert opinion support the importance of duration of ambulation loss and the severity of neurologic deficit (muscle strength, bladder function) in prediction of neurologic recovery among patients with symptomatic MESCC. Efforts to reduce the duration of ambulation loss and to prevent progression of neurologic deficits should be made to improve the probability of neurologic recovery.

Level of evidence: 2.

111 Jong JM, Oprea-Lager DE, Hooft L, de Klerk JM, Bloemendal HJ, Verheul HM, et al. **Radiopharmaceuticals for Palliation of Bone Pain in Patients with Castration-resistant Prostate Cancer Metastatic to Bone: A Systematic Review**. Eur Urol 2016;70(3):416-26.

**Abstract:** CONTEXT: The majority of patients with castration-resistant prostate cancer develop bone metastatic disease. It is often challenging to optimally palliate malignant bone pain. In case of multifocal pain due to diffuse osteoblastic metastases, treatment with bone-seeking radiopharmaceuticals can be considered.

OBJECTIVE: This systematic review evaluates the efficacy of different bone-seeking radiopharmaceuticals for palliation of malignant bone pain from prostate cancer.

EVIDENCE ACQUISITION: The PubMed (Medline) and Embase databases were searched for publications on 89-strontium-chloride ((89)Sr), 153-samarium-EDTMP ((153)Sm), 186-rhenium-HEDP ((186)Re), 188-rhenium-HEDP ((188)Re), and 223-radium-chloride ((223)Ra). Randomised controlled trials and prospective cohort studies were included. Metastatic bone pain had to be registered as outcome measure for prostate cancer patients separately.

EVIDENCE SYNTHESIS: This review included 36 articles of which 13 randomised trials and 23 prospective studies. Of all trials, 10 studies used (89)Sr, 7 (153)Sm, 12 (186)Re, 2 (188)Re, and 2 (223)Ra; three reported on a combination of different radionuclides. Only a few trials contained a blinding procedure and several studies contained incomplete follow-up or lack of intention-to-treat analysis. It was not possible to calculate a pooled estimate of pain response to treatment with any of the radionuclides because different definitions of pain response were used.

CONCLUSIONS: Overall, pain response percentages greater than 50-60% were seen with each radionuclide. Haematological toxicity was reported in 26 of the 36 studies and more than half of these trials stated no grade 3/4 leukopenia or thrombocytopenia occurred.

PATIENT SUMMARY: In this report we reviewed the efficacy of bone-seeking radionuclides for treating bone pain from metastatic prostate cancer. Overall, treatment with bone-seeking radionuclides resulted in pain responses greater than 50-60%.

112 James N, Pirrie S, Pope A, Barton D, Andronis L, Goranitis I, et al. **TRAPEZE: a randomised controlled trial of the clinical effectiveness and cost-effectiveness of chemotherapy with zoledronic acid, strontium-89, or both, in men with bony metastatic castration-refractory prostate cancer**. Health Technology Assessment (Winchester, England) 2016;20(53):1-288.

**Abstract:** BACKGROUND: Bony metastatic castration-refractory prostate cancer is associated with a poor prognosis and high morbidity. TRAPEZE was a two-by-two factorial randomised controlled trial of zoledronic acid (ZA) and strontium-89 (Sr-89), each combined with docetaxel. All have palliative benefits, are used to control bone symptoms and are used with docetaxel to prolong survival. ZA, approved on the basis of reducing skeletal-related events (SREs), is commonly combined with docetaxel in practice, although evidence of efficacy and cost-effectiveness is lacking. Sr-89, approved for controlling metastatic pain and reducing need for subsequent bone treatments, is generally palliatively used in patients unfit for chemotherapy. Phase II analysis confirmed the safety and feasibility of combining these agents. TRAPEZE aimed to determine the clinical effectiveness and cost-effectiveness of each agent.

METHODS: Patients were randomised to receive six cycles of docetaxel plus prednisolone: alone, with ZA, with a single Sr-89 dose after cycle 6, or with both. Primary outcomes were clinical progression-free survival (CPFS: time to pain progression, SRE or death) and cost-effectiveness. Secondary outcomes were SRE-free interval (SREFI), total SREs, overall survival (OS) and quality of life (QoL). Log-rank test and Cox regression modelling were used to determine clinical effectiveness. Cost-effectiveness was assessed from the NHS perspective and expressed as cost per additional quality-adjusted life-year (QALY). An additional analysis was carried out for ZA to reflect the availability of generic ZA.

Results:

PATIENTS: 757 randomised (median age 68.7 years; Eastern Cooperative Oncology Group scale score 0, 40%; 1, 52%; 2, 8%; prior radiotherapy, 45%); median prostate-specific antigen 143.78ng/ml (interquartile range 50.8-353.9ng/ml). Stratified log-rank analysis of CPFS was statistically non-significant for either agent (Sr-89, p=0.11; ZA, p=0.45). Cox regression analysis adjusted for stratification variables showed CPFS benefit for Sr-89 [hazard ratio (HR) 0.845, 95% confidence interval (CI) 0.72 to 0.99; p=0.036] and confirmed no effect of ZA (p=0.46). ZA showed a significant SREFI effect (HR 0.76; 95% CI 0.63 to 0.93; p=0.008). Neither agent affected OS (Sr-89, p=0.74; ZA, p=0.91), but both increased total cost (vs. no ZA and no Sr-89, respectively); decreased post-trial therapies partly offset costs [net difference: Sr-89 1341; proprietary ZA (Zometa(), East Hanover, NJ, USA) 1319; generic ZA 251]. QoL was maintained in all trial arms; Sr-89 (0.08 additional QALYs) and ZA (0.03 additional QALYs) showed slight improvements. The resulting incremental cost-effectiveness ratio (ICER) for Sr-89 was 16,590, with 42,047 per QALY for Zometa and 8005 per QALY for generic ZA.

CONCLUSION: Strontium-89 improved CPFS, but not OS. ZA did not improve CPFS or OS but significantly improved SREFI, mostly post progression, suggesting a role as post-chemotherapy maintenance therapy. QoL was well maintained in all treatment arms, with differing patterns of care resulting from the effects of Sr-89 on time to progression and ZA on SREFI and total SREs. The addition of Sr-89 resulted in additional cost and a small positive increase in QALYs, with an ICER below the 20,000 ceiling per QALY. The additional costs and small positive QALY changes in favour of ZA resulted in ICERs of 42,047 (Zometa) and 8005 for the generic alternative; thus, generic ZA represents a cost-effective option. Additional analyses on the basis of data from the Hospital Episode Statistics data set would allow corroborating the findings of this study. Further research into the use of ZA (and other bone-targeting therapies) with newer prostate cancer therapies would be desirable.

STUDY REGISTRATION: Current Controlled Trials ISRCTN12808747.

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113 James D, Hillery R, Freeman L, Kumari A, Kearney N. **Radium-223: Treating metastatic castration-resistant prostate cancer**. Intern Med J 2016;46 (Supplement 1):30-1.

**Abstract:** Background: Prostate cancer is the second most common cause of cancer related deaths in Australia. An increasing number of patients develop resistive mutations to treatments resulting in their disease advancing to metastatic castration-resistant prostate cancer (mCRPC). 223Radium dichloride is a newly developed radionuclide treatment for mCRPC. It is an alphaemitting radiopharmaceutical with a short-range and high-energy output. Mimicking calcium it forms complexes with hydroxyapatite crystals, specifically targeting bone metastases. Aim: The aim of the poster is to assess the advantages and disadvantages of 223Radium-dichloride in the treatment of metastatic castration-resistant prostate cancer. Methods: A literature search was conducted to investigate the use of 223Radium-dichloride in the treatment metastatic castration-resistant prostate disease. Results: Early clinical trials demonstrated 223Ra was well tolerated with no dose-limiting toxic effects. Subsequent randomized control trials in symptomatic prostate cancer patients resulted in a 30% reduction in risk of death, reduced pain and improved quality of life among 223Ra patients vs. placebo. Ongoing studies of 223Ra treatment in the ALSYMPCA trial have demonstrated low myelosuppression with no further development of bone metastases. Conclusion: 223Radium dichloride treatment in patients with mCRPC has been successful in improving both patient survival time and quality of life. Future studies are set to explore the efficacy of 223Ra in treating other cancers, such as breast and osteosarcoma, associated with bone metastases.

114 Hendriks LE, Hermans BC, van den Beuken-van Everdingen MH, Hochstenbag MM, Dingemans AM. **Effect of Bisphosphonates, Denosumab, and Radioisotopes on Bone Pain and Quality of Life in Patients with Non-Small Cell Lung Cancer and Bone Metastases: A Systematic Review**. Journal of Thoracic Oncology: Official Publication of the International Association for the Study of Lung Cancer 2016;11(2):155-73.

**Abstract:** Bone metastases are common in patients with non-small cell lung cancer (NSCLC), often causing pain and a decrease in quality of life (QoL). The effect of bone-targeted agents is evaluated by reduction in skeletal-related events in which neither pain nor QoL are included. Radioisotopes can be administered for more diffuse bone pain that is not eligible for palliative radiotherapy. The evidence that bone-targeted agents relieve pain or improve QoL is not solid. We performed a systematic review of the effect of bone-targeted agents on pain and QoL in patients with NSCLC. Our systematic literature search included original articles or abstracts reporting on bisphosphonates, denosumab, or radioisotopes or combinations thereof in patients with bone metastases (>=5 patients with NSCLC), with pain, QoL, or both serving as the primary or secondary end point. Of the twenty-five eligible studies, 13 examined bisphosphonates (one also examined denosumab) and 12 dealt with radioisotopes. None of the randomized studies on bisphosphonates or denosumab evaluated pain and QoL as the primary end point. In the single-arm studies of bisphosphonates a decrease in pain or analgesic consumption was found for 38% to 77% of patients. QoL was included in five of 13 studies, but improvement was found in only two. No high-level evidence that bisphosphonates or denosumab reduce pain or improve QoL was found. Although the data are limited, radioisotopes seem to reduce pain with a rapid onset of action and duration of response of 1 to 3 months. The evidence that bisphosphonates or denosumab reduce or prevent pain in patients with NSCLC and bone metastases or that they have an influence on QoL is very weak. Radioisotopes can be used to reduce diffuse pain, although there is no high-level evidence supporting such use.

115 Health Quality O. **Vertebral Augmentation Involving Vertebroplasty or Kyphoplasty for Cancer-Related Vertebral Compression Fractures: A Systematic Review**. Ont Health Technol Assess Ser 2016;16(11):1-202.

**Abstract:** BACKGROUND: Cancers that metastasize to the spine and primary cancers such as multiple myeloma can result in vertebral compression fractures or instability. Conservative strategies, including bed rest, bracing, and analgesic use, can be ineffective, resulting in continued pain and progressive functional disability limiting mobility and self-care. Surgery is not usually an option for cancer patients in advanced disease states because of their poor medical health or functional status and limited life expectancy. The objectives of this review were to evaluate the effectiveness and safety of percutaneous image-guided vertebral augmentation techniques, vertebroplasty and kyphoplasty, for palliation of cancer-related vertebral compression fractures.

METHODS: We performed a systematic literature search for studies on vertebral augmentation of cancer-related vertebral compression fractures published from January 1, 2000, to October 2014; abstracts were screened by a single reviewer. For those studies meeting the eligibility criteria, full-text articles were obtained. Owing to the heterogeneity of the clinical reports, we performed a narrative synthesis based on an analytical framework constructed for the type of cancer-related vertebral fractures and the diversity of the vertebral augmentation interventions.

RESULTS: The evidence review identified 3,391 citations, of which 111 clinical reports (4,235 patients) evaluated the effectiveness of vertebroplasty (78 reports, 2,545 patients) or kyphoplasty (33 reports, 1,690 patients) for patients with mixed primary spinal metastatic cancers, multiple myeloma, or hemangiomas. Overall the mean pain intensity scores often reported within 48 hours of vertebral augmentation (kyphoplasty or vertebroplasty), were significantly reduced. Analgesic use, although variably reported, usually involved parallel decreases, particularly in opioids, and mean pain-related disability scores were also significantly improved. In a randomized controlled trial comparing kyphoplasty with usual care, improvements in pain scores, pain-related disability, and health-related quality of life were significantly better in the kyphoplasty group than in the usual care group. Bone cement leakage, mostly asymptomatic, was commonly reported after vertebroplasty and kyphoplasty. Major adverse events, however, were uncommon.

CONCLUSIONS: Both vertebroplasty and kyphoplasty significantly and rapidly reduced pain intensity in cancer patients with vertebral compression fractures. The procedures also significantly decreased the need for opioid pain medication, and functional disabilities related to back and neck pain. Pain palliative improvements and low complication rates were consistent across the various cancer populations and vertebral fractures that were investigated.

116 Haugen BR, Alexander EK, Bible KC, Doherty GM, Mandel SJ, Nikiforov YE, et al. **2015 American Thyroid Association Management Guidelines for Adult Patients with Thyroid Nodules and Differentiated Thyroid Cancer: The American Thyroid Association Guidelines Task Force on Thyroid Nodules and Differentiated Thyroid Cancer**. Thyroid 2016;26(1):1-133.

**Abstract:** Background: Thyroid nodules are a common clinical problem, and differentiated thyroid cancer is becoming increasingly prevalent. Since the American Thyroid Association's (ATA's) guidelines for the management of these disorders were revised in 2009, significant scientific advances have occurred in the field. The aim of these guidelines is to inform clinicians, patients, researchers, and health policy makers on published evidence relating to the diagnosis and management of thyroid nodules and differentiated thyroid cancer. Methods: The specific clinical questions addressed in these guidelines were based on prior versions of the guidelines, stakeholder input, and input of task force members. Task force panel members were educated on knowledge synthesis methods, including electronic database searching, review and selection of relevant citations, and critical appraisal of selected studies. Published English language articles on adults were eligible for inclusion. The American College of Physicians Guideline Grading System was used for critical appraisal of evidence and grading strength of recommendations for therapeutic interventions. We developed a similarly formatted system to appraise the quality of such studies and resultant recommendations. The guideline panel had complete editorial independence from the ATA. Competing interests of guideline task force members were regularly updated, managed, and communicated to the ATA and task force members. Results: The revised guidelines for the management of thyroid nodules include recommendations regarding initial evaluation, clinical and ultrasound criteria for fine-needle aspiration biopsy, interpretation of fine-needle aspiration biopsy results, use of molecular markers, and management of benign thyroid nodules. Recommendations regarding the initial management of thyroid cancer include those relating to screening for thyroid cancer, staging and risk assessment, surgical management, radioiodine remnant ablation and therapy, and thyrotropin suppression therapy using levothyroxine. Recommendations related to long-term management of differentiated thyroid cancer include those related to surveillance for recurrent disease using imaging and serum thyroglobulin, thyroid hormone therapy, management of recurrent and metastatic disease, consideration for clinical trials and targeted therapy, as well as directions for future research. Conclusions: We have developed evidence-based recommendations to inform clinical decision-making in the management of thyroid nodules and differentiated thyroid cancer. They represent, in our opinion, contemporary optimal care for patients with these disorders. © Copyright 2016, Mary Ann Liebert, Inc. 2016.

117 Hashmi AH, Guckenberger M, Kersh R, Gerszten PC, Mantel F, Grills IS, et al. **Reirradiation stereotactic body radiation therapy (SBRT) for spinal metastases: A multi-institutional outcome analysis**. International Journal of Radiation Oncology 2016;96 (2 Supplement 1):S123-S4.

**Abstract:** Purpose/Objective(s): We report the largest multi-institutional pooled analysis specific to imaging-based local control in patients previously radiated with conventional external beam radiation (cEBRT) and salvaged with re-irradiation spine stereotactic body radiotherapy (SBRT). Materials/Methods: A retrospective review of 247 patients from seven different institutions was performed. Overall survival (OS) was based on per patient treated with SBRT, while local control was based on the spinal target volume treated, using the Kaplan Meier method. Local control was defined as imaging based progression within the SBRT target volume. Equivalent dose in 2 Gy fractions (EQD2) were calculated for the cEBRT and SBRT course and summed to yield the cumulative dose with an a/s of 10 for tumor and 2 for both spinal cord and cauda equina. Results: The median total dose and number of fractions of the initial cEBRT was 30 Gy and 10, respectively. The median SBRT total dose and number of fractions was 18 Gy and 1, respectively. Sixty percent were treated with single fraction SBRT (median, 18 Gy and EQD2/10 = 36.8 Gy), and 40% with multiple fraction SBRT (median, 24 Gy in 3 fractions and EQD2/10 = 36 Gy). The median time interval from cEBRT to reirradiation SBRT was 13.5 months and median patient follow up was 8.1 months. OS at 6 and 12 months was 64% and 48%, respectively. Thirteen percent of patients suffered a local failure, and the local control rate at 6 months and 12 months was 93% and 83%, respectively. Multivariate analysis identified (Karnofsky performance Status) KPS <70 as a significant prognostic factor for worse OS, and single fractionated SBRT as a significant predictive factor for better local control. There were no cases of radiation myelopathy, and the vertebral compression fracture rate was 4.5%. Conclusion: Re-irradiation spine SBRT is effective in yielding imagingbased local control with a clinically acceptable safety profile. A randomized trial would be required to determine the optimal fractionation.

118 Harris SR. **Differentiating the Causes of Spontaneous Rib Fracture After Breast Cancer**. Clin Breast Cancer 2016;16(6):431-6.

**Abstract:** Spontaneous rib fracture after treatment for primary breast cancer is not uncommon. Although metastatic disease accounts for about 30% of spontaneous rib fractures and should constitute the first line of diagnostic investigation, other possible contributors include primary osteoporosis or secondary osteoporosis resulting from cancer treatments. Chemotherapy-induced menopause, aromatase inhibitors, radiation therapy, and long-term bisphosphonate use can all contribute to bone fragility, including spontaneous rib fractures in the latter 3. Drawing on recent breast cancer practice guidelines as well as population-based studies of fracture risk for women with a history of breast cancer and systematic reviews, this Perspective will provide an update on recent developments in understanding how to differentiate the possible reasons for non-traumatic rib fracture in women treated for breast cancer. In addition to describing the various possible causes of spontaneous rib fracture, the recommended medical and imaging procedures for differentiating among the potential causes will be presented.

119 Harries M, Malvehy J, Lebbe C, Heron L, Amelio J, Szabo Z, et al. **Treatment patterns of advanced malignant melanoma (stage III-IV) - A review of current standards in Europe**. Eur J Cancer 2016;60:179-89.

**Abstract:** Aims and background With the recent emergence of immunotherapies and novel targeted treatments for advanced and metastatic melanoma such as selective B-Raf inhibitors and checkpoint inhibitors, the treatment landscape in Europe has changed considerably. The aim of this review was to provide an overview of current treatment pathways in Europe for the treatment of advanced melanoma, unresectable stage III-IV. Methods A literature search of four databases was conducted to identify publications reporting on the treatment patterns of advanced and metastatic melanoma (stage III-IV) in European populations. Results Seven full-text publications and two conference abstracts reported on observational studies of melanoma treatment practices in France, Italy and the United Kingdom. Treatment patterns were identified for two time periods: 2005-2009 and 2011-2012. Common treatments reported for both periods included chemotherapy with dacarbazine, fotemustine or temozolomide. The main differences between the two periods were the introduction and prescription of immunotherapy ipilimumab and targeted therapy vemurafenib between 2011 and 2012. Across the three countries studied, the types of treatments prescribed between 2005 and 2009 were relatively similar, however, with noticeable differences in the frequency and priority of administration. Conclusion Treatment practices for advanced melanoma vary markedly across different European countries and continue to evolve with the introduction of new therapies. The results of this review highlight a considerable evidence gap with regards to recent treatment patterns for advanced melanoma in Europe, especially post-2011 after the introduction of novel therapeutic agents, and more recently with the introduction of programmed cell death 1 inhibitors. Copyright © 2016 Elsevier Ltd.

120 Guerra Liberal FDC, Tavares AAS, Tavares J. **Palliative treatment of metastatic bone pain with radiopharmaceuticals: A perspective beyond Strontium-89 and Samarium-153**. Appl Radiat Isot 2016;110:87-99.

**Abstract:** PURPOSE: The present review article aims to provide an overview of the available radionuclides for palliative treatment of bone metastases beyond (89)Sr and (153)Sm. In addition, it aims to review and summarize the clinical outcomes associated with the palliative treatment of bone metastases using different radiopharmaceuticals.

MATERIALS AND METHODS: A literature search was conducted on Science Direct and PubMed databases (1990 - 2015). The following search terms were combined in order to obtain relevant results: "bone", "metastases", "palliative", "care", "therapy", "treatment", "radiotherapy", "review", "radiopharmaceutical", "phosphorus-32", "strontium-89", "yttrium-90", "tin-117m", "samarium-153", "holmium-166", "thulium-170", "lutetium-177", "rhenium-186", "rhenium-188" and "radium-223". Studies were included if they provided information regarding the clinical outcomes.

RESULTS AND CONCLUSIONS: A comparative analysis of the measured therapeutic response of different radiopharmaceuticals, based on previously published data, suggests that there is a lack of substantial differences in palliative efficacy among radiopharmaceuticals. However, when the comparative analysis adds factors such as patient's life expectancy, radionuclides' physical characteristics (e.g. tissue penetration range and half-life) and health economics to guide the rational selection of a radiopharmaceutical for palliative treatment of bone metastases, (177)Lu and (188)Re-labeled radiopharmaceuticals appear to be the most suitable radiopharmaceuticals for treatment of small and medium/large size bone lesions, respectively.

121 Guan J, Yuan ZC, Liu B. **Research progress of <sup>125</sup>I seeds implantation for metastatic spinal tumors. [Chinese]**. Chinese Journal of Cancer Prevention and Treatment 2016;23(20):1392-7.

**Abstract:** OBJECTIVE: The primary therapy for spinal metastases patients is to relieve the pain, improve quality of life and the prognosis. Brachytherapy, especially <sup>125</sup>I seeds for treating spinal metastases showed a greater advantage. This paper summarized the recent researches of the <sup>125</sup>I Particle Therapy in the mechanisms of spinal metastases, the impact on the human body and the surrounding tissues and the related clinical applications for the treatment of spinal metastases. METHODS: Relevant articles were searched with "<sup>125</sup>I seed, brachytherapy, molecular biology, spinal metastases, et al" as keywords in pubmed, CNKI, Wanfang, VIP, CBD database from 2000 to 2016. Totally 39 papers were selected and analyzed according to the inclusion criteria as follows: the molecular biology mechanisms of <sup>125</sup>I seeds for treating cancer, the effect of <sup>125</sup>I seeds implantation on body and surrounding tissue, the <sup>125</sup>I seeds implantation for treating spinal metastases'efficacy and prognosis, and the exclusion criteria are as follows: the experimental design is unreasonable, non-randomized controlled trials, the total number of samples or the total number of cases is less than 15 cases. RESULTS: <sup>125</sup>I seeds brachytherapy can effectively kill tumor cells, the organ function of vital organs and spinal cord nerve function had no significant effect, and can effectively relieve neuropathic pain. <sup>125</sup>I seeds in the treatment of spinal metastases, a higher local control rate of the tumor, pain relief effect is obvious, can relieve spinal cord compression symptoms; <sup>125</sup>I seeds implantation combined with vertebroplasty in the treatment of spinal metastases can also be Further increase the rate of pain relief and restore the stability of the spine, a superposition effect and complementary advantages. Spinal metastases osteolytic destruction involving the small joints leading to spinal instability and the emergence of more severe symptoms of spinal cord compression in patients with <sup>125</sup>I seeds can be combined with surgical treatment, is a minimally invasive, safe, effective, concurrent Low incidence of disease treatment, effective relief of pain, improve spinal nerve function, local tumor control, reconstruction of spinal stability.CONCLUSIONS: Compared with conventional External radiation therapy, <sup>125</sup>I seeds brachytherapy for the spinal metastases provides a new way for treatment. It has advantage, but still needs further researches in order to get better treatment effect. Copyright © 2016, Editorial Board of Chinese Journal of Cancer Prevention and Treatment. All right reserved.

122 Groenen KHJ, Pouw MH, Hannink G, Hosman AJF, Van der Linden YM, Verdonschot N, et al. **The effect of radiotherapy, and radiotherapy combined with bisphosphonates or RANK ligand inhibitors on bone quality in bone metastases. a systematic review**. Journal of Orthopaedic Research Conference 2016;34(Supplement 1).

**Abstract:** INTRODUCTION: Without treatment, patients with bone metastases may suffer from debilitating skeletal complications such as pathological fractures or, when vertebrae are affected, neurological complaints such as spinal cord compression [1]. The clinical experience of many clinicians is that radiotherapy (RT) strengthens bone due to re-calcification. However, scientific data underlining this stabilizing effect are scarce. Bisphosphonates (BPs) and RANKL inhibitors have already been shown to play a role in improving bone strength [2, 3]. The effect of combining RT, BPs, and RANKL inhibitors on bone quality is, however, unknown. As these treatments have different mechanisms of action, these treatment combinations might prevent pathological fractures and possible accompanying neurological problems more effectively. Therefore, the aims of this systematic review were to assess the effects of (1) RT, (2) RT combined with BPs, and (3) RT combined with RANKL inhibitors, on bone quality and bone strength parameters in bone metastases originating from solid tumors. METHODS: Pubmed, EMBASE and the Cochrane Library were searched for articles concerning the effect of RT or RT combined with either BPs or RANKL inhibitors on bone mineral density, bone quality and bone strength in patients with solid bone metastases. Any type of study design and type and dose of RT, BPs and RANKL inhibitors were allowed. Only articles in English, German, or Dutch were included. Outcome measures related to bone quality and bone strength were extracted and subsequently divided in five principal outcome categories: 1) Radiologic response (any qualitative description of re-calcification), 2) bone density (any quantitative description of bone density), 3) micro-architecture, 4) bone strength, and 5) pathological fractures. The Quality Assessment Tool for Quantitative Studies (QATQS) [4] was used to assess methodological quality. Data were analyzed qualitatively. RESULTS: The search strategy retrieved 2782 unique records. Thirty articles (3 animal studies, 27 patient studies) were included in this systematic review. Methodological quality was rated as 'strong', 'moderate', and 'weak' in four, 16 and 10 of the included studies, respectively. Animal studies: Animal studies showed that RT had similar effects on bone density, micro-architecture, and strength as receiving a negative control (no treatment), whereas adding BPs to RT restored bone quality and strength to those of healthy bone. Correlations between changes in bone mineral density, bone quality and strength were not reported. Patient studies: Radiotherapy - Studies reporting on radiological response rates following RT used a wide range of definitions. Response rates ranged from 25 to 80%. Studies reporting on bone density after RT showed the same trend: bone density increased after RT. It was unclear whether multi fraction RT had a positive effect on bone density increase compared to single fraction RT. Pathological fracture rates after primary RT ranged from 0 to about 15%. Whereas some studies reported more pathological fractures after single fraction RT than after multi fraction RT, others did not confirm this effect. Only one study assessed both bone density and fracture rate and demonstrated that the density change of patients with a pathological fracture was lower than those of patients without a pathological fracture. Radiotherapy combined with bisphosphonates - One study reported on response rate and showed that the response rate after RT was significantly higher in patients receiving both RT and BPs compared to those receiving only RT. Bone density increased after treatment with RT and BPs, which was significant from about 3 months onwards. Studies comparing RT with RT + BPs found similar fracture rates in both treatment groups. One study assessed both radiological response and fracture rate, but did not report correlations between both outcome measures. Radiotherapy combined with RANKL inhibitors - None of the included studies addressed the effect of RT combined with RANKL inhibitors on b ne density, bone micro-architecture, bone strength or related outcome parameters. DISCUSSION: In clinical practice, patients are often treated with a combination of local RT and systemic treatments (e.g. chemotherapy or hormonal therapy, BPs and RANKL inhibitors). In this systematic review we only focused on BPs and RANKL inhibitors as treatments additional to RT, as these treatments intend to improve the bone mass. In contrast, other anticancer treatments are primarily used to attack tumor tissue and decrease lesion size. There was a lot of variation between studies in terms of defining and quantifying radiological response and bone density. The use of different methods and definitions complicated comparison of results between studies and might have resulted in the inability to identify changes in bone quality and fracture rate after radiotherapy. Therefore, it would be beneficial if such outcome measures would be standardized for use in future studies. All studies on bone density after RT showed the same trend: bone density increased after treatment with RT. However, as these studies lacked a control group (no treatment), it cannot be concluded that the increase in bone density was due to the RT. In addition, co-medication, including BPs, was allowed in most patient studies. As BPs are known to increase bone density, the observed increase in bone density could also be caused by the BPs. It was unclear whether multi fraction RT resulted in less pathological fractures than single fraction RT. However, most studies reporting on pathological fractures were not designed to measure fracture rates. To be able to assess the actual effect of RT on fracture risk, studies should be designed with fracture rate as the primary outcome measure. In addition, all factors affecting the fracture risk, such as lesion size and pre-existing impending fractures, should be taken into account in the study design. From clinical experience it is believed that RT strengthens bones due to re-calcification. No correlations between changes in bone density, bone micro-architecture, and bone strength were reported in the animal studies and barely in the patient studies. Without correlating these outcome measures, no conclusions can be drawn on whether it is the process of re-calcification that leads to improved bone strength or not. To understand the role that RT possibly has in stabilizing metastatic bone lesions, future studies should, therefore, determine both bone quality and bone strength or fracture rate within the same animal or patient. Despite the clinical experience that radiotherapy is an effective treatment for bone metastases, based on this review it was concluded that there was no sufficient evidence that radiotherapy had a positive effect on bone quality and fracture risk. In addition, animal studies showed that the addition of BPs to RT restored bone quality and bone strength to that of healthy bone, whereas this is not yet proven in patients. Furthermore, there were neither animal nor patient studies addressing the effect of RANKL inhibitors as an adjunct to RT on bone quality and bone strength. SIGNIFICANCE: Preventing pathological fractures and possible accompanying neurological problems is very important in patients suffering from bone metastases. This systematic review thoroughly analyses the currently available studies on the potentially stabilizing effect of RT, and RT combined with BPs or RANKL inhibitor in bone metastases originating from solid bone metastases and, therefore, aids in the clinical treatment decision making process.

123 Groenen KH, Pouw MH, Hannink G, Hosman AJ, van der Linden YM, Verdonschot N, et al. **The effect of radiotherapy, and radiotherapy combined with bisphosphonates or RANK ligand inhibitors on bone quality in bone metastases. A systematic review**. Radiother Oncol 2016;119(2):194-201.

**Abstract:** PURPOSE: The role of radiotherapy in stabilizing metastatic bones is unclear. This systematic review assessed the effects of (1) radiotherapy, (2) radiotherapy combined with bisphosphonates, and (3) radiotherapy combined with RANK ligand (RANKL) inhibitors on bone quality and bone strength in bone metastases originating from solid tumors.

METHODS: Pubmed, EMBASE and the Cochrane Library were searched. Any type of study design and type and dose of radiotherapy, bisphosphonates and RANKL inhibitors were allowed.

RESULTS: 39 articles were identified. Animal studies showed that radiotherapy had similar effects on bone quality and strength as receiving no treatment, whereas adding bisphosphonates to radiotherapy restored bone quality and strength. In patient studies, bone density increased after radiotherapy and radiotherapy combined with bisphosphonates. However, due to the often non-optimal study design and study quality, it was unclear whether this increase could be attributed to these treatments. There was insufficient evidence to assess the additional effect of bisphosphonates or RANKL inhibitors.

CONCLUSION: Despite the clinical experience that radiotherapy is an effective treatment for bone metastases, there was no sufficient evidence for a positive effect on bone quality and fracture risk. Animal studies showed that adding bisphosphonates to radiotherapy restored bone quality and strength, whereas this was not proven in patients. There were no studies addressing the adjunct effect of RANKL inhibitors to radiotherapy. Although associated with several methodological, practical and ethical challenges, randomized controlled trials are needed.

124 Goodwin CR, Yanamadala V, Ruiz-Valls A, Abu-Bonsrah N, Shankar G, Sankey EW, et al. **A Systematic Review of Metastatic Hepatocellular Carcinoma to the Spine**. World Neurosurg 2016;91:510-7.e4.

**Abstract:** BACKGROUND: Hepatocellular carcinoma (HCC) frequently metastasizes to the spine. The impact of medical and/or surgical intervention on overall survival has been examined in a limited number of clinical studies, and herein we systematically review these data.

METHODS: We performed a literature review using PubMed, Embase, CINAHL, and Web of Science to identify articles that reported survival, clinical outcomes, and/or prognostic factors associated with patients diagnosed with spinal metastases. The methodologic quality of each review was assessed using the Preferred Reporting Items for Systematic Reviews and Meta-Analyses tool.

RESULTS: There were 26 articles (152 patients) that met the inclusion criteria and were treated with either surgery, radiotherapy, chemotherapy, and/or observation. There were 3 retrospective cohort studies, 17 case reports, 5 case series, and 1 longitudinal observational study. Of the patients with known overall survival after diagnosis of spinal metastasis, survival at 3 months, 6 months, 1 year, 2 years, and 5 years was 95.2%, 83.0%, 28.6%, 2.0%, and 1.4%, respectively. The median survival after diagnosis of the metastasis was 0.7 months in the patients who received no treatment, 7 months in the patients treated with surgical intervention alone, 6 months for patients who received chemotherapy and/or radiation, and 13.5 months in the patients treated with a combination of surgery and medical management. All other clinical or prognostic parameters were of low or insufficient strength.

CONCLUSIONS: Patients diagnosed with HCC spinal metastasis have a 10.6-month overall survival. Further analysis of patients in prospective controlled trials will be essential to the development of treatment algorithms for these patients in the future.

125 Goodwin CR, Sankey EW, Liu A, Elder BD, Kosztowski T, Lo SF, et al. **A systematic review of clinical outcomes for patients diagnosed with skin cancer spinal metastases**. Journal of Neurosurgery Spine 2016;24(5):837-49.

**Abstract:** OBJECT Surgical procedures and/or adjuvant therapies are effective modalities for the treatment of symptomatic spinal metastases. However, clinical results specific to the skin cancer spinal metastasis cohort are generally lacking. The purpose of this study was to systematically review the literature for treatments, clinical outcomes, and survival following the diagnosis of a skin cancer spinal metastasis and evaluate prognostic factors in the context of spinal skin cancer metastases stratified by tumor subtype. METHODS The authors performed a literature review using PubMed, Embase, CINAHL, and Web of Science to identify articles since 1950 that reported survival, clinical outcomes, and/or prognostic factors for the skin cancer patient population with spinal metastases. The methodological quality of reviews was assessed using the PRISMA (Preferred Reporting Items for Systematic Reviews and Meta-Analyses) tool. RESULTS Sixty-five studies met the preset criteria and were included in the analysis. Of these studies, a total of 25, 40, 25, and 12 studies included patients who underwent some form of surgery, radiotherapy, chemotherapy, or observation alone, respectively. Sixty-three of the 65 included studies were retrospective in nature (Class of Evidence [CoE] IV), and the 2 prospective studies were CoE II. Based on the studies analyzed, the median overall survival for a patient with a spinal metastasis from a primary skin malignancy is 4.0 months; survival by tumor subtype is 12.5 months for patients with basal cell carcinoma (BCC), 4.0 months for those with melanoma, 4.0 months for those with squamous cell carcinoma, 3.0 months for those with pilomatrix carcinoma, and 1.5 months for those with Merkel cell carcinoma (p < 0.0001). The overall percentage of known continued disease progression after spine metastasis diagnosis was 40.1% (n = 244/608, range 25.0%-88.9%), the rate of known recurrence of the primary skin cancer lesion was 3.5% (n = 21/608, range 0.2%-100.0%), and the rate of known spine metastasis recurrence despite treatment for all skin malignancies was 2.8% (n = 17/608, range 0.0%-33.3%). Age greater than 65 years, sacral spinal involvement, presence of a neurological deficit, and nonambulatory status were associated with decreased survival in patients diagnosed with a primary skin cancer spinal metastasis. All other clinical or prognostic parameters were of low or insufficient strength. CONCLUSIONS Patients diagnosed with a primary skin cancer metastasis to the spine have poor overall survival with the exception of those with BCC. The median duration of survival for patients who received surgical intervention alone, medical management (chemotherapy and/or radiation) alone, or the combination of therapies was similar across interventions. Age, spinal region, and neurological status may be associated with poor survival following surgery.

126 Goodwin CR, Abu-Bonsrah N, Boone C, Ruiz-Valls A, Sankey EW, Sarabia-Estrada R, et al. **Non-hepatocellular carcinoma spinal metastases**. J Clin Neurosci 2016;27:22-7.

**Abstract:** Metastases to the spine from non-hepatocellular carcinomas, such as cholangiocarcinoma and angiosarcoma, occur rarely. With improvements in oncologic care, the number of patients diagnosed with metastatic cancer is expected to increase. We performed a systematic review of the literature to assess the clinical presentation, treatment, outcome and survival of patients diagnosed with non-hepatocellular carcinoma spinal metastasis using PubMed, Embase, CINAHL, Cochrane Library and Web of Science. We identified 19 cases of spinal metastases from non-hepatocellular carcinomas that fit our pre-specified criteria. The mean age at presentation was 62.3 years and cholangiocarcinoma was the most common subtype. Patients frequently presented with pain, weakness or paraparesis and at the time of diagnosis, most of them had multi-level involvement of the spine. A majority of patients with spinal metastasis were treated either with radiation or chemotherapy or received no treatment. A minority of the reports included information on survival, which revealed a median survival of 1.5 months following diagnosis of the spinal metastasis. Although there is a paucity of published literature on non-hepatocellular carcinoma spinal metastasis, this systematic review provides descriptive clinical characteristics of these patients. Copyright © 2015 Elsevier Ltd.

127 Gendi K, Hennessy D, Heiner J. **The burden of metastatic disease of the femur on the Medicare system**. Springerplus 2016;5(1):1916.

**Abstract:** BACKGROUND: In the United States, over 1,650,000 new cases of cancer are being diagnosed yearly with almost 50 % of them being the top five bone-seeking cancers. Since cancer risk increases with age, this suggests that orthopedic oncology services may be a strain on the Medicare system. The femur is the most common site of long bone metastases. Prophylactic fixation techniques prevent pathologic fractures, reduce morbidities, and enhance the quality of life of patients with femoral metastases. This study aims to assess the rate of metastatic disease to the skeleton and evaluate the use and financial burden of femoral prophylactic fixation techniques on the Medicare system.

QUESTIONS/PURPOSES: (1) In the Medicare population, has the number of skeletal metastases increased? (2) In the Medicare population, has the use of prophylactic fixation techniques increased? (3) How has the financial burden of prophylactic fixation changed over the study period?

METHODS: The Medicare database was searched between 2005 and 2014 with the assistance of PearlDiver Technologies Inc. and the RBRVS DataManager Online from the American Medical Association. Searches were completed by using International Classification of Disease-9 (ICD-9) and current procedural terminology (CPT) codes for secondary malignant neoplasms and prophylactic fixation techniques. Facility charges, Medicare reimbursement and length of hospital stay were extracted from the Medicare database. Simple linear regression was performed to test the significance of yearly changes and the coefficient of determination was used to assess the strength of the correlation.

RESULTS: (1) In the Medicare population, has the number of skeletal metastases increased? While the number of Medicare patients with skeletal metastases has increased from 132,452 in 2005 to 155,819 in 2012 (p = 0.01, r<sup>2</sup> = 0.72), the prevalence of skeletal metastases in this population remained constant at 30.66 cases per 10,000 Medicare patients in 2012 (p = 0.56, r<sup>2</sup> = 0.06). (2) In the Medicare population, has the use of prophylactic fixation techniques increased? The number of prophylactic fixation techniques has not increased from 2005 to 2014 (p = 0.68, r<sup>2</sup> = 0.02); however, the rate of prophylactic fixation among those diagnosed with skeletal metastases has significantly decreased from 94.6 per 10,000 in 2005 to 82.72 per 10,000 in 2012 (p = 0.006, r<sup>2</sup> = 0.74). (3) How has the financial burden of prophylactic fixation changed over the study period? Both total and average hospital charges increased after adjusting for inflation in the total Medicare population; however, only the average Medicare reimbursement changed to reflect this. The total amount Medicare spent on prophylactic fixation techniques in 2012 was $20,245,957 after adjusting to 2014. Despite the increase in hospital charges and average Medicare reimbursement, the average length of hospital stay in the total Medicare population showed a significant decreased trend-down from 7.51 days in 2005 to 5.86 days in 2012 (p = 0.02, r<sup>2</sup> = 0.81).

CONCLUSIONS: Although the prevalence of metastatic disease to the skeleton remained stable between 2005 and 2012 in the Medicare population, prophylactic femoral fixation techniques declined in elderly adults between 2005 and 2014. This most likely signifies an increase in other treatment modalities that can prevent pathologic fractures such as prophylactic hemiarthroplasty, bisphosphonates, and/or radiation therapy.

LEVEL OF EVIDENCE: Level IV, Cross-sectional Study.

128 Garbe C, Peris K, Hauschild A, Saiag P, Middleton M, Bastholt L, et al. **Diagnosis and treatment of melanoma. European consensus-based interdisciplinary guideline - Update 2016**. Eur J Cancer 2016;63:201-17.

**Abstract:** Cutaneous melanoma (CM) is potentially the most dangerous form of skin tumour and causes 90% of skin cancer mortality. A unique collaboration of multi-disciplinary experts from the European Dermatology Forum, the European Association of Dermato-Oncology and the European Organisation of Research and Treatment of Cancer was formed to make recommendations on CM diagnosis and treatment, based on systematic literature reviews and the experts' experience. Diagnosis is made clinically using dermoscopy and staging is based upon the AJCC system. CMs are excised with 1-2 cm safety margins. Sentinel lymph node dissection is routinely offered as a staging procedure in patients with tumours >1 mm in thickness, although there is as yet no clear survival benefit for this approach. Interferon-alpha treatment may be offered to patients with stage II and III melanoma as an adjuvant therapy, as this treatment increases at least the disease-free survival and less clear the overall survival (OS) time. The treatment is however associated with significant toxicity. In distant metastasis, all options of surgical therapy have to be considered thoroughly. In the absence of surgical options, systemic treatment is indicated. For first-line treatment particularly in BRAF wild-type patients, immunotherapy with PD-1 antibodies alone or in combination with CTLA-4 antibodies should be considered. BRAF inhibitors like dabrafenib and vemurafenib in combination with the MEK inhibitors trametinib and cobimetinib for BRAF mutated patients should be offered as first or second line treatment. Therapeutic decisions in stage IV patients should be primarily made by an interdisciplinary oncology team ('Tumour Board'). Copyright © 2016 Elsevier Ltd. All rights reserved.

129 De la Garza-Ramos R, Benvenutti-Regato M, Caro-Osorio E. **Vertebroplasty and kyphoplasty for cervical spine metastases: a systematic review and meta-analysis**. Int J Spine Surg 2016;10:7.

**Abstract:** BACKGROUND: Vertebroplasty (VP) and kyphoplasty (KP) are two minimally invasive techniques used to relieve pain and restore stability in metastatic spinal disease. However, most of these procedures are performed in the thoracolumbar spine, and there is limited data on outcomes after VP/KP for cervical metastases. The purpose of this article is to evaluate the safety and efficacy of VP and KP for treating pain in patients with cervical spine metastases.

METHODS: A systematic review of the literature was conducted using the PubMed and Medline databases. Only studies that reported five or more patients treated with VP/KP in the cervical spine were included. Levels of evidence and grades of recommendation were established based on the Oxford Centre for Evidence-Based Medicine guidelines. Data was pooled to perform a meta-analysis for pain relief and complication rates.

RESULTS: Six studies (all level 4 studies) met the inclusion criteria, representing 120 patients undergoing VP/KP at 135 vertebrae; the most common addressed level was C2 in 83 cases. The average volume of injected cement was 2.5 +/- 0.5 milliliters at each vertebra. There were 22 asymptomatic cement leaks (16%; 95% CI, 9.8% - 22.2%) most commonly occurring in the paraspinal soft tissue. There were 5 complications (4%; 95% CI, 0.5% - 7.5%): 3 cases of mild odynophagia, 1 case of occipital neuralgia secondary to leak, and 1 case of stroke secondary to cement embolism. Pain relief was achieved in 89% of cases (range: 80 - 100%). The calculated average pain score decreased significantly from 7.6 +/- 0.9 before surgery to 1.9 +/- 0.8 at last evaluation (p=0.006).

CONCLUSION: Although the calculated complication rate after VP/KP in the cervical spine is low (4%) and the reported pain relief rate is approximately 89%, there is lack of high-quality evidence supporting this. Future randomized controlled trials are needed.

130 Dabestani S, Marconi L, Bex A. **Metastasis therapies for renal cancer**. Curr Opin Urol 2016;26(6):566-72.

**Abstract:** PURPOSE OF REVIEW: Although novel targeted therapies for metastatic renal cell carcinoma (RCC) are emerging, metastasectomy still remains the only potentially curable intervention and plays an important role both in disease control, cancer-specific survival (CSS) and overall survival (OS). A systematic review was conducted in 2014 by the European Association of Urology RCC guidelines panel to summarize evidence on the subject at hand. The purpose of this review is to update the current evidence base.

RECENT FINDINGS: A total of 17-19% of initially nonmetastatic patients with later RCC metastasis are potentially curable. Complete metastasectomy still remains the sole curative option, continues to show improved OS and CSS and is suggested to defer time to palliative targeted therapy. Resectability, long time to recurrence, good performance status and oligometastatic disease have better benefit of metastasectomy. Stereotactic radiotherapy remains an excellent option for local tumor control and symptom control in patients with RCC brain and bone metastases. Minimal-invasive options such as thermal ablation are evolving, albeit the evidence base is small. Novel trials are investigating sequencing of metastasectomy and targeted therapy with results pending.

SUMMARY: Metastasectomy continues to be supported as beneficial for OS, CSS and progression-free survival in patients with good prognostic factors.

131 Collinson L, Kvizhinadze G, Nair N, McLeod M, Blakely T. **Economic evaluation of single-fraction versus multiple-fraction palliative radiotherapy for painful bone metastases in breast, lung and prostate cancer**. J Med Imaging Radiat Oncol 2016;60(5):650-60.

**Abstract:** INTRODUCTION: Single- and multiple-fraction external beam radiotherapy (SFX-EBRT and MFX-EBRT) are palliative treatment options for localized metastatic bone pain. MFX is the preferred choice in many developed countries. Evidence shows little difference in how effectively SFX and MFX reduce pain. However, SFX is associated with higher retreatment and (in one meta-analysis) pathological fracture rates. MFX is, however, more time-consuming and expensive. We estimated the cost-effectiveness of SFX versus MFX for metastatic bone pain in breast, prostate and lung cancer in New Zealand.

METHODS: We constructed a Markov microsimulation model to estimate health gain (in quality-adjusted life-years or QALYs), health system costs (in real 2011 NZ dollars) and cost-effectiveness. The model was populated using effect estimates from randomized controlled trials and other studies, and New Zealand cancer and cost data. Disability weights from the 2010 Global Burden of Disease study were used in estimating QALYs.

RESULTS: Across all three cancers, QALY gains were similar for SFX compared to MFX, and per patient costs were less for SFX than MFX, with a difference of NZ$1469 (95% uncertainty interval $1112 to $1886) for lung cancer, $1316 ($810 to $1854) for prostate cancer and $1344 ($855 to $1846) for breast cancer. Accordingly, from a cost-effectiveness perspective, SFX was the preferable treatment option. Various sensitivity analyses did not overturn the clear preference for SFX.

CONCLUSION: For all three cancers, SFX was clearly more cost-effective than MFX. This adds to the case for desisting from offering MFX to patients with metastatic bone pain, from a cost-effectiveness angle.

132 Cives M, Rizzo F, Simone V, Bisceglia F, Stucci S, Seeber A, et al. **Reviewing the Osteotropism in Neuroendocrine Tumors: The Role of Epithelial-Mesenchymal Transition**. Neuroendocrinology 2016;103(3-4):321-34.

**Abstract:** Background: Neuroendocrine tumors (NETs) metastasize to the bone. However, the incidence, clinical features, management and pathogenesis of bone involvement in NET patients have been poorly investigated. Methods: We reviewed all published reports of histologically confirmed bone metastatic NETs and explored clinical, radiological, prognostic and therapeutic characteristics in a population of 152 patients. We then evaluated immunohistochemical expression of a panel of eight epithelial-mesenchymal transition (EMT)-related factors including SNAIL, TGF-beta1, CTGF, IL-11, PTHrP, EpCAM, CXCR4 and RANK in an independent cohort of 44 archival primary NETs. Biomarker expression was correlated with clinicopathological variables, including skeletal involvement, and tested for survival prediction. Results: We found that 55% of NET patients with bone metastases were male, with a median age of 55 years at diagnosis. Metastases were restricted to the skeleton in 34% of the NET population, and axial and osteoblastic lesions were prevalent. NETs differently expressed proteins involved in EMT activation. High CXCR4 (p < 0.0001) and low TGF-beta1 levels (p = 0.0015) were significantly associated with increased risk of skeletal metastases, suggesting that EMT is implicated in NET osteotropism. By applying an algorithm measuring distinct immunohistochemical predictors of osteotropism on primary tumors, we were able to identify NET patients with bone metastases with a sensitivity and specificity of 91 and 100%, respectively (p < 0.0001). Patients whose primary tumors expressed CTGF (p = 0.0007) as well as the truncated form of EpCAM (p = 0.06) showed shorter survival. Conclusion: Although underestimated, bone metastases are a prominent feature of NETs, and the tumor expression of EMT markers at diagnosis may predict concurrent or subsequent skeleton colonization. Copyright © 2015 S. Karger AG, Basel.

133 Chiu N, Chiu L, Popovic M, De Angelis C, Lutz S, Zhang N, et al. **Re-irradiation for painful bone metastases: Evidence-based approach**. Support Care Cancer 2016;24 (1 Supplement 1):S96.

**Abstract:** Introduction: The prognosis of patients with bone metastases has improved with the advent of increasingly effective systemic treatment and better supportive care. A growing number of bone metastases patients now outlive the duration of benefits from their initial treatment of radiotherapy (RT) while some patients fail to initially respond to RT. As such, re-irradiation (re-RT) may be required. Objectives: Recent research has provided an increased understanding in the area of re-RT. The current review updates the literature on findings in the area of re-RT. Methods: A literature search was conducted in Ovid Medline, Old Medline, Embase, Embase Classic, and Cochrane Central Register of Controlled Trials using relevant subject headings and keywords such as: "Re-irradiation," "bone metastases," and "radiotherapy." Results: The recent publication of the NCIC CTG SC20 trial shows that an 8 Gy treatment in a single fraction for re-RT is non-inferior and less toxic than 20 Gy in multiple fractions. Furthermore, patients responding to re-RT experience superior QoL and complain of less functional interference from pain; this provides a strong case in support of bone metastases patients being offered re-treatment. However, some specific patients will never respond to initial radiation or re-RT. New findings have found significant differences in bone markers between responders and non-re-sponders, thus opening the possibility for further research into the use of such biomarkers for predicting prognosis and for the guidance of consequent treatment decisions. Conclusions: The area of re-RT has undergone advances following recently published research. The current review updates the literature on findings in the area of re-RT.

134 Chiu N, Chiu L, Lutz S, Zhang N, Lechner B, Pulenzas N, et al. **Incorporation of life expectancy estimates in the treatment of palliative care patients receiving radiotherapy: Treatment approaches in light of incomplete prognostic models**. Support Care Cancer 2016;24 (1 Supplement 1):S221-S2.

**Abstract:** Introduction: Physician estimates of patients' survival times have historically been inaccurate. Several prognostic models have been created to aid physicians in providing more accurate estimates. Emerging evidence that prognosis may also depend on treatment has rendered most predictive models of survival incomplete. Objectives: Given evidence-based treatment options in a wide variety of patient populations, radiation oncologists need no longer rely so heavily on the precise prognostic capacity of survival models. The aim of this study was to investigate and discuss evidence-based practices in light of incomplete survival models. Methods: A literature search was conducted in Ovid Medline, OldMedline, Embase, Embase Classic, and Cochrane Central Register of Controlled Trials using relevant subject headings and keywords such as: "life expectancy estimates," "palliative care," "prognostic models," and "radiotherapy." Results: Relevant articles were extracted and discussed. Patients of different age demographics and survival prognoses benefit from palliative radiation treatment. For uncomplicated bone metastases, a single 8 Gy fraction of radiation is equally effective for palliation regardless of whether a patient will have a short or long duration of survival. Certain patients with complicated bone metastases may benefit from multiple fraction radiotherapy. There is no difference in neurologic function improvement or overall survival with the use of altered whole brain dose fractionation schedules when compared with standard fractionation schedules (30 Gy in ten fractions or 20 Gy in five fractions). Conclusions: Radiation oncologists need not rely as heavily on survival estimates in guiding their treatment decisions. However, further research is required to incorporate treatment factors in future survival prediction models.

135 Chang JH, Shin JH, Yamada YJ, Mesfin A, Fehlings MG, Rhines LD, et al. **Stereotactic Body Radiotherapy for Spinal Metastases: What are the Risks and How Do We Minimize Them?** Spine (Phila Pa 1976) 2016;41 Suppl 20:S238-S45.

**Abstract:** STUDY DESIGN: Systematic literature review.

OBJECTIVES: To summarize the risks of 3 key complications of stereotactic body radiotherapy (SBRT) for spinal metastases, that is, radiation myelopathy (RM), vertebral compression fracture (VCF), and epidural disease progression, and to discuss strategies for minimizing them.

SUMMARY OF BACKGROUND DATA: RM, VCF and epidural disease progression are now recognized as important risks following SBRT for spine metastases. It is unclear at this stage exactly how large these risks are and what strategies can be employed to minimize these risks.

METHODS: A systematic review of the literature using MEDLINE and a review of the bibliographies of reviewed articles on SBRT for spinal metastases were conducted.

RESULTS: The initial literature search revealed a total of 376 articles, of which 38 were pertinent to the study objectives. The risk of RM following SBRT was found to be dependent on the maximum dose to the spinal cord and estimated to be <=5% if the recommended published thecal sac dose constraints are adhered to. The crude risk of VCF was 13.7% (range: 0.7%-40.5%), and, on average, 45% were surgically salvaged. It has been shown that the risk of VCF is dependent on several anatomic and tumor-related factors including the SBRT dose per fraction. The crude risk of local failure at 1 year was 21.4% (range: 12%-27%) of which 67% (range: 38%-96%) occurred within the epidural space. The grade of epidural disease has been shown to be associated with the risk of local failure.

CONCLUSION: The risk of RM after spinal SBRT is low in particular if recommended dose metrics are adhered to. There is a significant risk of both VCF and epidural disease progression after spinal SBRT. These risks can potentially be minimized by identifying the risk factors for these complications, and performing careful radiotherapy and surgical planning.

Level of evidence: 2.

136 Batista N, Tee J, Sciubba D, Sahgal A, Laufer I, Weber M, et al. **Emerging and established clinical, histopathological and molecular parametric prognostic factors for metastatic spine disease secondary to lung cancer: Helping surgeons make decisions**. J Clin Neurosci 2016;34:15-22.

**Abstract:** Metastatic lung cancer to the spine occurs at high rates with patients usually given poor prognoses. Recent studies have observed that patients with certain genetic and molecular aberrations have better responses to adjuvant therapy. As such, current metastatic spine disease treatment algorithms grading all lung primaries' prognosis as poor may lead to inadequate treatment of spinal metastases. The aims of this study are to determine current survival patterns in metastatic spine disease secondary to lung cancer and identify relevant parameters that influence the prognostication of these patients. A systematic review in accordance with PRISMA guidelines was conducted for literature published between January 1, 1996 and September 31, 2015. The 27 studies identified were Level IV retrospective studies with an overall 'low' level of evidence. The overall median survival of patients with spine involved metastatic lung cancer was poor, ranging from 3.6 to 9 months. Median survival of patients with non-small cell lung cancer being treated with epidermal growth factor receptor (EGFR) inhibitors were observed to be better, with survival of up to 18 months. This review reports a subset of lung cancer patients with oncogenic molecular mutations that appear to confer a better overall survival. In these patients, individualized assessment rather than strict adherence to current metastatic scoring algorithms when determining management may be preferred. Copyright © 2016 Elsevier Ltd

137 Bakar D, Tanenbaum JE, Phan K, Alentado VJ, Steinmetz MP, Benzel EC, et al. **Decompression surgery for spinal metastases: a systematic review**. Neurosurg Focus 2016;41(2):E2.

**Abstract:** OBJECTIVE The aim of this study was to systematically review the literature on reported outcomes following decompression surgery for spinal metastases. METHODS The authors conducted MEDLINE, Scopus, and Web of Science database searches for studies reporting clinical outcomes and complications associated with decompression surgery for metastatic spinal tumors. Both retrospective and prospective studies were included. After meeting inclusion criteria, articles were categorized based on the following reported outcomes: survival, ambulation, surgical technique, neurological function, primary tumor histology, and miscellaneous outcomes. RESULTS Of the 4148 articles retrieved from databases, 36 met inclusion criteria. Of those included, 8 were prospective studies and 28 were retrospective studies. The year of publication ranged from 1992 to 2015. Study size ranged from 21 to 711 patients. Three studies found that good preoperative Karnofsky Performance Status (KPS >= 80%) was a significant predictor of survival. No study reported a significant effect of time-to-surgery following the onset of spinal cord compression symptoms on survival. Three studies reported improvement in neurological function following surgery. The most commonly cited complication was wound infection or dehiscence (22 studies). Eight studies reported that preoperative ambulatory or preoperative motor status was a significant predictor of postoperative ambulatory status. A wide variety of surgical techniques were reported: posterior decompression and stabilization, posterior decompression without stabilization, and posterior decompression with total or subtotal tumor resection. Although a wide range of functional scales were used to assess neurological outcomes, four studies used the American Spinal Injury Association (ASIA) Impairment Scale to assess neurological function. Four studies reported the effects of radiation therapy and local disease control for spinal metastases. Two studies reported that the type of treatment was not significantly associated with the rate of local control. The most commonly reported primary tumor types included lung cancer, prostate cancer, breast cancer, renal cancer, and gastrointestinal cancer. CONCLUSIONS This study reports a systematic review of the literature on decompression surgery for spinal metastases. The results of this study can help educate surgeons on the previously published predictors of outcomes following decompression surgery for metastatic spinal disease. However, the authors also identify significant gaps in the literature and the need for future studies investigating the optimal practice with regard to decompression surgery for spinal metastases.

138 Anonymous. **Denosumab (Xgeva)**. Canadian Agency for Drugs and Technologies in Health 2016;11:11.

**Abstract:** Bone is a common site of metastasis for many cancers including breast, prostate, thyroid, lung, renal, and melanoma. Skeletal metastatic disease is the cause of considerable morbidity in patients with advanced cancer and has been associated with an increase in cancer-related pain, hypercalcemia, fractures, spinal instability, and compression of the spinal cord. Denosumab is a human monoclonal antibody binding to human receptor activator of nuclear factor kappa-B ligand (RANKL). Denosumab has a Health Canada indication for reducing the risk of developing skeletal-related events (SREs) in patients with bone metastases from breast cancer, prostate cancer, non-small cell lung cancer, and other solid tumours. Denosumab is not indicated for reducing the risk of developing SREs in patients with multiple myeloma. The drug plans that participate in the CADTH Common Drug Review (CDR) process have requested that denosumab be evaluated for reimbursement for reducing the risk of developing SREs in patients with bone metastases from solid tumours (except breast and prostate cancer). The objective of this report was to perform a systematic review of the beneficial and harmful effects of denosumab for reducing the risk of developing SREs in patients with bone metastases from solid tumours (except from breast cancer or prostate cancer).

139 Altaf F, Weber M, Dea N, Boriani S, Ames C, Williams R, et al. **Evidence-Based Review and Survey of Expert Opinion of Reconstruction of Metastatic Spine Tumors**. Spine (Phila Pa 1976) 2016;41 Suppl 20:S254-S61.

**Abstract:** STUDY DESIGN: Systematic review and consensus expert opinion.

OBJECTIVE: To provide surgeons and other health care professionals with guidelines for surgical reconstruction of metastatic spine disease based on evidence and expert opinion.

SUMMARY OF BACKGROUND DATA: The surgical treatment of spinal metastases is controversial. Specifically two aspects of surgical reconstruction are addressed in this study: (i) choice of bone graft used during surgery for metastatic spine tumors and (ii) the design of reconstruction or construct to stabilize.

METHODS: A systematic review of the available medical literature from 1980 to 2015 was conducted, and combined with consensus expert opinion from a recent survey of spine surgeons who treat metastatic spine tumors.

RESULTS: There is very little evidence in the literature to provide guidance on the use of bone graft in metastatic tumor reconstruction. There is little evidence in the literature to support the preferential use of one graft type over the other. Approximately, 41% of respondents said they used bone graft or bone graft substitutes to accomplish fusion. There were 17 studies that described the use of a prefabricated prosthetic, 10 studies describing the use of polymethyl methacrylate (PMMA) bone cement, and only three studies describing the use of bone graft for anterior column reconstruction. The use of structural allograft was most popular among the experts for anterior reconstruction, followed by cage reconstruction, and PMMA bone cement.

CONCLUSION: Achieving bony union may be of importance for the maintenance of spinal stability in the long term after reconstruction. Whether bony union is required for patients with shorter life expectancies is debatable. The literature supports the use of anterior reconstruction with either a prefabricated prosthetic or PMMA bone cement. It also supports the use of an anterior construct reinforced with bilateral posterior instrumentation when performing a three-column reconstruction.

Level of evidence: n/a.

140 Zaheer A, Wadhwa V, Oh J, Fishman EK. **Pearls and pitfalls of imaging metastatic disease from pancreatic adenocarcinoma: A systematic review**. Clin Imaging 2015;39(5):750-8.

**Abstract:** Pancreatic adenocarcinoma is a systemic disease due to the presence of metastatic disease at the time of diagnosis and local recurrence as well as distant metastatic disease after treatment in a majority of patients. Recognition of these metastatic sites may help in accurate staging and assessment of therapeutic response. The authors discuss and illustrate imaging findings of metastatic disease from pancreatic adenocarcinoma in different organ systems with emphasis on entities that can mimic metastatic pancreatic cancer. Copyright © 2015 Elsevier Inc.

141 Yousef YA, Alkilany M. **Characterization, treatment, and outcome of uveal melanoma in the first two years of life**. Hematology/ Oncology and Stem Cell Therapy 2015;8(1):1-5.

**Abstract:** Background and objectives Features and characteristics of uveal melanoma are well described in adults, but little is known about the presentation of uveal melanoma in infancy. Design Systematic literature review. Methods A review of published, peer-reviewed literature reporting on uveal melanoma presenting during the first two years of life. Outcome measures included demographics, clinical features, histopathological findings, extent of the disease, therapeutic interventions, management outcomes, association with skin lesions or systemic diseases, and survival data. Results This review revealed 13 reported cases (seven boys and six girls) of uveal melanoma diagnosed within the first two years of life. The median age at diagnosis was seven months. Orbital mass and proptosis were the most common presentations (38%); only one tumor (8%) was melanotic, and pathologically 10 tumors (77%) had epithelioid component. Associated pigmented skin lesions (cutaneous disease) were seen in six cases (46%). All affected eyes were surgically removed; three patients received chemotherapy, and one received radiotherapy. At a median follow-up of 25 months, two patients (15%) had metastasis, and one of them (8%) was dead at six months' follow-up with liver and multi-organ metastasis. Conclusions Uveal melanoma can present within the first two years of life. In very rare cases, it can present as an intraocular tumor that simulates retinoblastoma, but it can also present as an orbital tumor. It has a tendency to affect patients with cutaneous diseases like familial atypical mole, melanoma syndrome, and dysplastic nevus syndrome. Despite this, uveal melanoma in this group has a more favorable prognosis than adult melanoma. Copyright © 2015 King Faisal Specialist Hospital & Research Centre.

142 Wells SA, Asa SL, Dralle H, Elisei R, Evans DB, Gagel RF, et al. **Revised American thyroid association guidelines for the management of medullary thyroid carcinoma**. Thyroid 2015;25(6):567-610.

**Abstract:** Introduction: The American Thyroid Association appointed a Task Force of experts to revise the original Medullary Thyroid Carcinoma: Management Guidelines of the American Thyroid Association. Methods: The Task Force identified relevant articles using a systematic PubMed search, supplemented with additional published materials, and then created evidence-based recommendations, which were set in categories using criteria adapted from the United States Preventive Services Task Force Agency for Healthcare Research and Quality. The original guidelines provided abundant source material and an excellent organizational structure that served as the basis for the current revised document. Results: The revised guidelines are focused primarily on the diagnosis and treatment of patients with sporadic medullary thyroid carcinoma (MTC) and hereditary MTC. Conclusions: The Task Force developed 67 evidence-based recommendations to assist clinicians in the care of patients with MTC. The Task Force considers the recommendations to represent current, rational, and optimal medical practice. Copyright © 2015 Mary Ann Liebert, Inc.

143 Wang Z, Qiao D, Lu Y, Curtis D, Wen X, Yao Y, et al. **Systematic literature review and network meta-analysis comparing bone-targeted agents for the prevention of skeletal-related events in cancer patients with bone metastasis**. Oncologist 2015;20(4):440-9.

**Abstract:** BACKGROUND: Complications from skeletal-related events (SREs) constitute a challenge in the care of cancer patients with bone metastasis (BM).

OBJECTIVES: This study evaluated the comparative effectiveness of pamidronate, ibandronate, zoledronate, and denosumab in reducing the morbidity of SREs in cancer patients with BM.

METHODS: Medline (1948 to January 2014), Embase (1980 to January 2014), the Cochrane Library (2014 issue 1), and Web of Science with Conference Proceedings (1970 to January 2014) were searched. Only randomized controlled trials assessing denosumab, bisphosphonates, or placebo in cancer patients with BM were included. The primary outcomes were SREs and SREs by type. The network meta-analysis (NMA) was performed with a random-effects Bayesian model.

RESULTS: The NMA included 14 trials with 10,192 patients. Denosumab was superior to placebo in reducing the risk of SREs (odds ratio [OR]: 0.49; 95% confidence interval [CI]: 0.31-0.75), followed by zoledronate (OR: 0.57; 95% CI: 0.41-0.77) and pamidronate (OR: 0.55; 95% CI: 0.41-0.72). Ibandronate compared with placebo could not reduce the risk of SREs. Denosumab was superior to placebo in reducing the risk of pathologic fractures (OR: 0.50; 95% CI: 0.32-0.79), followed by zoledronate (OR: 0.61; 95% CI: 0.43-0.86). Denosumab was superior to placebo in reducing the risk of radiation (OR: 0.51; 95% CI: 0.35-0.75), followed by pamidronate (OR: 0.67; 95% CI: 0.52-0.86) and zoledronate (OR: 0.70; 95% CI: 0.52-0.96).

CONCLUSION: This NMA showed that denosumab, zoledronate, and pamidronate were generally effective in preventing SREs in cancer patients with BM. Denosumab and zoledronate were also associated with reductions in the risk of pathologic fractures and radiation compared with placebo. Denosumab was shown to be the most effective of the bone-targeted agents.

144 Tunio M, Al Asiri M, Al Hadab A, Bayoumi Y. **Comparative efficacy, tolerability, and survival outcomes of various radiopharmaceuticals in castration-resistant prostate cancer with bone metastasis: a meta-analysis of randomized controlled trials**. Drug Des Devel Ther 2015;9:5291-9.

**Abstract:** BACKGROUND: A meta-analysis was conducted to assess the impact of radiopharmaceuticals (RPs) in castration-resistant prostate cancer (CRPC) on pain control, symptomatic skeletal events (SSEs), toxicity profile, quality of life (QoL), and overall survival (OS).

MATERIALS AND METHODS: The PubMed/MEDLINE, CANCERLIT, EMBASE, Cochrane Library database, and other search engines were searched to identify randomized controlled trials (RCTs) comparing RPs with control (placebo or radiation therapy) in metastatic CRPC. Data were extracted and assessed for the risk of bias (Cochrane's risk of bias tool). Pooled data were expressed as odds ratio (OR), with 95% confidence intervals (CIs; Mantel-Haenszel fixed-effects model).

RESULTS: Eight RCTs with a total patient population of 1,877 patients were identified. The use of RP was associated with significant reduction in pain intensity and SSE (OR: 0.63, 95% CI: 0.51-0.78, I(2)=27%, P,0.0001), improved QoL (OR: 0.71, 95% CI: 0.55-0.91, I(2)=65%, three trials, 1,178 patients, P=0.006), and a minimal improved OS (OR: 0.84, 95% CI: 0.64-1.04, I(2)=47%, seven trials, 1,845 patients, P=0.11). A subgroup analysis suggested an improved OS with radium-223 (OR: 0.68, 95% CI: 0.51-0.90, one trial, 921 patients) and strontium-89 (OR: 0.21, 95% CI: 0.05-0.91, one trial, 49 patients). Strontium-89 (five trials) was associated with increased rates of grade 3 and 4 thrombocytopenia (OR: 4.26, 95% CI: 2.22-8.18, P=0.01), leucopenia (OR: 7.98, 95% CI: 1.82-34.95, P=0.02), pain flare (OR: 6.82, 95% CI: 3.42-13.55, P=0.04), and emesis (OR: 3.61, 95% CI: 1.76-7.40, P=0.02).

CONCLUSION: The use of RPs was associated with significant reduction in SSEs and improved QoL, while the radium-223-related OS benefit warrants further large, RCTs in docetaxel naive metastatic CRPC patients.

145 Todenhofer T, Stenzl A, Hofbauer LC, Rachner TD. **Targeting Bone Metabolism in Patients with Advanced Prostate Cancer: Current Options and Controversies**. Int J Endocrinol 2015;2015 (no pagination)(838202).

**Abstract:** Maintaining bone health remains a clinical challenge in patients with prostate cancer (PC) who are at risk of developing metastatic bone disease and increased bone loss due to hormone ablation therapy. In patients with cancer-treatment induced bone loss (CTIBL), antiresorptive agents have been shown to improve bone mineral density (BMD) and to reduce the risk of fractures. For patients with bone metastases, both zoledronic acid and denosumab delay skeletal related events (SREs) in the castration resistant stage of disease. Novel agents targeting the Wnt inhibitors dickkopf-1 and sclerostin are currently under investigation for the treatment of osteoporosis and malignant bone disease. New antineoplastic drugs such as abiraterone, enzalutamide, and Radium-223 are capable of further delaying SREs in patients with advanced PC. The benefit of antiresorptive treatment for patients with castration sensitive PC appears to be limited. Recent trials on the use of zoledronic acid for the prevention of bone metastases failed to be successful, whereas denosumab delayed the occurrence of bone metastases by a median of 4.1 months. Currently, the use of antiresorptive drugs to prevent bone metastases still remains a field of controversies and further trials are needed to identify patient subgroups that may profit from early therapy. Copyright © 2015 Tilman Todenhofer et al.

146 Stomeo D, Tulli A, Ziranu A, Perisano C, De Santis V, Maccauro G. **Acrometastasis: A literature review**. Eur Rev Med Pharmacol Sci 2015;19(15):2906-15.

**Abstract:** OBJECTIVE: Acrometastases are a rare observation, and account for approximately 0.1% of metastases. Every age can be affected, with a male predominance. The most common primary cancer site is the lung, followed by the colo-rectal, breast and genito-urinary tract. They are most commonly seen in pre-terminal patients with wide-spread disseminated disease. Rarely, they may be the first presentation of occult silent cancer, mimicking a benign condition. There is no standard treatment.We reviewed last 20 years literature in order to describe the most common sites of primary tumours and the more commonly used treatments. MATERIALS AND METHODS: We searched the Cochrane Central Library (CENTRAL), MEDLINE/ PubMed (from 1940 to February 2014), SCOPUS database, and EMBASE/Ovid using a combination of controlled vocabulary and text word terms. RESULTS: Lung cancer was the first most common cause of acrometastases both in hands and feet, with 32.9% of all the cases; 20% of cases were renal cell cancer (RCC) metastases, followed by breast (12.9%) and colon (10%). Primary malignancies and site of metastasis (hand vs foot) suggest that the tumour cells reach the bones through the circulation and not the lymphatic system; in foot acrometastases Batson's plexus may play a fundamental role in dissemination. CONCLUSIONS: Treatment depends on staging and tumor extent. Amputation or disarticulation is the most common approach. It allows a wide margin resection and pain control. In some cases palliative treatment with radiation therapy, bisphosphonates and chemotherapy have been attempted with good results. The prognosis of the patients with acrometastases is poor; the mean survival time after diagnosis is 7 (+/-7) months. Special reference needs to be made to metastasis from renal cell carcinoma; if treated with radical surgical resection and nephrectomy a better outcome and survival rate shall be expected.

147 Sourbeer KN, Howard LE, Moreira DM, Amarasekara HS, Chow LD, Cockrell DC, et al. **Practice patterns and predictors of followup imaging after a negative bone scan in men with castration resistant prostate cancer: results from the SEARCH database**. J Urol 2015;193(4):1232-8.

**Abstract:** PURPOSE: We investigated imaging practice patterns in men with nonmetastatic (M0) castration resistant prostate cancer.

MATERIALS AND METHODS: We analyzed data on 247 patients with documented M0 CRPC from the SEARCH database. Patients were selected regardless of primary treatment modality and all had a negative bone scan after a castration resistant prostate cancer diagnosis. Cox models were used to test associations of time to a second imaging test with several demographic and clinical factors.

RESULTS: During a median followup of 29.0 months (IQR 12.9-43.5) after a post-castration resistant prostate cancer bone scan was negative, 190 patients (77%) underwent a second imaging test. On univariable analysis patients with higher prostate specific antigen (HR 1.13, p = 0.016), shorter prostate specific antigen doubling time (HR 0.79, p < 0.001) and faster prostate specific antigen velocity (HR 1.01, p < 0.001) were more likely to undergo a second imaging test. Treatment center was also a significant predictor of a second imaging test (p = 0.010). No other factor was a significant predictor. Results were similar on multivariable analysis. It was estimated that approximately 20% of men with a prostate specific antigen doubling time of less than 3 months did not undergo an imaging test in the first year after a post-castration resistant prostate cancer negative bone scan. However, 50% of patients with prostate specific antigen doubling time 15 months or greater underwent a second imaging test in the first year.

CONCLUSIONS: Clinicians use some known predictors of positive imaging tests to determine which patients with M0 castration resistant prostate cancer undergo a second imaging test . However, there may be under imaging in those at high risk and over imaging in those at low risk. Further studies are needed to identify risk factors for metastasis and form clear imaging guidelines in patients with M0 castration resistant prostate cancer.

148 Solmaz U, Ekin A, Dereli ML, Mat E, Gezer C, Sanci M. **Clear cell adenocarcinoma of cervix and vagina misdiagnosed as myoma: Case report and literature review**. Turk Jinekolojik Onkoloji Dergisi 2015;18(1):29-34.

**Abstract:** Clear cell adenocarcinoma (CCA) is a rare variant of mucinous adenocarcinoma of the cervix and vagina. The most common presenting symptom is abnormal vaginal bleeding. Here, we report a case and literature review of CCA of cervix and vagina which was incidentally diagnosed after surgery performed for myoma uteri. Since CCA is an extremely rare disease, standard screening tests, diagnostic tools and treatment methods have not been completely established yet. These features of CCA make it difficult to diagnose preoperatively. Hence, additional studies are needed to diagnose CCA correctly and determine definitive management and treatment principles through meta-analysis using multicenter data. Copyright © 2015, Gunes Kitap Kirtasiye. All rights reserved.

149 Sapkaroski D, Osborne C, Knight KA. **A review of stereotactic body radiotherapy - is volumetric modulated arc therapy the answer?** J Med Radiat Sci 2015;62(2):142-51.

**Abstract:** Stereotactic body radiotherapy (SBRT) is a high precision radiotherapy technique used for the treatment of small to moderate extra-cranial tumours. Early studies utilising SBRT have shown favourable outcomes. However, major disadvantages of static field SBRT include long treatment times and toxicity complications. Volumetric modulated arc therapy (VMAT) and intensity modulated radiotherapy (IMRT) may potentially mitigate these disadvantages. This review aims to assess the feasibility of emerging VMAT and IMRT-based SBRT treatment techniques and qualify which offers the best outcome for patients, whilst identifying any emerging and advantageous SBRT planning trends. A review and synthesis of data from current literature up to September 2013 was conducted on EMBASE, Medline, PubMed, Science Direct, Proquest central, Google Scholar and the Cochrane Database of Systematic reviews. Only full text papers comparing VMAT and or IMRT and or Static SBRT were included. Ten papers were identified that evaluated the results of VMAT/IMRT SBRT. Five related to medically inoperable stage 1 and 2 non-small-cell lung cancer (NSCLC), three to spinal metastasis, one related to abdominal lymph node malignancies, with the final one looking at pancreatic adenocarcinoma. Overall treatment times with VMAT were reduced by 66-70% for lung, 46-58% for spine, 42% and 21% for lymph node and pancreatic metastasis respectively, planning constraints were met with several studies showing improved organs at risk sparing with IMRT/VMAT to static SBRT. Both IMRT and VMAT were able to meet all planning constraints in the studies reviewed, with VMAT offering the greatest treatment efficiency. Early clinical outcomes with VMAT and IMRT SBRT have demonstrated excellent local control and favourable survival outcomes.

150 Safarpour D, Tavassoli F, Jabbari B. **Intramedullary metastasis from ovarian cancer: A systematic review of the literature**. Neurology Conference: 67th American Academy of Neurology Annual Meeting, AAN 2015;84(SUPPL. 14).

**Abstract:** Objective: The literature was reviewed to assess the prevalence of intramedullary metastasis from ovarian cancer and describe location, clinical features, survival, and treatment of such metastasis. Background: Intramedullary spinal cord metastasis (ISCM) is rare (0.1[percnt] to 2.0[percnt] among all cancers). The data on intramedullary ovarian metastasis is sparse. Design/Methods: We searched the literature using Yale's search engine to include but not limited to PubMed and Scopus on the subject of intramedullary metastasis from ovarian cancer since 1990 (the era of magnetic resonance imaging). Results: The prevalence of ovarian cancer metastasis to spinal cord ranged from 1[percnt] to 2.2[percnt] based on five reported series. There were 8 detailed case descriptions reported between1992-2012. The location of metastasis was cervical (4 cases), thoracic (3 cases) and in the conus-medullaris and cauda equine regions (1 case). Concurrent brain metastasis was present in 3 cases. The pathology of the primary tumor was described in 7 patients; 6 had serous adenocarcinoma, 4 of which were poorly differentiated, while the diagnosis was provided simply as poorly differentiated carcinoma and not otherwise specified in the 7th case. The average time between diagnosis of the primary tumor in the ovary to diagnosis of the intramedullary metastasis was 32 months. Of those who were reported deceased, the average survival was 7.1 months (range 5 to 10 months). Four studies reported patients to be alive 10, 16, 24 and 32 months after the detection of the intramedullary metastatic tumor. After diagnosis of intramedullary metastasis, all patients (8 patients) received radiotherapy, 6 underwent surgery and half of the patients (4 patients) received steroids. Conclusion: intramedullary metastasis from ovarian tumor accounts for 1-2.2[ percnt] of all intramedullary metastasis. The tumor types reported included serous adenocarcinoma and poorly differentiated carcinoma-not otherwise specified. Survival beyond two years have been reported with combination of resection and radiotherapy.

151 Sabanathan D, Gurney H, Hayden A. **The use of stereotactic radiotherapy for bone metastases from renal cell carcinoma-a systematic review**. Asia Pac J Clin Oncol 2015;3):63-4.

**Abstract:** Background: Renal cell carcinoma (RCC) is one of the top ten malignancies in Australia. Approximately a third of patients present with metastatic disease, of which 20-50% have bone metastases. Local control rates following treatment with conventional palliative radiotherapy have been suboptimal. Stereotactic body radiotherapy (SBRT), characterized by precision and high dose per fraction, may improve the local control and palliation of cancers such as RCC traditionally considered 'radio-resistant'. There is currently limited evidence regarding the outcomes and toxicities associated with SBRT in this setting. This study aims to critically evaluate and provide an overall summary of the evidence. The objective of this study is to report the outcomes following SBRT for bone metastases from renal cell carcinoma. Methods: A systematic literature search of databases (Medline, PubMed and Embase) was conducted in March 2015 to identify studies reporting outcomes following SBRT for bone metastases secondary to RCC. The primary objective was local control rate and secondary objectives included pain response, rate of vertebral compression fractures and toxicity Results: A total of nine studies were identified, including 355 patients treated with SBRT for 525 bone metastases. Prescribed doses ranged from 8-42 Gy in 1-5 fractions. At a median follow up period of 12.7 months (0.2-55 months), the mean local control rate was 88.9% (82-100%), and the mean pain response was 71% (60-89%). The median 12 month progression free survival rate was 87.8% (71-100%). In studies which reported vertebral compression fracture rates (n = 5), the mean risk of vertebral compression fracture was 16%. The incidence of grade 3 toxicities ranged from 0-10% with which included anemia, nausea, and fatigue. Conclusions: Current evidence suggests that SBRT is an effective treatment modality for renal cell carcinoma metastatic to bone with excellent local control rates and low rates of toxicity. Further research into patient selection, long-term toxicity, and sequencing with systemic therapy is warranted.

152 Sabanathan D. **The use of stereotactic radiotherapy for bone metastases from renal cell carcinoma-a systematic review**. Asia Pac J Clin Oncol 2015;2):38-9.

**Abstract:** Background: Renal cell carcinoma (RCC) is one of the top ten malignancies in Australia. Approximately a third of patients present with metastatic disease, of which 20-50% have bone metastases. Local control rates following treatment with conventional palliative radiotherapy have been suboptimal. Stereotactic body radiotherapy (SBRT), characterised by precision and high dose per fraction, may improve the local control and palliation of cancers such as RCC traditionally considered 'radio-resistant'. There is currently limited evidence regarding teh outcomes and toxicities associated with SBRT in this setting. This study aims to critically evaluate and provide an overall summary of the evidence. Objective: To report the outcomes following SBRT for bone metastases from renal cell carcinoma. Methods: A systematic literature search of databases (Medline, PubMed and Embase) was conducted in March 2015 to identify studies reporting outcomes following SBRT for bone metastases secondary to RCC. The primary objective was local control rate and secondary objectives included pain response, rate of vertebral compression fractures and toxicity. Results: A total of nine studies were identified, including 355 patients treated with SBRT for 525 bone metastases. Prescribed doses ranged from 8-42 Gy in 1-5 fractions. At a median follow up period of 12.7 months (0.2-55 months), the mean local control rate was 88.9% (82-100%), and the mean pain response was 71% (60-89%). The median 12 month progression free survival rate was 87.8% (71-100%). In studies which reported vertebral compression fracture rates (n = 5), the mean risk of vertebral compression fracture was 16%. The incidence of grade 3 toxicities ranged from 0-10% with which included anaemia, nausea, and fatigue. Conclusion: Current evidence suggests that SBRT is an effective treatment modality for renal cell carcinoma metastatic to bone with excellent local control rates and low rates of toxicity. Further research into patient selection, long-term toxicity, and sequencing with systemic therapy is warranted.

153 Ribeiro DFF, Lucena F. **Nuclear medicine therapies applied to small animals**. Eur J Nucl Med Mol Imaging 2015;1):S846.

**Abstract:** Introduction - Nuclear Medicine (NM) procedures have been used in the field of Veterinary Medicine (VM) for some years, with a recent increasing interest in Radionuclide Therapy (RNT), especially in hyperthyroidism and bone metastasis. Aims - Describe RNT applications in VM, with focus on well established procedures for small animals. A new therapeutic approach with 177Lu-DOTMP will also be included. Methods - A systematic review was conducted based on key-words, "Radioactive iodine therapy", "Iodine 131 therapy", "Radioiodine treatment", "hyperthyroidism", "therapies with radiopharmaceuticals", "Palliation treatment with radiopharmaceuticals", "radionuclide therapy", "veterinary", "153Sm-EDTMP", "dogs", "177Lu-DOTMP", "animals" and "small animals", and relevance of the content. Twenty articles were included and the analysis was focused on precautions prior and post therapy, therapeutic procedures and adverse effects of therapies with 131I, 153Sm-EDTMP and 177Lu-DOTMP. Results - The research included review articles (N=2; 15.38%), experimental articles (N=6; 46.15%), official documents (N=3; 23.08%) and official webpages (N=2; 15.38%). 131I therapy represents the most common treatment in VM due to its effectiveness and less disadvantages. Prior to the therapy it is advisable to determine thyroxine blood concentration, blood pressure and renal and cardiac function. Animals should by isolated no less then 7 days, in a quiet environment with shielded cages. The administered activity may be determined by: fixed activity; based on a scoring system; or by kinetic models. After the therapy renal function should be monitored. Regarding bone metastasis, 153Sm-EDTMP and 177Lu-DOTMP are being used as they represent attractive therapies although 177Lu-DOTMP seems to be more effective since it doesn't deteriorate the urinary tract. Prior to the therapy, erythrocytes, leucocytes and platelets levels should be evaluated and a bone scintigraphy is also advisable. The activities for each radiopharmaceutical should be determined based on the animal's weight, and motorization should be provided until 14 days post therapy. Although none of these two therapies are considered for the first therapeutic approach, they are often used as palliative treatment and might potentiate the effects of radiotherapy. Conclusion - RNT allied with simple therapeutic procedures provides an effective therapeutic approach in VM, giving the animals better chances of survival, with low incidence of adverse effects. Although 131I is the better established RNT, both the 153Sm-EDTMP and 177Lu- DOTMP appear promising and are slowly gaining their way into the VM community.

154 Qu S, Meng HL, Liang ZG, Zhu XD, Li L, Chen LX, et al. **Comparison of Short-Course Radiotherapy Versus Long-Course Radiotherapy for Treatment of Metastatic Spinal Cord Compression: A Systematic Review and Meta-Analysis**. Medicine 2015;94(43):e1843.

**Abstract:** In this study, we evaluate the efficacy of short-course radiotherapy (SCRT) versus long-course radiotherapy (LCRT) in the treatment of metastatic spinal cord compression (MSCC).PubMed, EMBASE, and Web of Science were searched up to April 2015. Relevant data were extracted based on inclusion and exclusion criteria. Methodological quality of randomized controlled trial (RCT) was evaluated using modified Jadad scale; non-RCT was evaluated using Newcastle-Ottawa Scale. Meta-analysis was performed using RevMan 5.3 software.Fourteen studies with 2239 patients were included. Results of meta-analysis showed that there were no significant differences between SCRT and long-course radiotherapy LCRT in 6-month overall survival rate (risk ratio [RR] = 0.97, 95% confidence interval [CI] 0.88, 1.07, P = 0.55), 1-year overall survival rate (RR = 0.94, 95% CI 0.85, 1.04, P = 0.22), motor function improvement (RR = 0.96, 95% CI 0.81, 1.13, P = 0.63), no change on motor function (RR = 0.98, 95% CI (0.88, 1.09), P = 0.74], and deterioration on motor function (RR = 0.96, 95% CI 0.71, 1.31, P = 0.78). Compared with SCRT, LCRT significantly increased 6-month local control rate (RR = 0.87, 95% CI 0.80, 0.95, P = 0.002), 1-year local control rate (RR = 0.83, 95% CI 0.71, 0.97, P = 0.02), and 2-year local control rate (RR = 0.83, 95% CI 0.79, 0.87, P < 0.00001).Both LCRT and SCRT provided similar survival rates and functional outcome, but LCRT showed better local control rates than SCRT. However, considering low cost and good patient's compliance, SCRT may be a better choice.

155 Pulenzas N, Cheon P, Wong E, Thavarajah N, Dennis K, Lutz S, et al. **A definition of "uncomplicated bone metastases" based on previous bone metastases radiation trials comparing single-fraction and multi-fraction radiation therapy**. Support Care Cancer 2015;1):S41-S2.

**Abstract:** Introduction: The most recent systematic review of randomized trials in patients with bone metastases has shown equal efficacy of single fraction (SF) and multiple fraction (MF) palliative radiation therapy in pain relief. It is important to determine the patient population to which the evidence applies. Objectives: This study aims to examine the eligibility criteria of the studies included in the systematic review to define characteristics of "uncomplicated" bone metastases. Methods: Inclusion and exclusion criteria of 21 studies included in the systematic review were compared. Common eligibility criteria were documented in hopes of defining the specific features of a common patient population representative of those in the studies. Results: More than half of the studies included patients with cytological or histological evidence of malignancy. Patients with impending and/or existing pathological fracture, spinal cord compression or cauda equina compression were excluded in most studies. Most studies also excluded patients receiving retreatment to the same site. Conclusions: "Uncomplicated" bone metastases can be defined as: presence of painful bone metastases unassociated with impending or existing pathologic fracture or existing spinal cord or cauda equina compression. Therefore, MF and SF have equal efficacy in patients with such presentations of bone metastases.

156 Puerta P, Guillen A, Mora J, Sunol M, Candela S, Ferrer E. **Isolated skull metastasis of ewing's sarcoma in a child**. Childs Nerv Syst 2015;31 (10):1952.

**Abstract:** Objective: Ewings sarcoma (ES) was described as a "diffuse hemangioendothelioma of bone". It affects long bones and pelvis. The predominant sites of metastases include lung, bone and bone marrow. Metastasis of ES to the central nervous system (CNS) is uncommon. We present an extremely rare case of skull metastasis of ES. Methods: We present a child affected of a metastatic ES of the skull and we describe our management based on a literature review through Pubmed Medline. Results: A 10-year-old male underwent resection of an ES in the left 5th rib 15 months previously, followed by chemotherapy and radiotherapy. He had a painless, progressive swelling over his right parietal area. CT showed an isodense parietal tumour which was homogeneously enhanced by contrast medium. It was partly extracranial and partly intracranial, with bone destruction. Gross total removal of the tumour was performed and the infiltrated dura was excised. We performed a duraplasty and a titanium mesh cranioplasty. The histology was identical to the specimens from the left rib tumour. The diagnosis was skull metastasis of ES. Adjuvant treatment was performed. Conclusion: ES is the second most common malignant bone tumour. It usually occurs in patients younger than 20 years of age and it's more frequent in males than females. Primary ES most often originates in long bone shafts, pelvic bones, ribs and vertebrae. This tumour frequently develops metastases. The principal sites of metastases are lung, bone and the bone marrow. Meningeal invasion and spinal cord compression are the best known forms of CNS involvement. The frequency of skull metastases of ES in children is unknown but, to our knowledge, there are only three cases previously reported. The multimodal treatment for ES is considered to be the optimal treatment method. Solitary skull metastasis should be removed totally, followed by systemic chemotherapy.

157 Ploussard G, Almeras C, Briganti A, Giannarini G, Hennequin C, Ost P, et al. **Management of Node Only Recurrence after Primary Local Treatment for Prostate Cancer: A Systematic Review of the Literature**. J Urol 2015;194(4):983-8.

**Abstract:** PURPOSE: We analyzed all available studies assessing the management of node only recurrence after primary local treatment of prostate cancer.

MATERIALS AND METHODS: We systematically reviewed the literature in January 2015 using the PubMed, Web of Sciences and Embase databases according to PRISMA guidelines. Studies exclusively reporting visceral or bone metastatic disease were excluded from analysis. Eight radiotherapy and 12 salvage lymph node dissection series were included in our qualitative study.

RESULTS: All 248 radiotherapy and 480 salvage lymph node dissection studies were single arm case series including a total of 728 patients. Choline positron emission tomography/computerized tomography was the reference imaging technique for nodal recurrence detection. Globally 50% of patients remained disease-free after short-term followup. Nevertheless, approximately two-thirds of patients received adjuvant hormone therapy, leading an overestimation of prostate specific antigen-free survival rates obtained after salvage treatment. Combining radiotherapy with salvage lymph node dissection may improve oncologic control in the treated region without improving the outfield relapse risk or the prostate specific antigen response. Great heterogeneity among series in adjuvant treatments, endpoints, progression definitions and study populations made it difficult to assess the precise impact of salvage treatment on the prostate specific antigen response and compare outcomes between radiotherapy and salvage lymph node dissection series. Toxicity after radiotherapy or salvage lymph node dissection was acceptable without frequent high grade complications. The benefit of early hormone therapy as the only salvage treatment remains unknown.

CONCLUSIONS: Although a high level of evidence is currently missing to draw any strong conclusion, published clinical series show that in select patients salvage treatment directed to nodal recurrence could lead to good oncologic outcomes. Although the optimal timing of androgen deprivation therapy in this setting is still unknown, such an approach could delay time to systemic treatment with an acceptable safety profile. Future prospective trials are awaited to better clarify this potential impact on well-defined endpoints.

158 Ost P, Bossi A, Decaestecker K, De Meerleer G, Giannarini G, Karnes RJ, et al. **Metastasis-directed therapy of regional and distant recurrences after curative treatment of prostate cancer: a systematic review of the literature**. Eur Urol 2015;67(5):852-63.

**Abstract:** CONTEXT: The introduction of novel imaging modalities has increased the detection of oligometastatic prostate cancer (PCa) recurrence, potentially justifying the use of a metastasis-directed therapy (MDT) with surgery or radiotherapy (RT) rather than a systemic approach.

OBJECTIVE: To perform a systematic review of MDT for oligometastatic PCa recurrence.

EVIDENCE ACQUISITION: This systematic review was performed according to Preferred Reporting Items for Systematic Reviews and Meta-analysis guidelines. We searched the Medline and Embase databases from 1946 to February 2014 for studies reporting on biochemical or clinical progression and/or toxicity or complications of MDT (RT or surgery). Reports were excluded if these end points could not be ascertained or separately analysed, or if insufficient details were provided. Methodological quality was assessed using an 18-item validated quality appraisal tool for case series.

EVIDENCE SYNTHESIS: Fifteen single-arm case series reporting on a total of 450 patients met the inclusion criteria. Seven studies were considered of acceptable quality. Oligometastatic PCa recurrence was diagnosed with positron emission tomography with coregistered computed tomography in most of the patients (98%). Nodal, bone, and visceral metastases were treated in 78%, 21%, and 1%, respectively. Patients were treated with either RT (66%) or lymph node dissection (LND) (34%). Adjuvant androgen deprivation was given in 61% of patients (n=275). In the case of nodal metastases, prophylactic nodal irradiation was administered in 49% of patients (n=172). Overall, 51% of patients were progression free 1-3 yr after salvage MDT, with most of them receiving adjuvant treatment. For RT, grade 2 toxicity was observed in 8.5% of patients, with one case of grade 3 toxicity. In the case of LND, 11% and 12% of grade 2 and grade 3 complications, respectively, were reported.

CONCLUSIONS: MDT is a promising approach for oligometastatic PCa recurrence, but the low level of evidence generated by small case series does not allow extrapolation to a standard of care.

PATIENT SUMMARY: We performed a systematic review to assess complications and outcomes of treating oligometastatic prostate cancer recurrence with surgery or radiotherapy. We concluded that although this approach is promising, it requires validation in randomised controlled trials.

159 Nguyen NT, Hotte S, Dayes I. **Long-term Survival in a Patient with Metastatic Spinal Cord Compression from a Prostate Cancer with Ultra-high PSA: Case Report and Review of the Literature**. Cureus 2015;7(1):e242.

**Abstract:** A 77-year-old man presented to the hospital for non-ambulation of 48 hours prior to admission. He was found to have a metastatic spinal cord compression (MSCC), a PSA exceeding 27,000, and biopsy-confirmed prostate cancer. After palliative radiation (RT) to the spine and medical treatment, the patient recovered his functions fully and survived for more than 7.5 years, far beyond what would be expected based on current published literature. A systematic review of the literature of MSCC in patients with prostate cancer was carried out. Prognostic factors of ambulation after RT included pre-treatment neurological status, duration of neurological deficits, and severity of the neurological impairment. Positive predictive factors of local control included single level of metastasis, time of development of motor deficits of more than 14 days, no prior androgen-deprivation therapy (ADT), age under 65, and longer course of RT (10 fractions of 2 Gy). Absence of prior ADT, pre-treatment ambulation, a single site of metastasis, and haemoglobin of less than 12g/L were positive predictors for survival.

160 Moreira DM, Howard LE, Sourbeer KN, Amarasekara HS, Chow LC, Cockrell DC, et al. **Predicting bone scan positivity in non-metastatic castration-resistant prostate cancer**. Prostate Cancer Prostatic Dis 2015;18(4):333-7.

**Abstract:** Background:To evaluate PSA levels and kinetic cutoffs to predict positive bone scans for men with non-metastatic castration-resistant prostate cancer (CRPC) from the Shared Equal Access Regional Cancer Hospital (SEARCH) cohort.Methods:Retrospective analysis of 531 bone scans of 312 clinically CRPC patients with no known metastases at baseline treated with a variety of primary treatment types in the SEARCH database. The association of patients' demographics, pathological features, PSA levels and kinetics with risk of a positive scan was tested using generalized estimating equations.Results:A total of 149 (28%) scans were positive. Positive scans were associated with younger age (odds ratio (OR)=0.98; P=0.014), higher Gleason scores (relative to Gleason 2-6, Gleason 3+4: OR=2.03, P=0.035; Gleason 4+3 and 8-10: OR=1.76, P=0.059), higher prescan PSA (OR=2.11; P<0.001), shorter prescan PSA doubling time (PSADT; OR=0.53; P<0.001), higher PSA velocity (OR=1.74; P<0.001) and more remote scan year (OR=0.92; P=0.004). Scan positivity was 6, 14, 29 and 57% for men with PSA<5, 5-14.9, 15-49.9 and >=50 ng ml -1, respectively (P-trend <0.001). Men with PSADT >=15, 9-14.9, 3-8.9 and <3 months had a scan positivity of 11, 22, 34 and 47%, correspondingly (P-trend <0.001). Tables were constructed using PSA and PSADT to predict the likelihood of a positive bone scan.Conclusions:PSA levels and kinetics were associated with positive bone scans. We developed tables to predict the risk of positive bone scans by PSA and PSADT. Combining PSA levels and kinetics may help select patients with CRPC for bone scans. Copyright © 2015 Macmillan Publishers Limited.

161 McDonald R, Lam H, Chow E, Rowbottom L, Soliman H. **International patterns of practice in radiotherapy for bone metastases: A review of the literature**. Support Care Cancer 2015;1):S279.

**Abstract:** Introduction: Radiation therapy is the standard treatment for symptomatic bone metastases. Several randomized control trials and meta-analyses have concluded a similar efficacy in pain relief when comparing single versus multiple fraction regimes. However, there continues to be reluctance to conform to published guidelines that recommend a single treatment for the palliation of painful bone metastases. Objectives: The objective of this present review is to summarize international patterns of practice and to determine if guidelines recommending single fraction treatment have been implemented in clinical care. Methods: A literature search was conducted in Ovid Medline, Embase, and Cochrane Central. Search words included, 'bone metastases', 'radiation therapy', 'radiotherapy', 'patterns of practice', and 'dose fractionation'. Both prospective and retrospective studies that investigated the prescription of radiotherapy to bone metastases using actual patient databases were included. Articles were excluded if they investigated hypothetical scenarios. Results: Six hundred and thirteen results were generated from the literature search. Twenty-six articles met the inclusion criteria. Of these, 11 were Canadian, 8 were European, 6 were American, and 1 was Australian. The use of single fraction radiotherapy (SFRT) ranged from 3% to 75%, but was generally lower in American studies. Choice of fractionation depended on a variety of factors, including patient age, prognosis, site of irradiation, and physician experience. Conclusions: Despite the publication of robust randomized control trials, meta-analyses, and clinical practice guidelines recommending the use of a single treatment to palliate uncomplicated bone metastasis, SFRT is internationally underutilized.

162 McDonald R, Chow E, Rowbottom L, DeAngelis C, Soliman H. **Incidence of pain flare in radiation treatment of bone metastases: A literature review**. Support Care Cancer 2015;1):S283.

**Abstract:** Introduction: Pain flare is a temporary increase in pain and is a potential side effect of radiotherapy treatment that can lead to decreased quality of life and hesitancy in receiving further treatment. Its incidence has been reported previously with great variability. A few studies have reported on the use of dexamethasone as a prophylactic agent in the prevention of pain flare. Objectives: Our objective is to present a review of the literature regarding the incidence of pain flare and use of prophylactic dexamethasone. Methods: A literature search was conducted in PubMed using subject keywords including "radiation therapy", "bone metastases", "pain flare", and "dexamethasone". The search was limited to English only but not restricted to any time period. A search was also conducted in the American Society for Therapeutic Radiology and Oncology 2014 book of published abstracts. Inclusion criteria were primary studies published with full text or abstracts only. Results: Seven articles investigated pain flare and/or dexamethasone use for conventional external beam radiation therapy (EBRT) while the remaining 4 investigated stereotactic body radiation therapy (SBRT). Pain flare incidence ranged from 2 to 44% for EBRT and 10 to 68% in SBRT. The use of dexamethasone is effective in both the prophylaxis and treatment of pain flare. Conclusions: Pain flare is an acute toxicity of both EBRT and SBRT. The use of dexamethasone in the prophylaxis of pain flare is efficacious. Future studies are required in order to optimize the reporting of pain and dexamethasone regimens in the prevention of pain flare.

163 McDonald R, Chow E, Rowbottom L, Bedard G, Lam H, Wong E, et al. **Quality of life after palliative radiotherapy in bone metastases: A literature review**. Journal of Bone Oncology 2015;4(1):24-31.

**Abstract:** OBJECTIVE: To investigate the quality of life (QOL) following palliative radiotherapy for painful bone metastases.

METHODS: A literature search was conducted in OvidSP Medline (1946-Jan Week 4 2014), Embase (1947-Week 5 2014), and the Cochrane Central Register of Controlled Trials (Dec 2013) databases. The search was limited to English. Subject headings and keywords included 'palliative radiation', 'cancer palliative therapy', 'bone metastases', 'quality of life', and 'pain'. All studies (prospective or retrospective) reporting change in QOL before and after palliative radiotherapy for painful bone metastases were included.

RESULTS: Eighteen articles were selected from a total of 1730. The most commonly used tool to evaluate QOL was the Brief Pain Inventory. Seventeen studies collected data prospectively. An improvement in symptoms and functional interference scores following radiotherapy was observed in all studies. The difference in changes in QOL between responders and non responders was inconsistently reported.

CONCLUSION: QOL improves in patients who respond to palliative radiotherapy for painful bone metastases.

164 Marin S, Coloma CS, Garde-Noguera J, Vidal OJ, Sanchez JG, Escoin C, et al. **Oligometastatic non-small-cell lung cancer and unresectable primary tumor: Safety and efficacy of radical treatment**. J Thorac Oncol 2015;2):S324.

**Abstract:** Background: Metastatic non-small cell lung cancer (NSCLC) is associated with a poor prognosis, and palliative chemotherapy is the mainstay of treatment. However, longtime survival has been observed in oligometastatic patients treated with locally ablative therapies to all sites of tumoral disease. Oligometastatic NSCLC with unresectable primary tumor at diagnosis represents a therapeutic challenge, and nowadays there is limited evidence about the benefit of the treatment with radical intention of both primary tumor and metastases. Methods: Retrospective study of patients with oligometastatic (3 or less lesions, in a unique location) and unresectable NSCLC treated with radical chemo-radiotherapy at primary tumor and with surgery or stereotactic radiation therapy to the metastases. We have done a systematic review of clinical histories from NSCLC advanced patients diagnosed between October 2011 and March 2015. The aim of our study is to analyze the safety and efficacy of this treatment strategy in terms of response rate, progression free survival (PFS) and overall survival (OS). Results: Twenty-three patients met inclusion criteria. Median age 57 year, eighteen male (78,3%) and ECOG (0-1) 95,7%. Histology: 15 adenocarcinoma (65,2%), 5 squamous carcinoma (5%), and 3 (13%) others. All patients had unresectable mediastinal lymph nodes infiltration. Location of metastases included the brain (n=12, 52.2%), lung metastases (n=6, 26,1%), bone metastases (n= 3, 13%), adrenal (n=1, 4,3%) and lymph node (n=1, 4,3%). Chemotherapy: 9 CDDP-Pemetrexed (39,1%), 9 CDDP-Vinorelbina (39,1%), 3 Carboplatinpaclitaxel, 1 CDDP-Gemcitabina (4.3%), 1 CDDP-Docetaxel (4.3%). Ten patients (43.5%) received sequential thoracic radiotherapy and 12 (52.2%) concomitant. Metastases treatment: 12 stererotactic radiation (52.2%), 7 external radiotherapy (30, 4%), 3 surgery (13%), 1 radiofrequency (4.3%). Toxicity: four patients (17,39%) developed G3 toxicity (2 hematological, 1 pneumonitis, 1 esophagitis). Median follow up was 15 months, median OS 18 m, median PFS 11 months. The 1-year OS were 73.9%, 2-year OS 21,7% and 3-year OS 8.7%. Conclusion: Radical treatment of oligometastatic and unresectable NSCLC patients is a safe therapeutic strategy. Despite the limited data and the small numbers of our study, it could be contemplated as an effective therapeutic alternative for selected patients.

165 Lukas RV, Mata-Machado NA, Nicholas MK, Salgia R, Antic T, Villaflor VM. **Leptomeningeal carcinomatosis in esophageal cancer: A case series and systematic review of the literature**. Dis Esophagus 2015;28(8):772-81.

**Abstract:** The aim of this study was to more clearly define the clinical course of leptomeningeal carcinomatosis due to esophageal cancer. A single institution retrospective case series was conducted. Additionally, a systematic review of the literature was performed. We present a large case series (n = 7) of leptomeningeal carcinomatosis due to esophageal cancer. Our case series and systematic review of the literature report similar findings. In our series, we report a predominance of male patients (86%) with adenocarcinoma histology (77%). Variable onset of leptomeningeal involvement of esophageal cancer in relation to the original diagnosis of the primary disease (5 months to 3 years and 11 weeks) was noted. Disease progresses quickly and overall survival is poor, measured in weeks (2.5-16 weeks) from the diagnosis of leptomeningeal involvement. Four of our patients initiated whole-brain radiation therapy with only two completing the course prior to clinical deterioration. Our patient with the longest survival (16 weeks) received intrathecal topotecan and oral temozolomide. Leptomeningeal carcinomatosis secondary to esophageal cancer has a poor prognosis. A clearly beneficial treatment modality is lacking. Copyright © 2015 International Society for Diseases of the Esophagus.

166 Li T, Thompson M, Tran D. **Metastatic-free survival and overall survival in prostate cancer**. Value Health 2015;18 (3):A14.

**Abstract:** Objectives: In clinical trials of early-stage prostate cancer, demonstration of an overall survival (OS) benefit is challenging because of prolonged patient survival. While the development of metastasis is a major milestone in the disease, payers are interested in understanding the clinical relevance of metastatic-free survival (MFS) as a surrogate endpoint and its relationship with long-term outcomes, in particular, OS. The objective of the current study was to identify empirical evidence evaluating MFS in patients with prostate cancer. Methods: A structured literature review was conducted in PubMed (1999-2014) to identify clinical trials in prostate cancer using MFS as a primary endpoint, and clinical and observational studies that evaluated the association between MFS and OS. Results: Three published clinical trials used MFS as a primary endpoint. The studies employed varying definitions for MFS (e.g., bone metastasis only or bone and soft tissue metastasis). In one long-term study comparing adjuvant radiotherapy to usual care, both MFS and OS outcomes were significantly improved with radiotherapy, suggesting a relationship between these two endpoints. Four additional studies examined the association between MFS and OS. One study reported that distant metastasis at three years met the Prentice criteria for surrogacy of prostate cancer-specific survival at 10 years. A second study reported that MFS was one of four independent prognostic variables for OS in prostate cancer. The remaining two studies demonstrated that time to metastasis was significantly associated with prostate cancer-specific mortality. Conclusions: MFS has been used as the primary endpoint in several prostate cancer studies, providing support for the clinical relevance of this outcome. Current evidence from the literature suggests an association between MFS and OS, however additional research is needed to further investigate this relationship.

167 Lee SH, Grant R, Kennedy C, Kilbride L. **Positioning and spinal bracing for pain relief in metastatic spinal cord compression in adults**. Cochrane Database of Systematic Reviews 2015;(9):CD007609.

**Abstract:** BACKGROUND: This is an updated version of the original Cochrane review published in Issue 3 (Lee 2012) on patient positioning (mobilisation) and bracing for pain relief and spinal stability in adults with metastatic spinal cord compression.Many patients with metastatic spinal cord compression (MSCC) have spinal instability, but their clinician has determined that due to their advanced disease they are unsuitable for surgical internal fixation. Mobilising may be hazardous in the presence of spinal instability as further vertebral collapse can occur. Current guidance on positioning (whether a patient should be managed with bed rest or allowed to mobilise) and whether spinal bracing is helpful, is contradictory.

OBJECTIVES: To investigate the correct positioning and examine the effects of spinal bracing to relieve pain or to prevent further vertebral collapse in patients with MSCC.

SEARCH METHODS: For this update, we searched for relevant studies from February 2012 to 31 March 2015. We searched the Cochrane Central Register of Controlled Trials (CENTRAL), MEDLINE and MEDLINE In Process, EMBASE, AMED, CINAHL, TRIP, SIGN, NICE, UK Clinical Research Network, National Guideline Clearinghouse and PEDro database. We also searched the metaRegister of Controlled Trials (mRCT), ClinicalTrials.gov, UK Clinical Trials Gateway (UKCTG), WHO International Clinical Trials Registry Platform (ICTRP) and Australia New Zealand Clinical Trials Registry (ANZCTR).For the original version, we searched the Cochrane Central Register of Controlled Trials (CENTRAL), MEDLINE, EMBASE, CINAHL, CANCERLIT, NICE, SIGN, AMED, TRIP, National Guideline Clearinghouse, and PEDro database, in February 2012.

SELECTION CRITERIA: We selected randomised controlled trials (RCTs) of adults with MSCC of interventions on positioning (mobilisation) and bracing.

DATA COLLECTION AND ANALYSIS: Two review authors independently assessed each possible study for inclusion and quality.

MAIN RESULTS: For the original version of the review, we screened 1611 potentially relevant studies. No studies met the inclusion criteria. Many papers identified the importance of mobilisation, but no RCTs of bed rest versus mobilisation have been undertaken. We identified no RCTs of bracing in MSCC.For this update, we identified 347 potential titles. We screened 300 titles and abstracts after removal of duplicates. We did not identify any additional studies for inclusion.

AUTHORS' CONCLUSIONS: Since publication of the original version of this review, no new studies were found and our conclusions remain unchanged.There is a lack of evidence-based guidance around how to correctly position and when to mobilise patients with MSCC or if spinal bracing is an effective technique for reducing pain or improving quality of life. RCTs are required in this important area.

168 Lai YL, Liang JA, Chien CR. **Is involved field target delineation safe in spinal palliative radiotherapy?** Eur J Cancer 2015;3):S208.

**Abstract:** Background: Bone metastases are a common manifestation of malignancy and cause pain and disability. Multiple randomized controlled trials and several systematic reviews have demonstrated that radiotherapy (RT) can provide significant palliation of painful bone metastases in 50-80% of patients. However, consensus definitions for target delineation in spinal palliative conventional fractionated radiotherapy have yet to be established. This study aimed to analyze the outcome after the involved field (tumor and adjacent sectors of spine) spinal palliative conventional fractionated radiotherapy [IF-SPCF-RT] following the International Spine Radiosurgery Consortium Consensus Guidelines for Target Volume Definition used in spinal stereotactic radiotherapy [Int J Radiation Oncol Biol Phys 2012; 83: e597-e605]. Material and Methods: Based on a prospectively established registry, we retrospectively collected clinical data on patients treated with IF-SPCF-RT within 2012-2014. Patients who received previous surgery or RT to the spine were excluded. We only included those with prescribed dose 30 to 37 Gray (Gy), with 2.5 to 3.0 Gy per fraction. Local failure was defined as image recurrence, retreatment (surgery or RT), or pain progression to the irradiated site. The local control (LC) rate was assessed based on each spinal segment treated and pain relief rate according to each patient treated. LC was calculated from the start of RT, using the Kaplan-Meier method. Results: We identified 38 patients with 95 treated spinal segments. The median follow-up was 4.7 months (range 0.6-30.2 months). 27 patients (71.1%) experienced pain relief. The 1, 3, 6, and 12 months LC rates were 90.5%, 74.6%, 47.2%, and 40.8%, respectively. There were only 10 in-field failures observed, including one with image alone, 3 with re-RT, and 6 with surgical treatment. No out-field failure was noted. Conclusions: IF-SPCF-RT yields acceptable rates of local tumor control and pain relief in patients with spinal bone metastasis. The possibility of out-field failure when target definition follows the International Spine Radiosurgery Consortium Consensus Guidelines for Target Volume Definition might be negligible.

169 Kothari G, Foroudi F, Gill S, Corcoran NM, Siva S. **Outcomes of stereotactic radiotherapy for cranial and extracranial metastatic renal cell carcinoma: a systematic review**. Acta Oncol 2015;54(2):148-57.

**Abstract:** BACKGROUND: Stereotactic radiotherapy is a non-invasive, ablative technique which may be particularly effective in treating metastatic renal cell carcinoma (RCC). The study objective was to analyse outcomes and toxicity of stereotactic radiotherapy in metastatic RCC.

MATERIAL AND METHODS: Following the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) guidelines, a systematic review of Medline was performed in March 2013. Exclusion criteria included mixed histology studies and case series. Local control, overall survival and toxicities were analysed.

RESULTS: From 148 publications identified, 16 and 10 publications for cranial and extracranial metastatic RCC met inclusion criteria, respectively. There were 810 intracranial patients and 2433 targets. The weighted local control was 92%. Overall survival ranged from 6.7 to 25.6 months. Significant Grade 3-4 toxicity ranged from 0% to 6%. The weighted rate of treatment-related mortality was 0.6%, all secondary to intratumoral haemorrhage. There were 389 extracranial patients and 730 targets. The weighted local control was 89%. Median overall survival ranged from 11.7 to 22 months. Grade 3-4 toxicity ranged from 0% to 4%. Treatment-related mortality was 0.5%.

CONCLUSION: Stereotactic radiotherapy is associated with excellent local control and low rates of toxicity for intracranial and extracranial metastatic RCC. Future randomised studies are required to confirm the additional benefit of Stereotactic Ablative Body Radiotherapy (SABR) above standard conservative or palliative approaches.

170 Kelly ML, Benzel EC. **Surgery Versus Radiation Therapy Alone in Treating Spinal Metastasis: A Perspective**. World Neurosurg 2015;83(6):1020-1.

171 Kai G, Chuan L, Fang L. **Minimally invasive treatments of spinal metastases: Vertebroplasty, radiofrequency ablation and radiation therapy. [Chinese]**. Chinese Journal of Tissue Engineering Research 2015;19(16):2613-8.

**Abstract:** BACKGROUND: The development of minimally invasive technology significantly reduces the occurrence of surgical complications due to spinal metastases. Currently, the minimally invasive treatment basically has three broad categories: vertebral cement augmentation, radiofrequency ablation combined with vertebroplasty, intraoperative radiotherapy combined with vertebroplasty. OBJECTIVE: To summarize the research progress of three kinds of minimally invasive treatments for spinal metastases. METHODS: PubMed and Wanfang databases were searched using the keywords of "spinal metastases, vertebroplasty, radiofrequency ablation, radiotherapy" in English and Chinese, respectively. RESULTS AND CONCLUSION: Vertebral cement augmentation with good analgesic effect has been used widely, and the efficiency is up to 80%-90%. But its effect to kill tumors is very limited that is unable to control tumor growth. Radiofrequency ablation and radiation can kill the tumor, but cannot rebuild the vertebral stability. Therefore, the combination of different technologies can improve the therapeutic effect on spinal tumors. In recent years, intraoperative radiation and implantation of radioactive particles or radioactive bone cement have been developed as new technologies. However, there is no conclusion that these new technologies have better outcomes than the vertebral cement augmentation because of less reports and lack of long-term follow-up. Especially in the metastatic patients with damaged vertebral posterior wall and tumors invaded into vertebral canal, the risk of nerve function damage caused by bone cement leakage is still very high, even after many attempts. Above all, there is no a perfect minimally invasive treatment for spinal metastases. Copyright © 2015, Chinese Journal of Tissue Engineering Research. All rights reserved.

172 Huisman M, Ter Haar G, Napoli A, Hananel A, Ghanouni P, Lovey G, et al. **International consensus on use of focused ultrasound for painful bone metastases: Current status and future directions**. Int J Hyperthermia 2015;31(3):251-9.

**Abstract:** Focused ultrasound surgery (FUS), in particular magnetic resonance guided FUS (MRgFUS), is an emerging non-invasive thermal treatment modality in oncology that has recently proven to be effective for the palliation of metastatic bone pain. A consensus panel of internationally recognised experts in focused ultrasound critically reviewed all available data and developed consensus statements to increase awareness, accelerate the development, acceptance and adoption of FUS as a treatment for painful bone metastases and provide guidance towards broader application in oncology. In this review, evidence-based consensus statements are provided for (1) current treatment goals, (2) current indications, (3) technical considerations, (4) future directions including research priorities, and (5) economic and logistical considerations. Copyright © 2014 Informa UK Ltd. All rights reserved.

173 Gomez Saez JM, Jimenez-Fonseca P, Santamaria Sandi J, Capdevila Castillon J, Navarro Gonzalez E, Zafon Llopis C, et al. **Spanish consensus for the management of patients with anaplastic cell thyroid carcinoma**. Endocrinologia y Nutricion 2015;62(3):e15-e22.

**Abstract:** Anaplastic thyroid cancer (ATC) is the most aggressive solid tumour known and is a rare but highly lethal form of thyroid cancer that requires a multidisciplinary team approach. No Spanish consensus exists for management of patients with ATC. The Thyroid Cancer Group of the Spanish Society of Endocrinology and Nutrition and the GETHI (Grupo Espanol de Enfermedades Huerfanas e Infrecuentes) of the Spanish Society of Oncology, in agreement with the Boards of these Societies, commissioned an independent task force to develop a wide consensus on ATC. The relevant literature was reviewed, including serial PubMed searches supplemented with additional articles. The consensus includes the characteristics, diagnosis, initial evaluation, establishment of treatment goals, approaches to locoregional disease (surgery, radiotherapy, systemic therapy, supportive care during active treatment), approaches to advanced/metastatic disease, palliative care options, monitoring, and long-term follow-up of ATC. For operable disease, a combination of radical surgery with adjuvant radiotherapy or chemotherapy, using agents such as doxorubicin, cisplatin and paclitaxel, is the best treatment strategy. Cytotoxic drugs are poorly effective for advanced/metastatic ATC. On the other hand, targeted agents may represent a viable therapeutic option. Patients with stage IVA/IVB resectable disease have the best prognosis, particularly if a multimodal approach is used, and some stage IVB unresectable patients may respond to aggressive therapy. Patients with stage IVC disease should be considered for clinical trials or for hospice/palliative care depending on their preference. This is the first Spanish consensus for ATC, and provides recommendations for management of this extremely aggressive malignancy. Novel systemic therapies are being tested, and more effective combinations are needed to improve patient outcomes. Although more aggressive radiotherapy has reduced locoregional recurrence, mean overall survival has not improved in the past 50 years. Copyright © 2014 SEEN.

174 Ghadjar P, Briganti A, De Visschere PJ, Futterer JJ, Giannarini G, Isbarn H, et al. **The oncologic role of local treatment in primary metastatic prostate cancer**. World J Urol 2015;33(6):755-61.

**Abstract:** PURPOSE: To determine the oncologic benefit or otherwise of local treatment of the prostate in patients with primary metastatic prostate cancer.

METHODS: A review of the literature was performed in April 2014 using the Medline/PubMed database. Studies were identified using the search terms "prostate cancer," "metastatic," "metastasis," "high risk," "radiation therapy," "radiotherapy" and "prostatectomy" from 1990 until April, 2014. Articles were also identified through searches of references of these articles.

RESULTS: Retrospective series and population-based data suggest that the use of local treatment of the prostate in patients with primary metastatic prostate cancer may improve cancer-specific survival and overall survival compared with treating these patients with androgen deprivation therapy alone. The clinical outcome in metastatic prostate cancer is largely determined by the extent of lymph node involvement and overall metastatic burden. Contemporary data are lacking to recommend one alternative of local therapy (radiotherapy or radical prostatectomy) over the other. The primary limitation of this literature review is the lack of published randomized trial assessing the role of local treatment in addition to systemic therapy.

CONCLUSIONS: Local treatment appears to improve oncologic outcomes in metastatic prostate cancer patients. Nevertheless, due to the lack of high-quality evidence, its role needs to be confirmed in future prospective trials. The selection of ideal candidates and optimal treatment alternative (radiotherapy, radical prostatectomy or other) warrants further investigation.

175 Galofre JC, Santamaria Sandi J, Capdevila J, Navarro Gonzalez E, Zafon Llopis C, Ramon y Cajal Asensio T, et al. **Consensus on the management of advanced medullary thyroid carcinoma on behalf of the Working Group of Thyroid Cancer of the Spanish Society of Endocrinology (SEEN) and the Spanish Task Force Group for Orphan and Infrequent Tumors (GETHI)**. Endocrinologia y Nutricion 2015;62(4):e37-e46.

**Abstract:** In Spain medullary thyroid carcinoma (MTC) would not exceed 80 new cases per year and less than half of them would be good candidates for systemic treatment with novel agents. Methods: Relevant literature was reviewed, including PubMed searches supplemented with additional articles. Results: The consensus summarizes the clinical outcomes in terms of activity and toxicity of each of the available drugs. A brief summary of the minimum requirements in terms of follow up and genetic counseling around MTC is also included. Conclusions: Only those patients with objective imaging progression in the last 12-14 months with large volume of disease are clear candidates to start systemic treatment. However, those patients with low disease volume should be considered for 'wait and see' strategy until symptoms of the disease appear. Multidisciplinary approach for the management of MTC patient is mandatory nowadays. Copyright © 2014 SEEN.

176 Fan HT, Wang L, Zhang P, Liu SB. **Photodynamic therapy in spinal metastases: a qualitative analysis of published results**. Int Surg 2015;100(4):712-9.

**Abstract:** The current study was to perform qualitative comparison of photodynamic therapy (PDT), based on previously published articles on spinal disease distribution status before and after treatment. Spinal metastasis, the migration of primary cancer cells and establishment of secondary tumors in the spine. We electronically searched CENTRAL (The Cochrane Library 2012), MEDLINE, EMBASE, CINAHL and AMED (from their beginning to December 31, 2012) to identify published studies assessing the effectiveness of PDT in spinal metastases. Our inclusion criteria resulted in only 4 articles, all in mice models. Due to study limitations and sparse data, the quality of evidence for all outcomes was low. Our analyses shows that effects on stereological and mechanical properties observed at the 1-week time point post-PDT are maintained at a longer 6-week time point, with combined PDT + bisphosphonate treatment being the most beneficial in terms of bone enhancement. Additionally, the combination of PDT + radiation therapy also demonstrated significant increases in stereological parameters, suggesting that previous radiation therapy treatment does not preclude the bone-enhancing effects of PDT and in fact may be synergistic in the longer term. The bone-enhancing effects of PDT in combination with conventional treatments, and its ability to destroy metastatic human breast cancer cells within bone, present PDT as an attractive novel treatment for spinal metastasis. The positive results from these preclinical studies might motivate future clinical translation of PDT for spinal metastasis.

177 Dore M, Cutuli B, Cellier P, Campion L, Blanc M. **Hypofractionated irradiation in elderly patients with breast cancer after breast conserving surgery and mastectomy: Analysis of 205 cases**. Radiat 2015;10 (1) (no pagination)(161).

**Abstract:** Background: Several randomized trials and meta-analyses confirmed a wide benefit of radiotherapy (RT), both after breast conserving surgery (BCS) and mastectomy. However, many elderly women don't receive RT. Hypofractionated (HF) RT allows << simplified >> and more accessible treatments with equivalent results to classic RT in three large randomized trials. However, there are few available data on HF-RT for nodal irradiation, as well as for the boost. Methods: We evaluated patients treated for IBC by HF-RT between 2004 and 2012 in two regional cancer centres. We used an original scheme delivering 45 Gy in 15 fractions three times a week, both after BCS or mastectomy, with or without nodal irradiation. After BCS, a 9 Gy boost in 3 fractions was delivered. Local, regional and distant recurrences were assessed, as well as acute and late cutaneous, cardiac or pulmonary toxicities. Results: 205 patients were analysed, 116 after BCS (57 %) and 89 after mastectomy (43 %). Median age was 81 years (range: 52-91); 44 % had axillary nodal involvement (pN+). The Nottingham Prognostic Index (NPI) scored 0, 1, 2 and 3 in 10 %, 27 %, 44 % and 19 % of the cases. A nodal HF-RT was delivered in 65 patients (32 %) and boost in 98 patients (84 % of BCS) by 9 Gy/3 fr scheme. Fifty (24 %) patients underwent chemotherapy and 156 (75 %) hormonal treatment. With a 49-month median follow-up, 3/116 (2.6 %) patients and 4/89 (4.5 %) had local recurrence (LR) after BCS and mastectomy, respectively. The overall 5-year LR rate was 4.4 %. In univariate and multivariate analysis, LR risk factors were: high NPI (HR 5.46; p = 0.028), and triple negative tumour (HR 9.78; p = 0.006). Only 8 (4.5 %) patients had grade III skin toxicity; 29 (14 %) late fibrosis and 16 (8 %) telangiectasia. No pulmonary or cardiac toxicity was observed. Conclusion: Our HF-RT scheme (with or without nodal irradiation) confirms in elderly patients the data from randomized trials, both after BCS or mastectomy. Toxicity seems very acceptable but requires a longer follow-up. A larger evaluation is still ongoing in several other centres in France. Copyright © 2015 Dore et al.

178 da Silva GT, Bergmann A, Santos Thuler LC. **Prognostic factors in patients with metastatic spinal cord compression secondary to lung cancer: a systematic review of the literature**. Eur Spine J 2015;24(10):2107-13.

**Abstract:** PURPOSE: The Metastatic spinal cord compression (MSCC) secondary to lung cancer (LC) has worse prognosis when compared to MSCC related to other solid tumors. The purpose of this study is to identify the survival time and the prognostic factors in the MSCC secondary to LC.

METHODS: A systematic review of the literature has been carried out. Studies published between January 2005 and March 2015 were identified through the electronic database PubMed and LILACS. Two independent reviewers selected the articles.

RESULTS: 7 studies were identified, which met the inclusion criteria, involving 1010 patients. The survival in 6 and 12 months ranged between 18 and 61%, and between 3.8 and 32%, respectively. The median survival ranged between 2.8 and 9 months. The variables related to the survival improvement were: female, performance status 1 or 2, pre-radiotherapy and postoperative ambulatory status, absence of bone metastases and visceral metastases, interval from cancer diagnosis to spinal metastases or radiotherapy of MSCC>15 months, slower (>7 days) development of motor deficit, and the neurological status at the postoperative.

CONCLUSIONS: The prognosis of the MSCC secondary to LC was poor. Considering the small number of studies identified, further research is needed to identify prognostic factors that are independent of the MSCC secondary to LC.

179 Cohen PR. **Zoledronic acid-associated symmetrical drug-related intertriginous and flexural exanthema (SDRIFE): Report of baboon syndrome in a woman with recurrent metastatic breast cancer after receiving zoledronic acid**. Dermatol Online J 2015;21 (8) (no pagination)(2).

**Abstract:** Background: Baboon syndrome is a distinctive skin reaction in which the patient typically develops erythematous buttocks that appear similar to those of a baboon. The non-contact allergenic variant of baboon syndrome is also referred to as symmetrical drug-related intertriginous and flexural exanthema (SDRIFE). Zoledronic acid is a bisphosphonate that is used in patients with metastatic cancer to prevent bone complications. Purpose: Zoledronic acid-associated baboon syndrome is described in a woman with recurrent metastatic breast cancer. Methods: PubMed was used to search the following terms, separately and in combination: baboon syndrome, breast cancer, symmetrical drug-related intertriginous and flexural exanthema, and zoledronic acid. All papers were reviewed and relevant manuscripts, along with their reference citations, were evaluated. Results: Zoledronic acid has infrequently been associated with mucocutaneous adverse reactions. However, baboon syndrome has not previously been observed in patients receiving zoledronic acid. The reported woman developed baboon syndrome after her initial exposure to zoledronic acid. Conclusions: Non-contact allergenic drug-induced baboon syndrome has most commonly been associated with antibiotics such as beta-lactams and penicillins. Zoledronic acid-associated baboon syndrome has not previously been observed in cancer patients. Baboon syndrome (SDRIFE variant) was observed in a woman with recurrent metastatic breast cancer after her first exposure to zoledronic acid. In summary, SDRIFE can occur in oncology patients receiving zoledronic acid and zoledronic acid should be added to the list of medications associated with the potential to cause non-contact allergenic drug-induced baboon syndrome. Copyright © 2015 by the article author(s).

180 Cheon PM, Wong E, Thavarajah N, Dennis K, Lutz S, Zeng L, et al. **A definition of "uncomplicated bone metastases" based on previous bone metastases radiation trials comparing single-fraction and multi-fraction radiation therapy**. Journal of Bone Oncology 2015;4(1):13-7.

**Abstract:** The most recent systematic review of randomized trials in patients with bone metastases has shown equal efficacy of single fraction (SF) and multiple fraction (MF) palliative radiation therapy in pain relief. It is important to determine the patient population to which the evidence applies. This study aims to examine the eligibility criteria of the studies included in the systematic review to define characteristics of "uncomplicated" bone metastases. Inclusion and exclusion criteria of 21 studies included in the systematic review were compared. Common eligibility criteria were documented in hopes of defining the specific features of a common patient population representative of those in the studies. More than half of the studies included patients with cytological or histological evidence of malignancy. Patients with impending and/or existing pathological fracture, spinal cord compression or cauda equina compression were excluded in most studies. Most studies also excluded patients receiving retreatment to the same site. "Uncomplicated" bone metastases can be defined as: presence of painful bone metastases unassociated with impending or existing pathologic fracture or existing spinal cord or cauda equina compression. Therefore, MF and SF have equal efficacy in patients with such bone metastases.

181 Chen B, Xiao S, Tong X, Xu S, Lin X. **Comparison of the Therapeutic Efficacy of Surgery with or without Adjuvant Radiotherapy versus Radiotherapy Alone for Metastatic Spinal Cord Compression: A Meta-Analysis**. World Neurosurg 2015;83(6):1066-73.

**Abstract:** BACKGROUND: Spinal metastases are 20 times more common than primary spinal tumors and often cause metastatic spinal cord compression (MSCC). Clinical manifestations (e.g., pain and neurologic dysfunction) adversely affect patients' quality of life. Radiotherapy (RT), chemotherapy, and surgery are the major therapeutic strategies for MSCC. There is some evidence that combining surgery with adjuvant RT may be a better option.

METHODS: This meta-analysis compared the therapeutic efficacy of surgery (with or without adjuvant RT) with RT alone in treatment of MSCC. Comparative studies of surgery (with or without adjuvant RT) versus RT alone for the treatment of MSCC were retrieved from the MEDLINE, EMBASE, and Cochrane Library databases. Primary (1-year survival) and secondary (motor function and complications) outcomes were compared by meta-analysis.

RESULTS: Of the 26 studies originally identified, 20 were excluded (not original research, lack of relevance, no group comparison, or lack of comparable data). Compared with RT alone, surgery (with or without adjuvant RT) was associated with improvement of ambulation (odds ratio = 1.74, 95% confidence interval = 1.35-2.25, P < 0.05), pain relief (odds ratio = 3.61, 95% confidence interval = 2.75-4.74, P < 0.05), and 1-year survival (odds ratio = 1.92; 95% confidence interval = 1.37-2.71, P < 0.01). No differences in regaining walking ability and substantially longer hospital stays were observed. Surgery showed better therapeutic efficacy than RT alone with regard to quality of life and life expectancy, without additional complications.

CONCLUSIONS: Further studies are needed to investigate the effects of these interventions on quality of life and to identify the best therapeutic strategy for patients with MSCC.

182 Broder MS, Gutierrez B, Cherepanov D, Linhares Y. **Burden of skeletal-related events in prostate cancer: unmet need in pain improvement**. Support Care Cancer 2015;23(1):237-47.

**Abstract:** PURPOSE: Up to 75% of patients with prostate cancer experience metastatic bone disease, which leads to an increased risk for skeletal-related events (SREs) including pathological bone fracture, spinal cord compression, and hypercalcemia of malignancy. Our objective was to systematically review the literature on the impact of SREs on quality of life (QOL), morbidity, and survival with a primary focus on the impact of SREs on pain in prostate cancer patients.

METHODS: We searched PubMed, limiting to peer-reviewed English-language human studies published in 2000-2010. The search was based on the US Food and Drug Administration and European Medicines Agency definition of an SRE, which includes pathologic fracture, spinal cord compression (SCC), hypercalcemia of malignancy, and radiotherapy or surgery to bone resulting from severe bone pain.

RESULTS: A total of 209 articles were screened, of which 173 were excluded, and 36 were included in this review. Patients with SREs had more pain and worse survival compared with no SREs. Pathologic bone fractures worsened QOL and were associated with shorter survival. Radiation therapy of SCC alleviated pain and improved morbidity. SCC was associated with decreases in patient survival. Radiation therapy and surgery to bone improved pain.

CONCLUSIONS: Specific SREs are associated with worse outcomes, including increased pain, poorer QOL, morbidity, and survival. Treatment of SREs is associated with improved pain, although there remains a need for more effective treatment of SREs in prostate cancer patients.

183 Anonymous. **Erratum : Direct decompressive surgery followed by radiotherapy versus radiotherapy alone for metastatic epidural spinal cord compression: A meta-analysis (Spine (2014) 39 (E587-E592))**. Spine (Phila Pa 1976) 2015;40(9):E562.