



Session 4, Wednesday 7 October, 10:00-11:00 and 16:30-17:30

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Tumour, epidemiology, basic science

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### **ASYMPTOMATIC CONSTRUCT FAILURE IN METASTATIC SPINE TUMOUR SURGERY**

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#### Introduction:

Implant/Construct failures in metastatic spine tumour surgery (MSTS) are under-reported (1.9-16%). These are based on clinical presentations or revisions required for symptomatic failures (SF). The phenomenon of asymptomatic construct failure (AsCF) after MSTS has not been described.

#### Aim:

To study the incidence, onset, underlying mechanism, natural history, and the associated factors leading to AsCF after MSTS.

#### Materials and Methods:

This retrospective review prospectively collected data of 288 patients who underwent MSTS from 2005-15. Data collected were patient demographics, oncological, operative, postoperative variables, number of levels instrumented/decompressed and fixation types. Construct failures were identified through studying available serial radiographs. Risk factors and survival duration were analysed. Competing risk regression analyses with AsCF as the event of interest and SF/death as competing events. Kaplan-Meier curves were obtained for patients with AsCF, SF & no failures.

#### Results:

AsCF was observed in 41/246 patients (16.7%). Average onset of AsCF after MSTS was 2 mths (1-9 mths). Early AsCF (<3mths from index surgery) accounted for 80.5%, while late AsCF (>3mths) were observed in 19.5%. Early AsCF occurred due to: 1) reduction of body height of the vertebra within the construct in patients with only posterior instrumentation (n=22); 2) cage subsidence/tilting in patients with anterior column reconstruction (n=11). Increasing age(p<0.02) and primary breast [(13/41)31.7%](p<0.01) tumours were associated

with higher rates of AsCF. The frequencies of various radiological failure were screw ploughing=15; loosening=15; pullout=3; cutout=8; breakage=2; and cage subsidence=6; displacement=1; breakage=0; rod breakage=1; and angular deformity (increase in kyphosis=25; decreased lordosis=4). Most common radiologically detectable AsCF mechanism was angular deformity (increase in kyphosis) in 29 patients, followed by screw ploughing or loosening in 15 patients each. There was a trend towards AsCF in patients with SINS $\geq$ 7, instrumentation across junctional regions and construct length of 6-9 levels, although the associations were not significant. Median survival of AsCF patients: 20mths (3-95mths) in patients with early failure and 41mths (11-92mths) in patients with late failure. Average follow-up duration was 20 mths. None of the AsCF patients underwent revision surgery during the study period.

#### Conclusion:

Majority of early AsCF were clinically inconsequential and need no intervention. Late failure was seen in patients who survived longer and maintained ambulation for a longer period. This may be due to the failure of fusion and/or late recurrence of tumours. Though AsCF does not need aggressive or urgent intervention, we recommend periodic investigations/follow-up to detect progressive construct failure. Increasing age and patients with primary breast tumour have a higher possibility of AsCF after MSTs.

#### Disclosures:

author 1: none; author 2: none; author 3: none; author 4: none

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### **ANALYSIS OF UNPLANNED READMISSIONS IN PATIENTS UNDERGOING METASTATIC SPINE TUMOUR SURGERY (MSTS)**

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#### Introduction:

Readmission rates indicate quality of care and identify target areas for quality improvement in patients undergoing metastatic spine tumour surgery (MSTS).

#### Aim:

To analyse the risk factors associated with unplanned readmission within 30, 90-days and 12-mths following MSTs.

#### Materials and Methods:

This is a retrospective study on patients who underwent MSTs from 2005-17. Patients were followed-up until 2-yrs post-op or until their demise, whichever occurred earlier. Of 303 patients, complete data were available for 272 for final analysis.

Outcome Measures include: Number of 30, 90-days and 12-mths readmissions following index MSTs, and index length of hospital stay (LOS).

Data collected included demographics, Charlson co-morbidity index, Tokuhashi & Bilsky scores, primary tumour type, radiotherapy (RT), operative details, blood loss, LOS and number of readmissions until 2 years post-operatively or until death, with reasons and duration of each readmission.

Definition of: 30-day readmission - any readmission  $\leq$ 30days excluding those with >30days' index hospital stay; 90-day readmission any readmission of >30 to  $\leq$ 90days; and 12-mths readmission - any readmission >90days to  $\leq$ 12mths all following index MSTs.

#### Results:

A total of 272 patients (127F:145M); mean age 60.3, were analysed. Subsidized:Private patients 203(75%): 69(25%). 205(75%) patients underwent open surgery, 65(24%) minimally invasive surgery (MIS) and 2(0.74%) hybrid surgery. Pre-op RT was administered to 42(15.5%) patients and post-op to 187(68.75%). Immediate post-op complications occurred in 87(32%) patients during index hospital stay, where 30 had non-surgical related infections. Forty (15%) patients had  $\geq$ one 30-day, 58(21.32%) had  $\geq$ one 90-day and 89(32.72%) had  $\geq$ one 12-mth readmissions. Pre-operative ECOG score significantly affected 30-day readmission ( $p=0.047$ ) while blood loss affected 90-day readmission ( $p=0.035$ ) and Tokuhashi score influenced 12-mth readmission ( $p<0.001$ ). We observed 318 unplanned readmissions, with 41 Thirty-day, 104 Ninety-day and 173 Twelve-mth readmissions. Analysing 30-day readmissions, 12.2%(5/41) were caused by wound infections and 7.32%(3/41) were disease-related causes (e.g. neutropenic fever, sepsis, worsening of disease-related symptoms). Wound infection led to 90-day readmissions in 1%(1/104) of patients, while disease-related complications resulted in 12.5%(13/104). 12-mth readmissions: 2.31%(4/173) were due to wound infections; 17%(29/173) were subsequent to disease-related complications.

#### Conclusion:

Unplanned readmissions are not uncommon and they are more frequent compared to other subspecialties. Most common reason for 30, 90-day and 12-mth readmission were urological, side-effects of definitive treatment (RT/CT) and loco-regional disease progression respectively. Readmissions >12 mths post-op arise due to visceral/skeletal metastatic spread secondary to resistance of tumour to mainline oncological treatment.

#### Disclosures:

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## **IS THERE AN OPTIMAL TIMING BETWEEN RADIOTHERAPY AND SURGERY TO REDUCE WOUND COMPLICATIONS IN SPINAL METASTASES? A SYSTEMATIC REVIEW**

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**Introduction:** Surgery with radiotherapy (RT) is more effective in treating spinal metastases, than RT alone. However, RT administered in close proximity to surgery may predispose to wound complications. Limited guidelines exist on the optimal timing between RT and surgery. **Aim:** To address whether pre-operative RT (preop-RT) and/or post-operative RT (postop-RT) is associated with wound complications and to define the safe interval between RT and surgery or vice versa.

**Materials and Methods:** This systematic review is based on published literature with inclusion criteria: (i) Articles in English (ii) Patients with age  $\geq$ 18 yrs (iii) Articles dealing with spinal metastases, treated with surgery and RT (preop-RT and/or postop-RT). The MeSH terms

included in the search criteria were spine, neoplasms, neoplasm metastasis, laminectomy, surgery, radiotherapy, wounds and injuries, wound healing, wound infection; and free text words included spinal, vertebra, cancer, malignancy, metastasis, vertebrectomy, corpectomy, radiation therapy, irradiation, stereotactic, wound problem, wound complication, wound dehiscence, major wound complication, and wound breakdown. The MeSH terms and free text words were used systematically to develop search strings and conduct our search in PubMed, Scopus and Embase databases (up to February 2019). We obtained 664, 165 and 1503 articles respectively, adding up to 2332 articles. After applying exclusion criteria and reading the titles and abstracts, we obtained 60 relevant articles. Further removal of duplicates resulted in 46 articles. We screened the full text of 46 articles and shortlisted 27 articles for data extraction. Fourteen additional articles were identified by hand-search, leading to a total of 41 articles, which have been included in this systematic review.

**Results:** All 41 articles mentioned wound complications/healing. Sixteen articles discussed preop-RT, 8 postop-RT, 15 both, and 2 mentioned intraoperative-RT with additional pre/postop-RT. Twenty studies mentioned surgery-RT time interval; where only one article concretely concluded that radiation-surgery interval of  $\leq 7$  days led to high wound complication rates. Seven studies reported significant association between preop-RT and wound complications. Of these, 4 studies observed a higher risk of infection in patients receiving preop-RT as compared to postop-RT.

**Conclusion:** The findings of this systematic review do not provide sufficient evidence to draw definite guidelines about the optimal radiation-surgery interval. However, based on published literature and expert opinions available, we conclude that an interval of 2 weeks with a minimum of 7 days is optimum between RT and surgery or vice versa; this can be reduced further by postop-stereotactic body RT. If the RT-surgery window is  $>12$  months, wound-complications rise. Postop-RT has fewer wound complications versus preop-RT.

Disclosures:

author 1: none; author 2: not indicated; author 3: none; author 4: none; author 5: none; author 6: none

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### **METASTATIC SPINAL CORD COMPRESSION IN THE PAEDIATRIC POPULATION-A SYSTEMATIC REVIEW AND FORMULATION OF NATIONAL GUIDELINES**

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**Study Design:** Systematic review

**Introduction:**

Metastatic Spinal Cord Compression (MSCC) has been noted in 3-5% of children with primary tumours. MSCC can be associated with permanent neurological deficits and prompt treatment is necessary. Our aim was to perform a systematic review on MSCC in children  $< 18$  years to help formulate national guidelines.

**Methods:**

A systematic review of the English language was undertaken using the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) guidelines. Search criteria included 'MSCC in children, paediatric and metastases' for papers published between January 1999-September 2019. Isolated case reports/case series with  $<10$  patients were excluded.

**Results:**

From a total of 17 articles identified, a final 4 were analysed (Level III/IV). Neuroblastoma

constituted the most common cause for MSCC in children (53.9%) followed by sarcoma (13%). Soft tissue sarcomas constituted the most frequent cause of MSCC in children >5 years old. The median age at time of diagnosis was 53.2 months. MSCC was the initial manifestation of the disease in 71% patients. A multimodality approach to treatment was utilised depending on the primary tumour. The prognosis for neurological recovery was found to be inversely proportional to the degree of neurological deficits and duration of symptoms. Conclusion:

In children with neuroblastoma/Ewing sarcoma/Lymphoma, chemotherapy was the primary treatment. Early surgery should be a consideration with rapid deterioration of neurology despite chemotherapy.

Multimodality approach including chemo-radiotherapy and surgery should be the treatment of choice in metastatic sarcomas. It is worth noting that multi-level laminectomy/decompression and asymmetrical radiation to the spine can lead to spinal column deformity in the future.

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### **NANOPARTICLE-FUNCTIONALIZED POLY-METHYL METHACRYLATE BONE CEMENT FOR SUSTAINED CHEMOTHERAPEUTIC DELIVERY**

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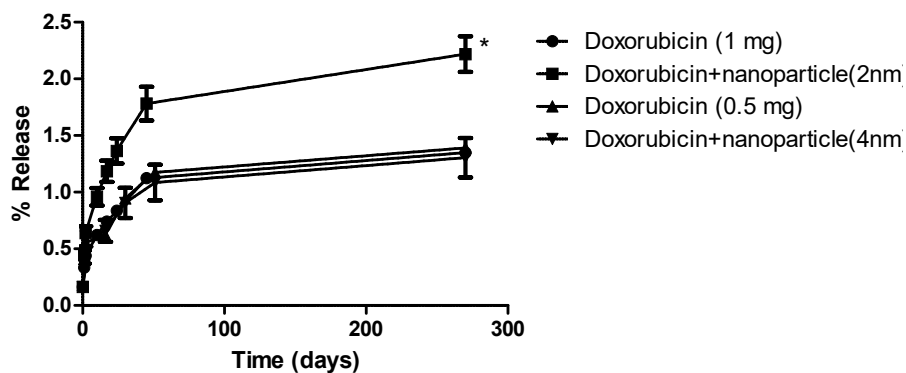
**INTRODUCTION:** Poly-methyl methacrylate (PMMA) bone cement is one of the most commonly used bone substitutes in spine surgery. In clinical practice it can be loaded with various drugs, such as antibiotics or anti-cancer therapeutics, as a means of local drug delivery. However, studies have shown that drugs loaded into PMMA cement tend to release in small bursts in the first 48-72 hours, and the remaining drug is trapped without any significant release over time. The objective of this study is to develop a nanoparticle-functionalized PMMA cement for use as a sustained doxorubicin delivery device. We hypothesize that PMMA cement containing mesoporous silica nanoparticles will release more doxorubicin than regular PMMA

**METHODS:** High viscosity SmartSet™ PMMA cement by DePuy Synthes was used in this study. The experimental group consisted of 3 replicates each containing 0.24 g of mesoporous silica nanoparticles (nanoparticle size was 2 μm with either 2 nm or 4 nm pore size), 1.76 g of cement powder, 1ml of liquid cement monomer and 0.5 or 1 mg of doxorubicin. The control group consisted 3 replicates each containing 2.0 g of cement powder, 1ml of liquid cement monomer and 0.5 or 1 mg of doxorubicin. The experimental group contained an average of 8.18 ± 0.008 % (W/W) mesoporous silica nanoparticles. Each replicate was casted into a cylindrical block and incubated in a PBS solution which was changed at predetermined intervals for 9 month. The concentration of eluted doxorubicin in each solution was measured using a florescent plate reader. The mechanical properties of cement were assessed by unconfined compression testing. The effect of the doxorubicin released from cement on breast tumor cell metabolic activity was assessed using the Alamar Blue test.

**RESULTS:** Following 9 month of incubation, it was noted that the initial amount of doxorubicin loaded onto the cement did not affect the rate of release. Furthermore, the

nanoparticles with 4nm pore size did not increase the amount of doxorubicin released from the cement. Finally, the PMMA cement functionalized with nanoparticles with 2 nm pore size released  $2.20 \pm 0.28$  % of the initially loaded doxorubicin which was more than the  $1.35 \pm 0.02$  % released by the control group ( $p < 0.002$ ). There was no statistically significant difference in Young's elasticity modulus between groups ( $p > 0.53$ ). Nanoparticle functionalized PMMA suppressed the metabolic activity of breast cancer cells by 69 % ( $p < 0.05$ ).

**CONCLUSIONS** Nanoparticle-functionalized PMMA cement can release up to 1.63 times more doxorubicin than the standard PMMA and can result in a sustained drug release over a period of 9 month. The use of mesoporous silica nanoparticles to improve drug release from PMMA cement shows promise. In the future, in vivo experiments are required to test the efficacy of released doxorubicin on tumor cell growth.



Doxorubicin release from PMMA cement over a 9 month period, \* denotes statistically significant difference ( $p < 0.05$ )

Disclosures:

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## FOSTERING PHYSICAL ACTIVITY AFTER COMPLEX LUMBAR SPINE SURGERY: LONG-TERM RESULTS OF A RANDOMIZED TRIAL

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**Background:** Many patients maintain sedentary lifestyles after lumbar surgery because of fear of injury, pain, deconditioning, and habit, and thus incur potential long-term adverse consequences (i.e. Sedentary Death Syndrome). We previously showed the effectiveness of an RCT intervention to increase prudent physical activity at the 4-month short-term follow-up. However, beneficial effects of activity interventions often are noted in the short-term, and extinguish with time.

**Purpose:** To determine the sustainability of an intervention to increased physical activity, primarily walking, after 12 months

**Sample:** 230 patients, enrolled 3 months after complex lumbar surgery, cleared by surgeons to increase physical activity, followed for 12 months

Outcome: Paffenbarger Physical Activity and Exercise Index (PAEI) at 12 months

Methods: During routine 3-month postop visits, 110 intervention patients received 1) a booklet about benefits of physical activity and national activity guidelines 2) instruction on how to increase lifestyle walking 3) a calibrated pedometer 4) made a self-contract specifying walking goals and 5) received periodic telephone encouragement early in the trial. 120 controls received information about safe physical activity. At enrollment all patients completed the valid 3-domain PAEI measuring number of blocks walked and stairs climbed daily and sports during the past week. Kcal/week were calculated for each domain and for an overall total. Operative records were reviewed and a Surgical Invasiveness Index (SII) value (reflecting complexity) was calculated (max 10 points/vertebral level). Multivariable analyses considered within-patient enrollment to 12-month follow-up change in Kcal/week, controlling for demographic and clinical characteristics.

Results: At enrollment intervention and control groups were similar in mean age (64 vs 63), men (55% vs 51%), median SII value (11 vs 11), PAEI walking Kcal/week (1418 vs 1311), and PAEI overall total Kcal/week (1786 vs 1754) (all  $p > .05$ ). Mean time from surgery to enrollment was 2.9 months, and from enrollment to long-term follow-up was 12.6 months. The within-patient mean increase in PAEI walking was 860 vs 365 Kcal/week; in multivariable analysis with change in PAEI walking as the dependent variable and controlling for age, sex, and surgical complexity, intervention group remained associated (estimate 563, 95% CI 70-1057,  $p = .03$ ). The increase in PAEI overall total was 1294 vs 758 Kcal/week; in similar multivariable analysis intervention group remained associated (estimate 642, 95% CI 75-1209,  $p = .03$ ).

Conclusions: A psychosocial intervention in the spine care setting was successful in increasing and then sustaining gains in physical activity up to 12 months after lumbar surgery. Our study highlights the potential for interventions to foster new physical activity habits that diminish sedentary lifestyles and thus promote long-term spine and overall health.

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