Vertebroplasty as a palliative treatment option for intractable pain in pediatric patients with spinal tumors

Leandro Cardarelli Leite[1], Shahrad Rassekh[2], Robert D'Ortenzio[3], and Manraj Heran[4]

[1]University of Western Ontario
[2]British Columbia's Childen's Hospital
[3]The University of British Columbia
[4]University of British Columbia

March 23, 2021

Abstract

Background: Primary and secondary malignant tumors of the spine are relatively uncommon in the pediatric population but are associated with high morbidity and significantly decreased quality of life due to pain. Local management of these tumors is often challenging due to the importance of maintaining vertebral mechanical integrity as well as the spinal growth potential. Typically, surgery and/or radiation therapy have been used in the primary management of these tumors. However, treatment options become more limited when there is relapse or refractory disease, with re-resection or additional radiotherapy often not being viable therapies. The purpose of this study was to assess the feasibility of percutaneous vertebroplasty as a palliative treatment for intractable pain secondary to malignant tumors affecting the spine. Procedure: A retrospective review of all cases of vertebroplasty performed at a single institution between 2003 and 2020. Results: A total of 11 vertebral levels were treated in 3 children with relapsed cancers (two with alveolar rhabdomyosarcoma, and one with Wilms tumor). All three had clinical benefit with sustained significant improvement in their pain. Conclusions: Vertebroplasty is a currently underutilized modality that might provide excellent pain palliation in cases of relapsed cancer in the spine. Future prospective studies of its use in pediatric oncology are needed.

Vertebroplasty as a palliative treatment option for intractable pain in pediatric patients with spinal tumors

Authors:

Leandro Cardarelli-Leite[1]; Shahrad Rod Rassekh[2]; Robert D'Ortenzio[3]; Manraj Kanwal Singh Heran[3,*]

[1]Division of Interventional Radiology, Department of Medical Imaging, Western University, London, ON, Canada

[2]Division of Hematology, Oncology and BMT, Department of Pediatrics, University of British Columbia, Vancouver, BC, Canada[3]Department of Radiology, University of British Columbia, Vancouver, BC, Canada

*Corresponding author:

M.K.S. Heran

BC Children's Hospital

4500 Oak St

Vancouver, BC

V6H 3N1

Tel.: +1 604 875 2131; fax: +1 604 875 2367

E-mail address: mheran@cw.bc.ca

Word count

Abstract: 206

Manuscript: 3165

Number of tables: 2

Number of figures: 1

Short running title: Vertebroplasty for intractable pain in children

Keywords: Pediatric cancer, vertebroplasty, spinal tumor, rhabdomyosarcoma, palliative care

Abbreviations

ALL	Acute lymphoblastic leukemia
CT	Computed-tomography
INR	International normalized ratio
IR	Interventional Radiologists
MRI	Magnetic resonance imaging
ODI	Oswestry disability index
PET	Positron emission tomography
PMMA	Polymethyl methacrylate
RT	Radiotherapy
VAS	Visual analog scale

Abstract:

Background: Primary and secondary malignant tumors of the spine are relatively uncommon in the pediatric population but are associated with high morbidity and significantly decreased quality of life due to pain. Local management of these tumors is often challenging due to the importance of maintaining vertebral mechanical integrity as well as the spinal growth potential. Typically, surgery and/or radiation therapy have been used in the primary management of these tumors. However, treatment options become more limited when there is relapse or refractory disease, with re-resection or additional radiotherapy often not being viable therapies. The purpose of this study was to assess the feasibility of percutaneous vertebroplasty as a palliative treatment for intractable pain secondary to malignant tumors affecting the spine.

Procedure: A retrospective review of all cases of vertebroplasty performed at a single institution between 2003 and 2020.

Results: A total of 11 vertebral levels were treated in 3 children with relapsed cancers (two with alveolar rhabdomyosarcoma, and one with Wilms tumor). All three had clinical benefit with sustained significant improvement in their pain.

Conclusions: Vertebroplasty is a currently underutilized modality that might provide excellent pain palliation in cases of relapsed cancer in the spine. Future prospective studies of its use in pediatric oncology are needed.

INTRODUCTION

Malignant spine tumors are relatively rare in the pediatric population, with primary tumors such as Ewing sarcoma and osteosarcoma comprising less than 1% of all spine tumors [1]. However, neoplasms such as lym-

phoma, neuroblastoma, and sarcoma can metastasize to the spinal axis and are not uncommon in clinical practice[2,3]. Although the development of new treatments may have improved overall survival, spinal tumors carry significant morbidity with risk of pathologic fracture and possible vertebral collapse with associated segment instability, spinal cord compression, and nerve root impingement [3]. These structural changes often require prompt treatment and may require a multidisciplinary approach involving neurosurgeons, orthopedic surgeons, oncologists, radiation oncologists, pain specialists and interventional radiologists (IR). In a palliative context where pain control is fundamental to improve the overall quality of life, spinal tumors often present a significant challenge in children [4].

Minimally invasive spinal procedures performed by IR, such as tumor ablation and cementoplasty (vertebroplasty or kyphoplasty), are well accepted treatments for cancer-related pain or local disease control in adults with spinal tumors [5,6]. These treatments can be used independently or in combination to provide pain relief and improve quality of life [6]. However, the epidemiology, tumor histologic types and comorbidities of adults are completely different from oncologic pediatric patients. The value of these procedures in the pediatric population are still being investigated, with limited published literature available. The purpose of this study was to assess the feasibility of percutaneous vertebroplasty in children as a palliative treatment for intractable pain secondary to malignant tumors affecting the spine.

METHODS

A retrospective review of the patient's charts, imaging, and electronic medical records was performed following approval from the Institutional Review Board to identify pediatric patients that underwent vertebroplasty between January 2003 and April 2020. Clinical success and long-term complications were assessed by retrospective chart review of hospital records. Baseline characteristics of the patients and their tumors, use of pain medications, overall clinical status, and performance status were collected before and after the procedures, as well as any adverse event related to the vertebroplasty procedure.

Case Selection

Indication for intervention included *(i)* vertebral fracture secondary to advanced cancer or its treatment *(ii)* with clinically significant pain that affected quality of life and function *(iii)* that was refractory to optimized pharmacological treatment or where radiotherapy was contra-indicated due to previous radiation or extent of disease. Decision to intervene was reached following discussion at the multidisciplinary tumor board involving clinical oncology, surgery, radiation oncology, orthopedic surgery, and IR.

Pre-vertebroplasty work-up

The patient and caregivers were informed of the risks and benefits of the procedure, as well as the paucity of evidence for the procedure in the pediatric setting, and written informed consent was obtained. Since all patients had spine, chest, or abdominal computed-tomography (CT) or magnetic resonance imaging (MRI) performed for other reasons less than 3 months prior to vertebroplasty, no further imaging was necessary prior to the intervention. Platelet count of >50,000/mcL and INR < 1.5 were required to proceed. Any supplementary laboratory workup deemed necessary by the anesthesiologist was completed.

Vertebroplasty technique

The patients were transferred to the IR suite, were intubated, and received general anesthesia. They were positioned prone on the fluoroscopy table and the skin of the back prepped and draped as per standard sterile technique. Using biplanar fluoroscopic-guidance, the interventional radiologist advanced a 13-gauge or 15-gauge bone needle via a costrotransverse (for thoracic vertebral bodies) or transpedicular (for lumbar vertebral bodies) approach using a surgical mallet, into the midline of the anterior third of the targeted vertebral body, following previously described technique in adults [7]. Under continuous fluoroscopy, the polymethyl methacrylate (PMMA) cement was injected. Care was taken to ensure no cement extravasated beyond the margins of the vertebral body, especially into the spinal canal, or into the venous system. After achieving adequate distribution within the vertebra and waiting the necessary time for polymerization of the cement, the needle was removed. Patients recovered in the acute care unit for 4-6 hours to recuperate

from anesthesia and then were transferred to the general ward for overnight observation with discharge the following morning.

Post-vertebroplasty follow-up

No specific imaging study was necessary to assess the treated vertebral body during follow-up unless there was no pain improvement after 2 weeks or if the patient developed new or acute worsening of back pain after initial clinical improvement.

RESULTS

Three patients were identified, with a total of 11 vertebral levels treated (Figure). All three patients had relapsed refractory solid tumors with multilevel metastatic disease. Demographics and procedure details have been summarized in Table 1.

Case 1

A 14-year-old patient presented with widely metastatic alveolar rhabdomyosarcoma and extensive disease throughout the pelvis, abdomen and chest and multiple bony metastases in the long bones and vertebrae. She was treated with 12 weeks of standard chemotherapy including vincristine, actinomycin and cyclophosphamide, and a PET-CT scan showed complete response. Given that the site of primary tumor was unclear at diagnosis and that radiation to all sites of disease was not possible, the patient received additional 12 weeks of chemotherapy, followed by consolidation with high dose chemotherapy with autologous stem cell rescue. There was disease progression at 9 months post treatment with widespread metastases in the chest, abdomen and pelvis, as well as in the T7 and T12 vertebral bodies, causing significant pain in the back and lower extremities. The patient received salvage chemotherapy with irinotecan and temozolomide, with good response. However, there was ongoing severe back pain (7/10) which was refractory to oral morphine 10 mg six times a day, and deterioration of the performance status with a Lansky score dropping from 100 to 70. Multidisciplinary decision was for vertebroplasty of the two levels, which occurred uneventfully. The pain reduced to 5/10 seven days after the procedure and the opioid intake decreased to oral morphine 10 mg twice a day. Over the next three weeks, the pain completely resolved (0/10) and the Lansky score improved to 100. The patient returned to playing competitive high-level basketball and participated in other high impact activities including skydiving. Palliative chemotherapy was continued, and the patient remained pain free and off all pain medications for three months, at which time there was tumor progression in the pelvis. Back pain returned seven months after vertebroplasty, shortly before the patient passing from pulmonary metastatic disease.

Case 2

A 9-year-old patient with Wilms tumor was treated with vincristine, actinomycin, doxorubicin and then upstaged due to poor response to more aggressive chemotherapy, including carboplatin, etoposide, doxorubicin, cyclophosphamide, and whole abdominal radiation. He presented three years later with a paravertebral mass at L3 with no other sites of disease. His relapse was not responsive to salvage chemotherapy with vincristine and temozolomide and re-irradiation was not possible. He was pain free and multidisciplinary decision was to perform vertebroplasty for local tumor control. The procedure was uneventful and was able to stabilize tumor growth for five months, when he developed intermittent right leg pain due to tumor progression. This required a combination of oral acetaminophen with codeine, and gabapentin for management. Chemotherapy was stopped and new vertebroplasty was done at the L3 level. His pain resolved over the next three weeks and he stopped all oral pain medications. His disease remained stable for 14 months, when it again relapsed at the L3 level, causing intermittent right leg pain requiring gabapentin. Cryoablation of the tumor was performed. His pain progressed during the first 48-hours post-procedure, requiring increased doses of gabapentin and codeine. Three weeks after the thermal ablation, his pain had completely resolved, with all pain medications discontinued. His pain returned three months later and was severe, requiring palliative radiation that stabilized his disease for the next 18 months. At age 13, he had further recurrence at the L3 level, which was again associated with severe pain requiring high doses of oral morphine and gabapentin. A

new vertebroplasty was done, with significant reduction in his pain medications over the next month. He passed five months after his last intervention.

Case 3

A 6-year-old patient with prostatic alveolar rhabdomyosarcoma presented with metastatic disease to lymph nodes and long bones, ribs, and numerous vertebrae. He developed disease progression at multiple vertebral levels 17 months after initial diagnosis, associated with significant back pain. Palliative radiation with 2000 cGy in four fractions was given to his spine from T5 to L4, with pain improvement. However, his pain returned three months later and was difficult to manage, requiring continuous fentanyl and ketamine infusions, clonazepam, acetaminophen, lorazepam and ibuprofen. He had multilevel vertebroplasty performed in two stages, one week apart. First, T1, T6, T7, and T9 were treated, followed by T11, L2, L3 and L4. His pain improved significantly over the next 30 days, and he was able to be discharged home with palliative care support and passed three months following his last intervention.

DISCUSSION

Primary pediatric spinal tumors are rare, however, up to 5% of children with extra-spinal solid malignancies develop metastasis to the spine secondary to contiguous invasion or hematogenous spread[8]. When curative intent is no longer achievable in patients with spinal malignancies, the main goals of treatment shift towards preservation of function and improving quality of life via pain control. Cancer-related pain can pose significant psychological and physical burden to pediatric patients, resulting in a negative impact on quality of life [9]. Adequate palliative pain management can be challenging, requiring multimodality treatment strategies to provide adequate control. This may include oral or intravenous medications, surgery, radiotherapy (RT) and minimally invasive procedures such as thermal ablation or cementoplasty[10].

Prescribing opioids is a valid initial strategy and is recommended by the World Health Organisation in their two-step approach for the treatment of severe cancer-related pain in children[10,11]. However, opioids have a well-established side effect profile including constipation, drowsiness, pruritis and nausea[12]. In addition, opioids pose other risks, such as tolerance, withdrawal, and dependence syndrome. For patients with pain refractory to optimized opioid dose escalation and despite other adjuvant medications (e.g., gabapentin or amitriptyline), alternatives become limited.

Continuous intravenous infusions of lidocaine or ketamine have been used to treat pain that is refractory to opioids [13,14]. Lidocaine infusion, unfortunately, requires admission to the intensive care unit for continuous monitoring during drug initiation and dose titration due to risks of bradycardia, respiratory depression and seizure [13]. Courade *et al* . recently published a prospective multicentric trial to evaluate the efficacy of continuous infusion of low-dose ketamine through the course of three days as adjunctive therapy in 38 children and adolescents with persistent pain[14]. Most of the patients in this study were being treated palliatively for solid malignancies and 97% of them were already receiving intravenous morphine for pain management. The continuous infusion of ketamine significantly reduced the visual analog scale of pain (VAS) in 50% of the studied population. However, opioid-sparing effect was only achieved in four of the 38 patients. More worrisome, 23% of the enrolled patients experienced poor tolerance to the trialed treatment. Even though these studies included patients with different tumor histologic types, they show that even non-invasive therapies may have complications and limitations. The potential advantages of vertebroplasty over infusion therapy might include shortened hospital stay after the procedure, elimination of the need for intensive care monitoring, the procedure being well tolerated even in young children, and the reduction in dose or elimination of the need for opioids following the intervention. Nevertheless, comparative prospective trials are needed to confirm these benefits.

Surgery for patients with advanced spinal tumors usually does not have a curative intent [15]. The most common surgical techniques in this population include laminectomy for spinal cord decompression, resection of metastatic intraspinal tumors to prevent neurological compromise, or removal of epidural disease to allow radiotherapy. Surgery frequently requires posterior stabilization with instrumentation to prevent instability [16]. Overall, invasive spine surgery in children poses a significant morbidity with reported complication rates

at 19-21% and include spinal cord shock and nerve root damage, with an inpatient mortality rate of 3%[16,17]. In patients with refractory pain and with poor oncological prognosis, minimally invasive techniques may provide a more reasonable option, especially if life expectancy is thought to be short. In this study, recurrent pain was observed only after disease progression and few weeks before the patients passing.

RT has an important role in the palliative treatment of pediatric spinal tumors [18]. A survey involving an international research consortium found that the most common indication for palliative radiation was pain management (43%), with the spine being the second most common targeted area (14%) [19]. Rao et al.[20] described pain relief in 83% of their treated patients, with 43% able to decrease their daily dose of opioids[20]. When compared to curative RT, palliative RT is better tolerated and has fewer side effects, with a grade [?]3 toxicity occurring in only 4% of patients [20,21].

Nonetheless, palliative RT still represents a small percentage of the indications in children when compared to the adult population[19]. Part of this may be explained by the fact that fewer investigations have been published in the pediatric literature and most practices are translated from the adults guidelines[22]. Another potential factor limiting the use of palliative RT in children may be the logistics involved in treatment. Younger patients may require anesthesia for adequate immobilization, and parents may face economic challenges involving travel costs and time away from work [19,23]. These can be problematic since palliative RT regimens frequently require multiple sessions[21]. It is also important to note that, as the median survival after palliative RT is 3.6 months, a patient having to repeatedly come to hospital for RT may not be ideal[20]. Vertebroplasty has the advantage of being able to be performed in a single setting, thereby decreasing the number of hospital visits and potential costs involved. Future cost-analysis studies are necessary to confirm this hypothesis.

Percutaneous vertebroplasty is a minimally invasive image-guided procedure that injects PMMA cement within a collapsed vertebral body, to provide pain relief and mechanical stabilization. The cement polymerisation generates an exothermic reaction, destroying tumor and bone nerve endings within a 3 mm margin of the cement[7]. Additionally, the cement consolidates and stabilizes fractured fragments and prevents further vertebral body collapse [7]. Vertebroplasty is recommended by several adult medical societies for the palliative treatment of painful oncologic fractures or weakened vertebral bodies secondary to neoplasms, with a reported clinical success of 92% and major complication rate $< 1\%$ [24–29]. Vertebroplasty can be performed under conscious sedation or general anesthesia and takes approximately 15-30 minutes, with an increment of 5-15 minutes for any additional vertebral level treated [7].

Vertebroplasty is associated with significant pain reduction and increase in the level of function, with sustained long-term benefit. A recently published systematic review included 1445 adults with spinal malignancies that underwent palliative vertebroplasty alone for the treatment of painful pathologic fractures [30]. Baseline weighted average Oswestry Disability Index (ODI) was 74.7, with a Visual Analog Scale (VAS) of 7.5. Both scores significantly decreased following intervention and demonstrated sustained long-term benefit, with ODI of 28.9 and VAS of 3.0 after 1-year follow-up [30]. This publication also confirmed the safety profile of the procedure, with a very low incidence of symptomatic complications (1.4%), which included radiating pain, transient chest pain, radiculopathy without palsy, hemothorax, hematoma, radicular neuritis, asymptomatic and symptomatic pulmonary embolisms, bilateral leg motor deficits, cauda equina, and complete paraplegia. Pain might increase immediately after the procedure and is likely related to muscular spasm, and the full pain relief benefit following intervention may take up to two weeks. Cement leak can occur but the vast majority are asymptomatic and usually of no clinical significance [30]. Since these studies were performed in adults, the true benefit and complication risks in the pediatric population still needs further investigation.

All three patients treated with vertebroplasty in this retrospective study described significant pain improvement, with Patient 1 and 2 no longer requiring oral medications. Few cases of vertebral augmentation for pain control have been reported in pediatric patients and are summarized in Table 2 [31–35]. Patients were treated with kyphoplasty and vertebroplasty in four of the five case reports and only two of the eight patients that were treated had an underlying malignancy [33,34]. There is no evidence of clinical superiority

of kyphoplasty over vertebroplasty, nor demonstration of lower incidence of complications [36]. Kyphoplasty may require longer procedural times due to its increased technical complexity, has higher equipment costs, and typically requires larger needles for access which theoretically could increase complication risks[36].

Vertebroplasty in the pediatric setting could potentially affect the normal development of the vertebral body due to mechanical restriction of growth or thermal disruption of the growth plate. Nonetheless, this has not been observed by other authors after a mean follow-up of 3 years (ranging from 3 months to 8 years) [34]. In pediatric patients with spine metastasis, the median survival of those who have the need to undergo radiation therapy or surgery, or who develop a pathologic fracture or spinal cord compression, is less than one year[37]. Therefore, the theoretical concerns of growth restriction should be weighed against the patient's symptoms and potential benefit of the procedure.

Although the patients in the current study had pain secondary to metastatic disease to the spine, vertebroplasty could be useful in managing pain in other pediatric oncological scenarios. For instance, in patients with acute lymphoblastic leukemia (ALL) since up to 16% may have vertebral fractures at the time of diagnosis [38]. Additionally, vertebroplasty could be a useful treatment in patients who develop painful vertebral fractures due to treatment-induced osteoporosis [39]. Since these indications were not assessed on the current study, further investigation is required.

This study has several limitations. First, it is retrospective and did not allow for homogeneous assessment of patient reported outcomes or quality of life measures to capture the overall impact of the intervention. Second, the number of patients included is very small. In addition, all three patients had metastatic disease to the spine rather than a primary bone-based malignancy, and the application of this intervention in patients with primary spine tumors is still unknown. Patient 1 received neoadjuvant chemotherapy at the time of vertebroplasty, and Patients 2 and 3 had received recent palliative radiation prior to the procedure. This may confound the reported improved pain post vertebroplasty and make it challenging to truly quantify the overall impact of the intervention. However, in all three cases where vertebroplasty was performed, there was significant reduction in pain and medication use, and there was evidence of sustained tumor and pain response in two cases. This improvement would be consistent with published data in the adult literature.

In conclusion, vertebroplasty in children with spinal bony metastases may provide improved pain control with attendant reduction in the need for pain medications. This procedure could provide an additional option to accompany medical or radiation therapies for pain control in the palliative context and increased awareness of this treatment option could improve the quality of life for children and adolescents with vertebral tumors.

Conflict of Interest Statement The authors have nothing to disclose.

Acknowledgments

None.

REFERENCES

1. Ravindra VM, Eli IM, Schmidt MH, Brockmeyer DL. Primary osseous tumors of the pediatric spinal column: review of pathology and surgical decision making. *Neurosurg Focus* . 2016;41(2):E3. doi:10.3171/2016.5.FOCUS16155

2. Kelley SP, Ashford RU, Rao AS, Dickson RA. Primary bone tumours of the spine: A 42-year survey from the Leeds Regional Bone Tumour Registry. *Eur Spine J* . 2007;16(3):405-409. doi:10.1007/s00586-006-0188-7

3. Kim HJ, McLawhorn AS, Goldstein MJ, Boland PJ. Malignant Osseous Tumors of the Pediatric Spine. *J Am Acad Orthop Surg* . 2012;20(10):646-656. doi:10.5435/JAAOS-20-10-646

4. Kaye EC, Friebert S, Baker JN. Early Integration of Palliative Care for Children with High-Risk Cancer and Their Families. *Pediatr Blood Cancer* . 2016;63(4):593-597. doi:10.1002/pbc.25848

5. Kam NM, Maingard J, Kok HK, et al. Combined Vertebral Augmentation and Radiofrequency Ablation in the Management of Spinal Metastases: an Update. *Curr Treat Options Oncol* . 2017;18(12):74.

doi:10.1007/s11864-017-0516-7

6. Lee SK, Weiss B, Yanamadala V, Brook A. Percutaneous Interventional Management of Spinal Metastasis. *Semin Intervent Radiol* . 2019;36(3):249-254. doi:10.1055/s-0039-1694698

7. Heran MKS, Legiehn GM, Munk PL. Current Concepts and Techniques in Percutaneous Vertebroplasty. *Orthop Clin North Am* . 2006;37(3):409-434. doi:10.1016/j.ocl.2006.05.001

8. Sciubba DM, Hsieh P, McLoughlin GS, Jallo GI. Pediatric Tumors Involving the Spinal Column. *Neurosurg Clin N Am* . 2008;19(1):81-92. doi:10.1016/j.nec.2007.09.008

9. Tutelman PR, Chambers CT, Stinson JN, et al. Pain in Children with Cancer. *Clin J Pain* . 2017;33(1):1. doi:10.1097/AJP.0000000000000531

10. Downing J, Jassal SS ing., Mathews L, Brits H, Friedrichsdorf SJ. Pediatric pain management in palliative care. *Pain Manag* . 2015;5(1):23-35. doi:10.2217/pmt.14.45

11. WHO guidelines on the pharmacological treatment of persisting pain in children with medical illnesses. In: *World Health Organization* . ; 2012. https://www.ncbi.nlm.nih.gov/books/NBK138354/

12. Caran EMM, Dias CG, Seber A, Petrilli AS. Clinical aspects and treatment of pain in children and adolescents with cancer. *Pediatr Blood Cancer* . 2005;45(7):925-932. doi:10.1002/pbc.20523

13. Gibbons K, DeMonbrun A, Beckman EJ, et al. Continuous Lidocaine Infusions to Manage Opioid-Refractory Pain in a Series of Cancer Patients in a Pediatric Hospital. *Pediatr Blood Cancer* . 2016;63(7):1168-1174. doi:10.1002/pbc.25870

14. Courade M, Bertrand A, Guerrini-Rousseau L, et al. Low-dose ketamine adjuvant treatment for refractory pain in children, adolescents and young adults with cancer: A pilot study. *BMJ Support Palliat Care* . Published online 2019:1-8. doi:10.1136/bmjspcare-2018-001739

15. Spratt DE, Beeler WH, de Moraes FY, et al. An integrated multidisciplinary algorithm for the management of spinal metastases: an International Spine Oncology Consortium report. *Lancet Oncol* . 2017;18(12):e720-e730. doi:10.1016/S1470-2045(17)30612-5

16. Horn SR, Dhillon ES, Poorman GW, et al. Epidemiology and national trends in prevalence and surgical management of metastatic spinal disease. *J Clin Neurosci* . 2018;53:183-187. doi:10.1016/j.jocn.2018.04.022

17. Spacca B, Giordano F, Donati P, Genitori L. Spinal tumors in children: Long-term retrospective evaluation of a series of 134 cases treated in a single unit of pediatric neurosurgery. *Spine J* . 2015;15(9):1949-1955. doi:10.1016/j.spinee.2015.04.012

18. Shweikeh F, Quinsey C, Murayi R, et al. Treatment patterns of children with spine and spinal cord tumors: national outcomes and review of the literature. *Child's Nerv Syst* . 2017;33(8):1357-1365. doi:10.1007/s00381-017-3433-y

19. Rao AD, Chen Q, Ermoian RP, et al. Practice patterns of palliative radiation therapy in pediatric oncology patients in an international pediatric research consortium. *Pediatr Blood Cancer* . 2017;64(11):1-7. doi:10.1002/pbc.26589

20. Rao AD, Figueiredo MLS, Yegya-Raman N, et al. Clinical practice and outcomes of palliative radiation therapy in pediatric oncology patients: An international comparison of experiences from two distinct countries and health care systems. *Radiother Oncol* . 2019;140:1-5. doi:10.1016/j.radonc.2019.05.017

21. Stachelek GC, Terezakis SA, Ermoian R. Palliative radiation oncology in pediatric patients. *Ann Palliat Med* . 2019;8(3):285-292. doi:10.21037/apm.2019.05.01

22. Lutz S, Balboni T, Jones J, et al. Palliative radiation therapy for bone metastases: Update of an ASTRO Evidence-Based Guideline.*Pract Radiat Oncol* . 2017;7(1):4-12. doi:10.1016/j.prro.2016.08.001

23. Tucker TL, Samant RS, Fitzgibbon EJ. Knowledge and utilization of palliative radiotherapy by pediatric oncologists. *Curr Oncol* . 2010;17(1):48-55. doi:10.3747/co.v17i1.460

24. Baerlocher MO, Saad WE, Dariushnia S, Barr JD, McGraw JK, Nikolic B. Quality improvement guidelines for percutaneous vertebroplasty. *J Vasc Interv Radiol* . 2014;25(2):165-170. doi:10.1016/j.jvir.2013.09.004

25. ACR–ASNR–ASSR–SIR–SNIS Practice Parameter for the Performance of Vertebral Augmentation. *Am Coll Radiol* . 2017;1076:1-18.

26. Tsoumakidou G, Too CW, Koch G, et al. CIRSE Guidelines on Percutaneous Vertebral Augmentation. *Cardiovasc Intervent Radiol* . 2017;40(3):331-342. doi:10.1007/s00270-017-1574-8

27. Rousing R, Ole A, Michael K, et al. Percutaneous vertebroplasty as treatment of malignant vertebral lesions : a systematic review and GRADE evaluation resulting in a Danish national clinical guideline.*Eur Spine J* . 2020;(0123456789). doi:10.1007/s00586-020-06392-w

28. Bollen L, Dijkstra SPD, Bartels RHMA, et al. Clinical management of spinal metastases—The Dutch national guideline. *Eur J Cancer* . 2018;104:81-90. doi:10.1016/j.ejca.2018.08.028

29. CLERK-LAMALICE O, BEALL DP, ONG K, LORIO MP. ISASS Policy 2018—Vertebral Augmentation: Coverage Indications, Limitations, and/or Medical Necessity. *Int J Spine Surg* . 2019;13(1):1-10. doi:10.14444/5096

30. Sørensen ST, Kirkegaard AO, Carreon L, Rousing R, Andersen MØ. Vertebroplasty or kyphoplasty as palliative treatment for cancer-related vertebral compression fractures: a systematic review. *Spine J* . 2019;19(6):1067-1075. doi:10.1016/j.spinee.2019.02.012

31. Carbó E, Riquelme Ó, García A, González JL. Vertebroplasty in a 10-year-old boy with Gorham–Stout syndrome. *Eur Spine J* . 2015;24:590-593. doi:10.1007/s00586-015-3764-x

32. Issa M, Lucas G, Violas P, Griffet J, Courvoisier A. Vertebroplasty for vertebral hemangioma in children: a report of two cases with 2-year follow-up. *Child's Nerv Syst* . 2015;31(11):2179-2183. doi:10.1007/s00381-015-2777-4

33. Kanatli U, Ataoğlu B, Özer M, Şenköylü A, Çetinkaya M. Kyphoplasty for intractable pain due to glucocorticosteroid-induced osteoporotic vertebra fracture of a 9-year-old patient with systemic lupus erythematosus: 8-Year follow-up. *J Pediatr Orthop* . 2015;35(6):e55-e59. doi:10.1097/BPO.0000000000000346

34. Hoashi JS, Thomas SM, Goodwin RC, Gurd DP, Hanna R, Kuivila TE. Balloon Kyphoplasty for Managing Intractable Pain in Pediatric Pathologic Vertebral Fractures. *J Pediatr Orthop* . 2017;37(4):e286-e291. doi:10.1097/BPO.0000000000000886

35. Thomas AM, Fahim DK. Stand-Alone Balloon Kyphoplasty for Treatment of Traumatic Burst Fracture in Pediatric Patient. *World Neurosurg* . 2019;125:475-480. doi:10.1016/j.wneu.2019.01.184

36. Chen AT, Cohen DB, Skolasky RL. Impact of Nonoperative Treatment, Vertebroplasty, and Kyphoplasty on Survival and Morbidity After Vertebral Compression Fracture in the Medicare Population. *J Bone Jt Surgery-American Vol* . 2013;95(19):1729-1736. doi:10.2106/JBJS.K.01649

37. Hernandez RK, Maegbaek ML, Liede A, Sørensen HT, Ehrenstein V. Bone Metastases, Skeletal-related Events, and Survival Among Children With Cancer in Denmark. *J Pediatr Hematol Oncol* . 2014;36(7):528-533. doi:10.1097/MPH.0000000000000106

38. Halton J, Gaboury I, Grant R, et al. Advanced vertebral fracture among newly diagnosed children with acute lymphoblastic leukemia: Results of the Canadian Steroid-Associated Osteoporosis in the Pediatric Population (STOPP) research program. *J Bone Miner Res* . 2009;24(7):1326-1334. doi:10.1359/jbmr.090202

39. van der Sluis IM, van den Heuvel-Eibrink MM. Osteoporosis in children with cancer. *Pediatr Blood Cancer* . 2008;50(S2):474-478. doi:10.1002/pbc.21407

LEGEND

Figure - (A) A 15-year-old with stage 4 alveolar rhabdomyosarcoma was treated with vertebroplasty at the T7 and T12 levels. (B) A child with metastatic Wilms tumor had repeated interventions at the L3 vertebral body between ages 9 and 13. (C) A 6-year-old with advanced rhabdomyosarcoma of the prostate required multiple-level vertebroplasty to treat his bony fractures which were causing him significant refractory pain.

Hosted file

`1_TABLE 1.pdf` available at https://authorea.com/users/403449/articles/514879-vertebroplasty-as-a-palliative-treatment-option-for-intractable-pain-in-pediatric-patients-with-spinal-tumors

Hosted file

`1_TABLE 2.pdf` available at https://authorea.com/users/403449/articles/514879-vertebroplasty-as-a-palliative-treatment-option-for-intractable-pain-in-pediatric-patients-with-spinal-tumors