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Hybrid therapy and use of carbon-fiber-reinforced polyetheretherketone instrumentation for management of mobile spine chordomas: A case series and review of the literature

Chi Shing Adrian Lam[1], Vicente de Paulo Martins Coelho[1], Seth Wilson[1], Joshua Palmer[2], Anas Bardeesi[1], Vikram Chakravarthy[1]

[1]Department of Neurological Surgery, The Ohio State University Wexner Medical Center, [2]Department of Radiation Oncology, The Ohio State University Comprehensive Cancer Center, Columbus, Ohio, United States.

E-mail: *Chi Shing Adrian Lam - chishing.lam@osumc.edu; Vicente de Paulo Martins Coelho - vicentecoelhojr@yahoo.com.br; Seth Wilson - seth.wilson@osumc.edu; Joshua Palmer - joshua.palmer@osumc.edu; Anas Bardeesi - anasmohammedwajdia.bardeesi@osumc.edu; Vikram Chakravarthy - vikram.chakravarthy@osumc.edu

***Corresponding author:**
Chi Shing Adrian Lam, Department of Neurological Surgery, The Ohio State University Wexner Medical Center, Columbus, Ohio, United States.

chishing.lam@osumc.edu

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ABSTRACT

Background: Mobile spine chordomas demonstrate varied surgical risk profiles compared to their sacral analogs. Often, the limitation to performing an *en bloc* resection of a mobile spine chordoma is tumor violation of the epidural space. Given these limitations, we propose the utilization of carbon fiber-reinforced polyetheretherketone (CFR-PEEK) instrumentation in separation surgery to enhance visualization for stereotactic body radiation therapy (SBRT) planning, allowing an ablative radiosurgical dose to be delivered.

Methods: We present two illustrative cases highlighting the advantages of hybrid therapy (separation surgery and adjuvant SBRT) with CFR-PEEK instrumentation in the management of mobile spine chordoma.

Results: Case 1 is a 62-year-old female with an L4 chordoma who underwent separation surgery and L3–5 posterior instrumented fusion using CFR-PEEK instrumentation. Case 2 is a 68-year-old female with a L3 chordoma who underwent revision separation surgery encompassing completion of L3 partial corpectomy and CFR-PEEK screw exchange of prior L2–4 titanium instrumentation. Both patients received postoperative ablative SBRT. At 18-month postoperative time points, both patients were clinically stable, with no signs of tumor recurrence or progression.

Conclusion: Mobile spine chordomas present a unique challenge in obtaining a margin negative *en bloc* resection. Separation surgery allows the ability to decrease surgical morbidity and deliver an ablative radiosurgical dose. Furthermore, the incorporation of CFR-PEEK instrumentation allows the utilization of multiparametric magnetic resonance imaging for long-term disease monitoring. Hybrid therapy, a less morbid alternative to standard *en bloc* spondylectomy, offers a better surgical morbidity profile by combining effectively with SBRT for optimal tumor control.

Keywords: Carbon fiber/polyetheretherketone, Chordoma, Hybrid therapy, Magnetic resonance imaging, Mobile spine, Separation surgery

INTRODUCTION

Chordomas of the mobile spine (C1-L5) are rare primary osseous neoplasms with an annual incidence of 0.05/100,000 people per year.[26] Epidemiological studies describe 58.3% of cases

as male with a mean age of 55 years.[55] Chordomas most often localize to the skull base (41.1%) or sacrum (31.4%), with the remainder presenting in the mobile spine (27.5%).[34] Skull base chordomas have a higher median survival at 162 months compared to the sacrum and mobile spine at 87 and 95 months, respectively.[34] Diagnosis of chordomas is often late in the disease course and requires histologic evaluation through percutaneous biopsy.

According to the Enneking staging system, chordomas are classified as low-grade malignant tumors, which fall under stages IA and IB.[5,16] As such, the standard of care for these patients has been *en bloc* resection with negative margins, often necessitating resection of the dura, followed by adjuvant radiation and/or chemotherapy.[4,8,54] Mainly influenced by intrinsic anatomic features, arising in the mobile spine typically discourages a more aggressive resection due to an unfavorable morbidity outlook.[40] These circumstances position separation surgery, where spinal column decompression and tumor resection occur with limited corpectomy, ensuring an adequate target for postoperative radiosurgery, as an appealing strategy for this location.[10,30] More recently, Lockney *et al*. have demonstrated the effectiveness of hybrid therapy, consisting of separation surgery followed by stereotactic body radiation therapy (SBRT), for newly diagnosed chordomas.[24] In a prospective study with 111 patients, Barzilai *et al*. demonstrated that hybrid therapy was effective at decreasing pain and improving quality of life for patients with metastatic epidural spinal cord compression.[3]

Shifting from therapeutic approaches, radiographic imaging to evaluate chordomas typically involves computed tomography (CT) scans and magnetic resonance imaging (MRI). On CT, these tumors have low density and may have cortical destruction.[15,27] On T1-weighted imaging, chordomas usually appear hypo- or iso-intense, whereas they are characteristically hyperintense on T2-weighted imaging.[11] Chordomas can appear with no, mild, or marked enhancement.[2] Histologically, the World Health Organization[51] has identified three subtypes of chordoma: conventional, dedifferentiated, and poorly differentiated. Conventional chordomas are the most common,[45] whereas poorly differentiated chordomas typically occur in the skull base.[15]

Innovations in surgical technology can assist in the multi-disciplinary nature of standard care for chordoma patients. Titanium-based surgical constructs produce artifacts on follow-up CT and MRI, creating challenges in radiation planning and oncologic surveillance.[7] Carbon fiber-reinforced polyetheretherketone (CFR-PEEK) is a type of composite material combining the strength and stiffness of carbon fiber with the biocompatibility and resistance to corrosion of polyetheretherketone. It has been used in various medical and surgical applications, including as an alternative to traditional titanium instrumentation in spine surgery.[38] Notably, CFR-PEEK does not create the same artifact on advanced imaging as titanium instrumentation and, thus, plays an integral role in adjuvant therapy planning. SBRT, compared to conventional radiotherapy, has been shown to provide excellent local tumor control for both primary and metastatic bone tumors.[44] CFR-PEEK hardware allows for more precise dosimetry contouring of the spinal cord and at-risk organs for patients requiring adjuvant therapy, allowing an ablative dose to be delivered.[35]

We report two cases of chordoma in the mobile spine where CFR-PEEK implants were utilized in separation surgery followed by adjuvant SBRT, reporting patient outcomes and benefits of this combined treatment modality.

MATERIALS AND METHODS

We describe two cases of mobile spine chordomas [Table 1]. Case 1 is a 62-year-old female with an L4 chordoma who was experiencing back pain, left-sided lower extremity radiculopathy, and paresthesia. The patient then underwent separation surgery, encompassing partial corpectomy at L4 and L3–5 posterior instrumented fusion with CFR-PEEK, followed by adjuvant SBRT.

Case 2 features a 68-year-old female presenting with back pain and bilateral lower extremity radiculopathy impacting ambulation. The patient underwent partial resection of L3 epidural tumor at an outside hospital, with vertebroplasty at the index level and titanium pedicle screw fixation from L2 to 4. Pathology confirmed chordoma and radiation was not performed. Six-month postoperative imaging revealed a residual tumor. The patient then underwent revision surgery with transpedicular L3 partial corpectomy and L2–4 pedicle screw exchange with CFR-PEEK to assist with postoperative radiation therapy planning.

Patient informed consent was obtained, and this case series has been reported in line with the CARE guidelines (for case reports).[36]

RESULTS

Case 1

A 62-year-old female presented with a 4-month history of axial low back pain with occasional left-sided anterior thigh radicular pain and intermittent paresthesia [Figure 1]. Her medical history was significant for hypertension, coronary artery disease, anxiety, osteoarthritis of her knee, and prior hip surgery. She also had a 20-pack year history of tobacco use. On physical examination, she grossly had 5/5 motor strength in all extremities.

Table 1: Demographics overview.

Characteristic	Case #1	Case #2
Age	62	68
Gender	Female	Female
Level	L4	L3
Underwent revision	No	Yes
Past medical history	HTN, CAD, anxiety, osteoarthritis of the knee, hip surgery, and current smoker	HTN, HLD, obesity, melanoma status post excision, gastric sleeve surgery, and ankle repair surgery
Symptoms preoperative	Back pain, radiculopathy, and paresthesia	Back pain, radiculopathy, and ambulatory difficulties
Last follow-up	Period: 19 Months Unremarkable	Period: 18 Months Unremarkable
KPS		
Pre-Op	90	90
1-Month Post-Op	90	90
4-Month Post-Op	90	100
6-Months Post-Op	80	-
12-Months post-Op	100	100
15-Months Post-Op	100	100
18-Months Post-Op	100	100

HTN: Hypertension, CAD: Coronary artery disease, HLD: Hyperlipidemia, KPS: Karnofsky performance scale, Pre-Op: Pre-operative, Post-Op: Post-Operative

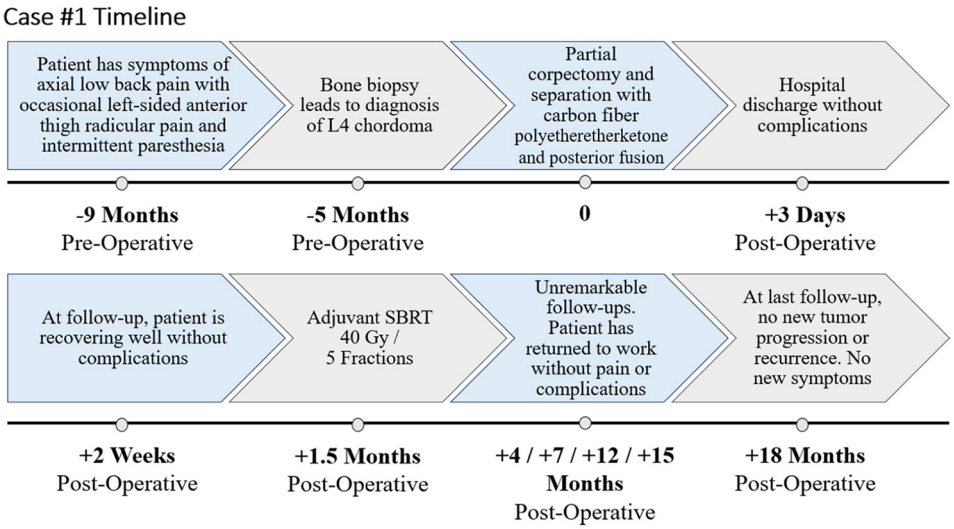

Figure 1: Timeline of important events for case #1.

Imaging revealed a T2 hyperintense destructive expansile lesion at L4, demonstrating cortical breakthrough into the anterior epidural space and anterior left prevertebral soft tissues [Figure 2]. In addition, there was severe stenosis at L4 secondary to epidural tumor extension.

Biopsy of the L4 vertebrae demonstrated chordoma consistent with the conventional subtype. Immunohistochemistry confirmed tumor cells positive for pancytokeratin, epithelial membrane antigen (EMA), and weak S100; paired box gene 8 and thyroid transcription factor 1 stain were negative. Expression of p53 was low, where 20% of tumor cell nuclei had intense p53 immunoreactivity, associated with improved prognosis and longer progression-free survival in chordomas.[43]

Thereafter, she underwent separation surgery, encompassing a partial transpedicular corpectomy of L4 with L3–5 cement-augmented posterior instrumented fusion, using CFR-PEEK instrumentation [Table 2]. There were no intraoperative

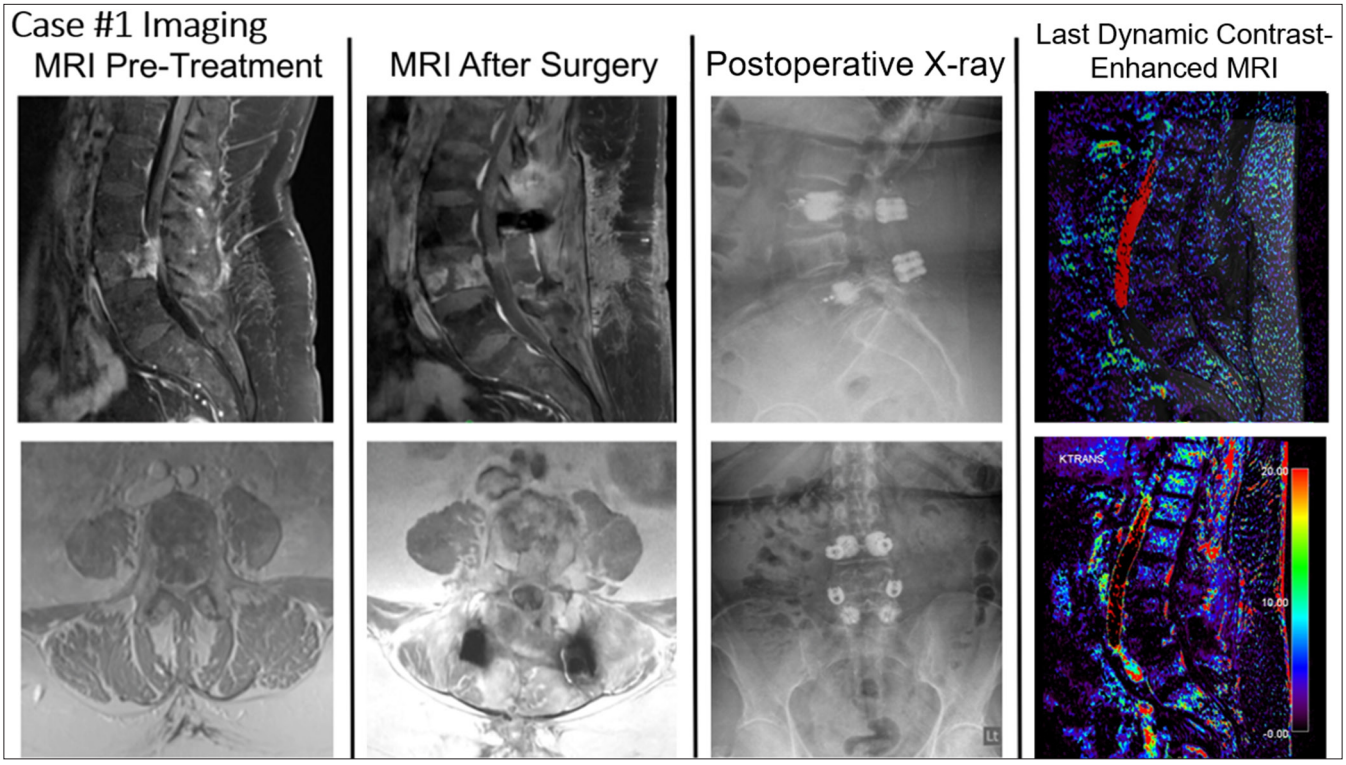

Figure 2: Relevant imaging for Case #1. The first column contains T1-weighted fat-suppressed magnetic resonance imaging (MRI) pre-treatment (top = sagittal, bottom = axial). The second column contains T1-weighted fat-suppressed MRI after surgery (top = sagittal, bottom = axial). The third column contains X-rays after surgery (top = lateral, bottom = anteroposterior). The last column contains the last dynamic contrast-enhanced-MRI (top = overlay, bottom = MR perfusion).

Table 2: Surgical overview.

Characteristic	Case #1	Case #2
Approach	Posterior	
Instrumentation	CFR-PEEK	
Removal of previous hardware	No	Yes
Partial corpectomy	L4	L3
Fused levels	L3-5	L2-4
Length of surgery (hours)	4.7	4.4
Estimated blood loss (mL)	1000	400
Intraoperative complications	None	
Postoperative complications	None	
Immunohistochemistry of pathological specimen	Positive for pancytokeratin, EMA, and weak S100. Negative for PAX8 and TTF-1	Positive for brachyury gene, AE1/AE3, CAM5.2, Oscar, EMA. Focally positive for S100 and HMB45

EMA: Epithelial membrane antigen, PAX8: Paired box gene 8, TTF-1: Thyroid transcription factor 1, HMB45: Human melanoma black 45, CFR-PEEK: Carbon fiber-reinforced polyetheretherketone

complications, the total surgical time was 4.7 h, and the estimated blood loss was 1 L. The patient was discharged home 3 days later without any complications during her stay.

At 1-month postoperative, imaging demonstrated adequate neural decompression. Thereafter, she underwent SBRT using 3 volumetric modulated arc therapy (VMAT) at 40 Gy in five fractions with 10 megavolts (MV) photons in a flattening filter-free (FFF) mode [Figure 3 and Table 3].

Three- and 6-month MRIs were stable, and the patient reported a Karnofsky Performance Scale (KPS) of 100 at 19 months postoperative. Dynamic contrast-enhanced MRI (DCE-MRI) scans were performed postoperatively at

3 weeks, 5 weeks, 4 months, 7 months, 10 months, 13, and 19 months to evaluate for progression. DCE-MRI revealed stable findings consistent with postoperative changes and no evidence of tumor activity or recurrence.

Case 2

A 68-year-old female presented with worsening back pain with radiation into bilateral lower extremities [Figure 4]. Her medical history was significant for melanoma status post excision (deemed cured), hypertension, hyperlipidemia, obesity, gastric sleeve surgery, and ankle repair surgery. The patient did not have a prior smoking history. Lumbar X-ray revealed a worsening sclerotic lesion in her L3 vertebral body and a new L3 compression fracture. In addition, MRI demonstrated an enhancing lesion (4.8 × 4.8 cm) with epidural extension, nearly obliterating the spinal canal at the level of L3 with involvement of the superior and inferior neural foramina [Figure 5].

She underwent laminectomy and partial facetectomies of L3 bilaterally, debulking of L3 epidural tumor, L3 vertebroplasty, and L2–4 pedicle screw fixation with titanium instrumentation at an outside institution. Pathology confirmed the diagnosis of chordoma, with tumor cells positive for multiple cytokeratins and the brachyury gene. Cytokeratins AE1/AE3, CAM5.2, and Oscar were found to be diffusely positive in tumor cells. EMA stained positive, while S100 and human melanoma black 45 were focally positive.

At 3 months postoperative, an MRI lumbar spine demonstrated a persistent marrow placing lesion. At 6 months postoperative, she presented to our institution for evaluation. MRI lumbar spine revealed residual chordoma

Table 3: Radiotherapy overview.

Characteristic	Case #1	Case #2
Target	L4	L3
Technique	VMAT	
Energy (MV)	10	
Delivered fractions	5	
Delivered dose (cGy)	4000	
Elapsed days	6	4
Complications	None	

VMAT: Volumetric modulated arc therapy, MV: Megavolts, cGy: Centigray

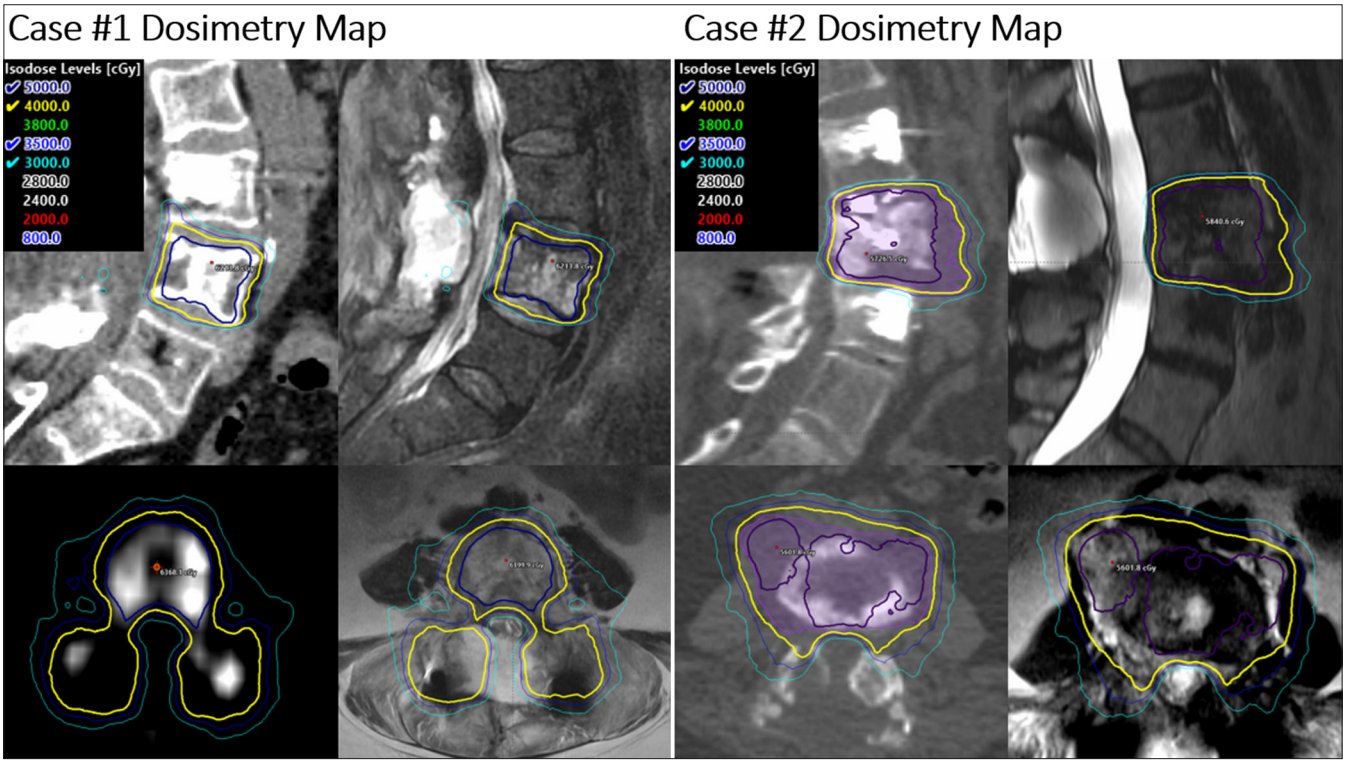

Figure 3: Dosimetry mapping for Case #1 (left) and Case #2 (right). This figure highlights typical volumetric modulated arc therapy spinal stereotactic body radiation therapy isocenter planning used in these cases, following consensus contouring guidelines. Of note, no hardware-related imaging artifact at the target volume allowed precise dose delineation.

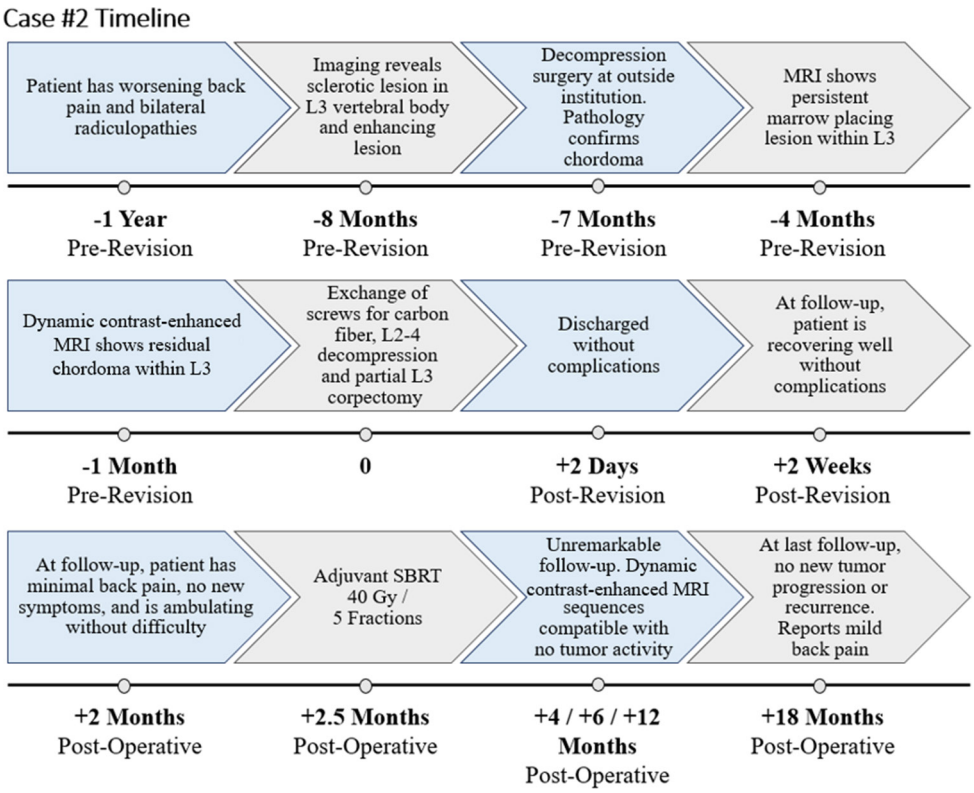

Figure 4: Timeline of important events for case #2.

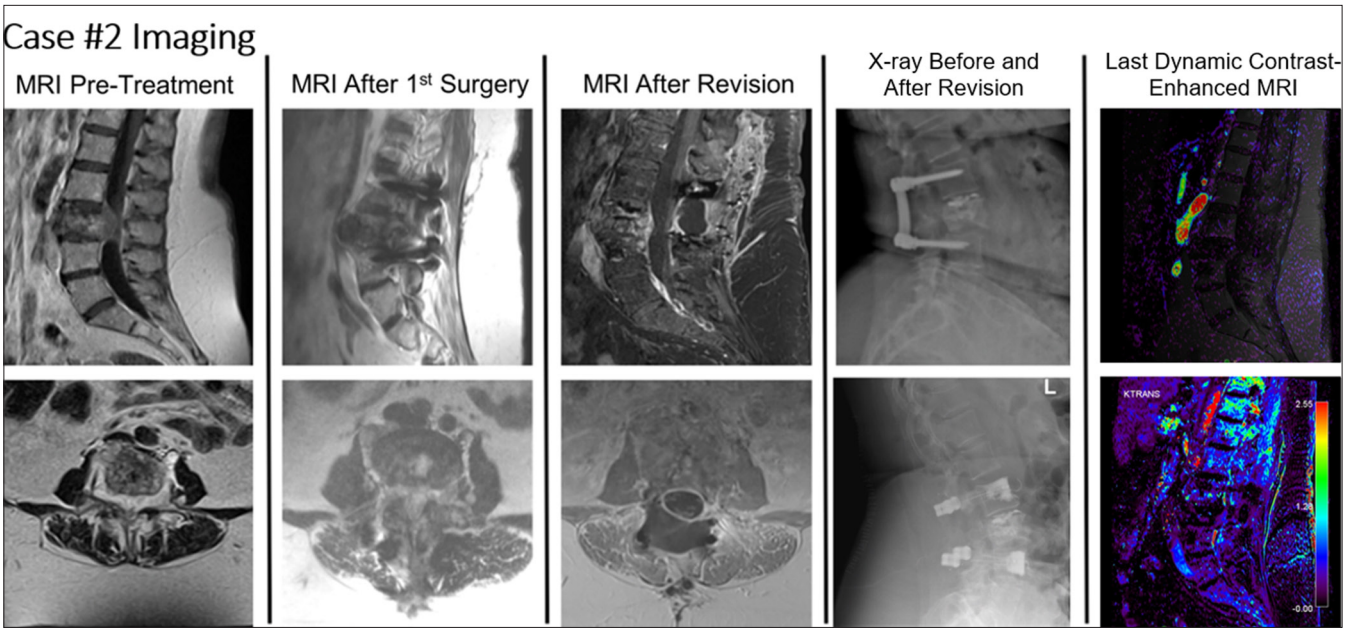

Figure 5: Relevant imaging for Case #2. The first column contains T1-weighted fat-suppressed magnetic resonance imaging (MRI) pre-treatment (top = sagittal, bottom = axial). The second column contains T1-weighted fat-suppressed MRI after her first surgery (top = sagittal, bottom = axial). The third column contains T1-weighted fat-suppressed MRI after her revision surgery (top = sagittal, bottom = axial). The fourth column contains sagittal X-rays before (top) and after (bottom) revision surgery. The last column contains the last dynamic contrast-enhanced-MRI (top = overlay, bottom = MR perfusion).

within the L3 vertebral body with increased right prevertebral extraosseous extension and bilateral L3–4 foraminal tumoral compression. The patient also experienced mechanical back pain, and a CT scan demonstrated loose hardware. On physical examination, she was neurologically intact, with 5/5 motor strength in all extremities.

Before the revision, KPS was 90. Revision surgery consisted of re-do decompression/epidural tumor debulking with L3 partial corpectomy and L3–5 instrumentation replacement with CFR-PEEK [Table 2]. Surgical time was 4.4 h, and estimated blood loss was 400 mL, with no intraoperative or postoperative complications. Pathology was consistent with chordoma. Immunohistochemistry was positive for AE1/AE3, CAM5.2, EMA, S100, HMB45, and Oscar. The patient was discharged home on postoperative day 2 without any complications during her stay.

The patient then underwent postoperative SBRT, consisting of a cumulative dose of 40 Gy in 5 fractions using 2 VMAT arcs with 10 MV photons in an FFF mode targeting the L3 vertebra [Figure 3 and Table 3]. KPS grades pre- and post-radiation therapy were 90. At 18 months post-op, the patient was doing well overall with mild back pain rated 1 out of 10, not requiring medications. The patient elected for conservative measures. The latest MRI and CT imaging demonstrated additional delayed height loss of the L3 vertebral body, which is being followed with interval scans. Her KPS grade was 100. Perfusion sequences at 2, 5, 7, 12, and 18 months postoperative showed "cold" patterns compatible with no metabolic tumor activity.

DISCUSSION

Overview of the management of mobile spine chordomas

Mobile spine chordomas demonstrate a slow, indolent growth rate, often diagnosed at later stages, with patients remaining asymptomatic for a lengthy period.[47] Despite their indolent presentation, chordomas have high rates of metastases and local recurrence.[9] In one of the largest cohorts specific for mobile spine chordomas, a 50-year retrospective study with 52 patients found the overall rate of local recurrence to be 66%, with 75% of recurrences occurring an average of 30 months after excision and radiation.[4]

Conventionally, chordomas have been thought of as radio- and chemo-resistant tumors that require aggressive surgical control.[46] While *en bloc* resection with negative margins has been considered the definitive treatment for sacral chordomas,[33] resection of mobile spine chordomas can be more challenging. Since these chordomas are located adjacent to vital structures in the axial skeleton, resection often risks damage to critical neurovascular elements, and anterior and lateral approaches can pose a risk of multiple access morbidity.

At present, gaps remain in the literature and consensus does not exist regarding the optimal strategy to manage patients with mobile spine chordomas. Debates remain in balancing aggressive surgical resections at the risk of sacrificing neurological function. In a retrospective study of 26 mobile spine chordoma patients who underwent surgical resection, 73% experienced complications, such as deep infection and neurological complications, with 35% requiring reoperation.[20] In the same study, the authors concluded that *en bloc* resections resulted in better oncological outcomes compared to more debulking-type resections and without an increase in complications.

Meanwhile, in a multi-institutional study of 32 patients with mobile spine chordomas, Molina *et al*.[29] showed that *en bloc* resection of C1–2, chordomas resulted in higher rates of complications and increased tumor recurrence compared to *en bloc* resection of subaxial cervical spine chordomas. This supports the need to explore additional methods to manage mobile spine chordoma patients with decreased surgical morbidity while maximizing oncological outcomes.

Furthermore, *en bloc* resection does not guarantee an R0 resection, and even if an R0 resection is achieved, there could still be microscopic residual disease. Over the years, studies have increasingly highlighted the importance of neoadjuvant or adjuvant high-dose radiotherapy for the management of spinal chordomas.[34] Jin *et al*.[17] performed a retrospective review of 35 mobile spine and sacral chordoma patients treated with definitive SBRT, intralesional gross-total resection, separation surgery, or *en bloc* resection. Patients who received high-dose SBRT had a higher 5-year local recurrence-free survival of 89.9% than those who did not undergo SBRT. Thus, even though conventional-dose radiotherapy has been ineffective in these patients, high-dose radiotherapy (SBRT) can help with local control.[21]

Further studies have suggested coupling intralesional, gross-total resections or separation surgery with postoperative SBRT can be an alternative technique to *en bloc* resections. In a single-institution study of 12 patients with mobile spine chordomas, Lockney *et al*.[24] showed those who underwent intralesional resection and SBRT as initial treatment had higher local control rates (80%) at the last follow-up compared to patients who only had initial surgical resection with SBRT at the time of recurrence (57.1%).

In a single institution study where 16 chordoma patients were treated with varying approaches, Akmansu *et al*.[1] found subtotal or gross total resection of tumor or radiotherapy dose and techniques were not associated with recurrence. These authors concluded for patients with small or residual tumors, SBRT may be more beneficial.

CFR-PEEK benefits over titanium for posttreatment monitoring and radiation effectiveness

A key principle in radiation planning is to maximize the tumoricidal dose, or the biologically effective dose while minimizing damage to the surrounding tissues. Having clear visualization for radiation therapy planning is key for radiation oncology treatments, staging scans, and dosimetry protocols.

As spine surgeons have transitioned away from using traditional autografts, the prevalence of interbody device materials has grown.[32] Two popular hardware materials currently used for pedicle screws, rods, and anterior column reconstruction are titanium and CFR-PEEK. The material and components used to create each construct are largely determined by patient pathology and surgeon experience.[14] Titanium possesses high osseointegrative capacity and elastic modulus,[32] but its radio-opaqueness causes it to generate artifacts on CT and MRI imaging.[23] While titanium has previously been the gold standard, CFR-PEEK poses several unique advantages that enhance surgical outcomes.[50]

Compared to traditional titanium implants, CFR-PEEK instrumentation provides a radiolucent biomaterial with similar clinical properties to the native spine.[39] This provides a better evaluation of microscopic disease. As such, many studies have advocated for CFR-PEEK instrumentation for postoperative radiation planning in the management of spinal tumors.[18,22,42]

Out of 1400 patients treated by the National Centre for Oncological Hadron Therapy with proton and carbon therapy, Mastella *et al*.[25] found seven patients with CFR-PEEK implants, including three mobile spine chordomas. Compared to titanium implants, CFR-PEEK instrumentation was found to cause fewer dose perturbations, CT artifacts, and delineation uncertainties. Although this is not a one-to-one parallel since the patients illustrated in our case studies received photon therapy, the benefits of using CFR-PEEK are similar.

In a retrospective study of ten patients with spinal metastases who underwent postoperative photon therapy, Müller *et al*.[31] compared CFR-PEEK to titanium implants for radiotherapy treatment planning. CFR-PEEK was found to cause fewer image artifacts and improved treatment plan quality for intensity modulated radiation therapy, although VMAT plan quality was similar.

In addition to enhanced visualization for adjuvant treatment, the use of CFR-PEEK instrumentation has demonstrated improved efficacy monitoring for local disease recurrence.[48]

While beneficial for all primary and metastatic spine diseases, this may play a significant role in the management of chordoma due to high reported rates of local recurrence.[13]

Dosimetry for enhanced SBRT efficacy in chordoma treatment

Proper dosing of adjuvant radiation therapy is key in chordoma management. Jin *et al*.[17] demonstrated that patients with high-dose stereotactic radiosurgery had significantly improved 5-year survival compared to those who did not undergo the same treatment. High doses are preferred as chordomas have demonstrated radioresistance.[52]

In a study completed by Chen *et al*.,[6] 28 patients with spinal chordomas, including 24 with mobile spine chordomas, were treated with SBRT at a median dose of 4000 cGy in five fractions. Overall, the 2-year survival rate was 92%, and the 2-year local control rate was 96%. This again emphasizes the importance of high-dose hypofractionated SBRT as a tool for local control of these persistent tumors.

The tumor that is located too close to the spinal cord may indicate the need for proton therapy, as dosing to the spinal cord is one of the main complications of SBRT.[19]

Although studies have found proton therapy to be advantageous to photon therapy due to the depth-dose characteristics of protons that allow for better sparing of normal tissues,[28,41] there exists limited data comparing the use of proton and photon therapies for mobile spine chordomas.

Yazici *et al*.[53] evaluated the impact of spinal implants on dosimetry and concluded care should be taken during adjuvant radiotherapy to avoid implants and that anterior rod instrumentation had the largest impact on unintended spinal cord dosing. Given that proper dosimetry is key in successfully treating chordoma, and it can be impacted by tumor location and the presence of spinal implants, CFR-PEEK can be a valuable tool that allows for more accurate dosing.

Multiparametric post-treatment monitoring

Radiographic imaging for evaluating chordomas typically involves CT and MRI. On CT, these tumors have low density and may have cortical destruction.[15,27]

Santos *et al*.[37] have investigated the limitations of conventional MRI and the advantages of DCE-MRI perfusion imaging in assessing chordoma treatment. They demonstrated that the indolent characteristics of this tumor challenge the monitoring of tumor progression with conventional MRI. In this regard, DCE-MRI perfusion studies provide more insights about underlying tumor vascularity and physiology, better evaluating posttreatment efficacy.

CFR-PEEK also allows for better disease monitoring. Titanium implants can cause artifacts, leading to an inability to use multiparametric studies reliably. These have shown

MRI to be significantly affected by titanium materials.[12] Recent studies suggest that with CFR-PEEK instrumentation, MRI provided similar benefits for treatment planning and monitoring as CT-myelography.[49] Our case studies specifically highlight the strengths of DCE-MRI for multiparametric monitoring. Pre- and post-radiation therapy MRI perfusion can serve as a useful diagnostic modality, especially when patients have CFR-PEEK instrumentation in place.

Limitations

Optimal management approaches for spine chordomas are debated. Although surgical resection is a mainstay, it is more challenging to obtain negative margin resection in mobile spine chordomas, given the anatomic constraints.

The present study is limited by its patient volume and longitudinal follow-up; further work will be required to determine whether CFR-PEEK hardware significantly affects the morbidity and mortality of patients with mobile spinal chordomas. Although a small series, early follow-up demonstrates a lack of metabolic activity supporting ablative treatment of the chordoma. Ongoing surveillance with DCE-MRI will confirm absence of active chordoma disease. While many pros of CFR-PEEK instrumentation have been highlighted, other factors for consideration include the cost comparison of titanium versus CFR-PEEK implants.

CONCLUSION

Inherent anatomic differences between the sacrum and mobile spine lead to consequently distinct morbidity outlooks for the traditional *en bloc* resection dogma. This scenario propels separation surgery as an appealing surgical strategy for this location. With advances in SBRT and the ability to deliver an ablative dose, inducing tumor apoptosis/necrosis, shifting prior paradigms of radiosensitivity. Hybrid therapy, integrating separation surgery and adjuvant SBRT, has recently demonstrated success in managing chordomas. This integrated approach may be a noteworthy advancement in the comprehensive care of mobile spine chordomas.

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