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Clinical study

Carbon fiber reinforced vs titanium implants for fixation in spinal metastases: A comparative clinical study about safety and effectiveness of the new “carbon-strategy”

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ABSTRACT

In spinal oncology traditional titanium implants could significantly impair evaluation of postoperative imaging because of artifacts, potentially affecting proper planning and execution of radiotherapy and adequate radiological follow-up to rule out progression of the disease. This is why carbon fiber reinforced (CFR)-PEEK implants have been developed for spinal fixation. The advantages of this system include fewer artifacts on imaging, potentially improving the execution and quality of radiotherapy, with also a reduced scattering effect to neighboring tissues.

A comparative clinical and radiological study between new CFR-PEEK and standard titanium implants is described. Data recorded for each case included patient demographics, clinical, radiological and surgical data, intra- and postoperative complications, follow-up information. The goal of this study was to verify the safety and effectiveness of CFR-PEEK devices compared to standard titanium implants.

A total number of 78 patients were reviewed. 36 patients underwent CFR-PEEK fixation, while titanium implants were used for 42 patients. Functional recovery was obtained in both groups and registered at last follow-up in terms of axial pain and neurological status. No significative differences were found between the two groups in terms of post-operative clinical complications and hardware-related complications.

CFR-PEEK implants constitute a feasible and effective way to restore stability in metastatic spine tumors. This study found a non inferior favorable profile in terms of intraoperative and postoperative complications and functional recovery, compared to titanium. Further prospective studies are needed to clarify the potential oncological advantage of their radiolucency.

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1. Introduction

In the last decades an exponential rise in the incidence of spinal metastases has been recorded and justified, above all, by the introduction of targeted therapies. The advancements in surgical techniques, radiosurgery, and immunotherapy revolutionized the treatment algorithm, enhancing the need for an essential multidisciplinary management of these patients [1–4].

Surgical indications involve the presence of instability, epidural compression and/or neurological impairment, severe axial pain, the need for diagnosis or for oncological cytoreduction or excision [1,5].

In case of overt, potential, or iatrogenic instability, fixation becomes mandatory. Traditional titanium implants have been demonstrated to possess sufficient stiffness and reliability and are currently widely used by surgeons for different pathologies involving the spine. In spinal oncology, however, titanium implants could significantly impair evaluation of postoperative imaging because of artifacts, potentially affecting proper planning and execution of radiotherapy and adequate radiological follow-up to rule out progression of disease [6].

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This is why carbon fiber reinforced (CFR)-PEEK implants have been developed for spinal fixation. The advantages of this system include fewer artifacts on imaging, potentially improving the execution and quality of radiotherapy with a reduced scattering effect to neighboring tissues [6,7].

In this article a comparative clinical and radiological comparison between new CFR-PEEK and standard titanium implants is described. The aim of this preliminary study was to prove the safety and the effectiveness of carbon devices for fixation in spinal metastases.

2. Materials and methods

In November 2017 the authors started performing spinal fixation for metastatic lesions using CFR-PEEK implants at the Neurosurgery Department of the “Città della Salute e della Scienza” in Turin (Italy). Patients with diagnosis of spinal metastasis requiring surgery for instability, severe pain, epidural compression, and/or neurological impairment were included in a prospective evaluation. Even if not strictly considered as metastases, myeloma and non-Hodgkin lymphoma (NHL) spinal lesions were included because of similar surgical management. Patients were included in the CFR-PEEK group in case of thoracic or lumbar locations requiring posterior fixation, or in case of cervical lesions requiring an anterior approach. These criteria were defined because of the absence, to the authors' best knowledge at the moment of evaluation, of CFR-PEEK posterior cervical stabilization devices. To achieve posterior fixation, a CFR-PEEK pedicle-based posterior stabilization system (Carboclear™, CarboFix Orthopedics, Herzliya, IL, USA) was used (Fig. 1). In this system pedicle screws are coated with titanium to enhance bone integration and visibility during surgery and fluoroscopy check. For cervical lesions requiring anterior approach, CFR-PEEK cervical plates (Black Armor, Icotec ag, Altstätten, CH) were implanted (Fig. 2). Replacement of the vertebral body was performed when needed (significant anterior column destruction and an estimated life expectancy above 1 year) with radiolucent implants such as PEEK cages (ECD and XRL expandable devices, Depuy Synthes, Raynham, Massachusetts, USA) or heterologous bone grafts.

The series of CFR-PEEK fixations was then compared to a retrospective series of metastatic patients that underwent traditional titanium pedicle screw fixation (ExpEDIUM or Mountaineer, Depuy

Synthes, Raynham, Massachusetts, USA) from January 2015 to November 2017.

Data recorded for each case included: sex; age; American Society of Anesthesiologists (ASA) score; tumor histology; spinal level; grade of instability, evaluated with the Spinal Instability Neoplastic Score (SINS) [8]; grade of epidural compression according to the ESCC scale [9]; preoperative and postoperative Numbering Rate Scale (NRS) for axial pain; preoperative, early postoperative, and last follow-up neurological status, according to the American Spinal Injury Classification (ASIA) Impairment scale (AIS); previous radiotherapy; extent and type of decompression; type of instrumentation, body replacement, when performed; duration of the procedure; intraoperative blood loss; intra- and postoperative complications; length of hospital stay; follow-up duration; local recurrence. Fixation was considered appropriate with a SINS > 6 points and/or if iatrogenic surgical instability was expected after intralesional debulking. Previously radiated lesions were not excluded, if the other inclusion criteria were met. Total corpectomy was defined as the removal of more than 95% of the vertebral body confirmed on a post-operative CT; partial corpectomy was defined as the removal of less than 95% of the vertebral body. Decompression was defined as circumferential bilateral, when bony and ligamentous structures together with tumor tissue were bilaterally removed to free the whole circumference of the spinal cord. When the procedure approached the vertebra, removal of the lamina, the pedicle, the transverse process, and the affected body only from one side was defined as circumferential monolateral decompression. Decompression was defined anterior if only the vertebral body was removed, while it was defined posterior in case of bilateral laminectomy, and postero-lateral if transverse processes and/or pedicles were removed from one side or both sides. Intraoperative neuromonitoring (IONM) was used during the procedures. All the patients received a postoperative CT scan before discharge. Follow-up clinical and radiographic controls performed by the surgeons' team were performed at 3, 6, 12 months and yearly thereafter, in order to assess hardware stability and local recurrence.

Statistical analysis was performed using SPSS v.21.0 (IBM Corp., Armonk, NY, USA). Comparisons were performed with Student's *t*-test for continuous variables. Statistical significance was defined with a *p*-value <0.01. Informed consent was obtained from all included patients to use clinical information for research purposes.

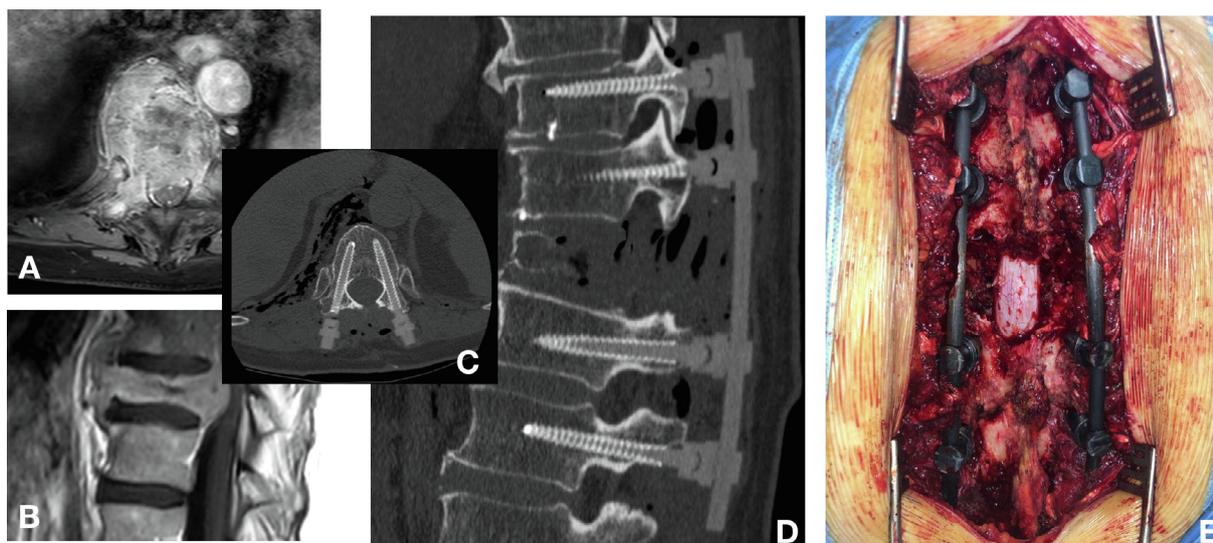


Fig. 1. Male, 61 years old. T11 NSCLC metastases with high grade epidural compression and paraparesis. (A,B) A dorso-lumbar fixation with CFR-PEEK implants and circumferential decompression were performed. (C,D,E) At the last follow-up (8 months) a total neurological recovery was observed.

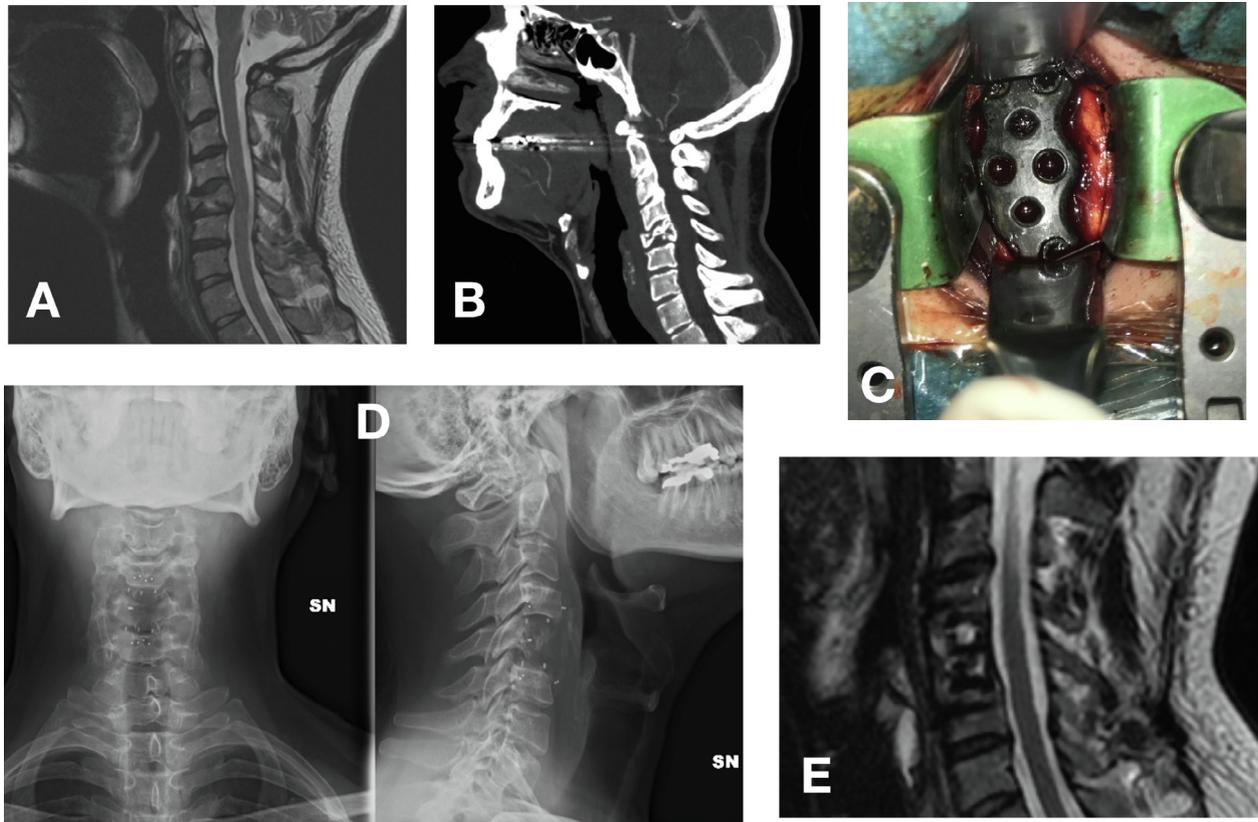


Fig. 2. Male, 32 years old. C5 myeloma with disabling axial pain. (A,B) An anterior approach was performed for intralaminar corpectomy. A PEEK cage and a CFR-PEEK anterior plate were used for replacement and fixation (C,D,E).

This work is coherent with the ethical standards proposed in the Helsinki declaration of Human Rights.

3. Results

Results are summarized in Tables 1–5. A total of 78 patients were reviewed. 36 patients underwent CFR-PEEK fixation, while titanium implants were used for 42 patients. The most common location was the thoracic spine. Non small cell lung cancer (NSCLC) was the most common primary tumor in both groups. The most represented SINS score in both groups was between 7 and 12 points (potentially unstable). In the majority of cases a high grade epidural compression was recorded (69.4% and 73% in the CFR-PEEK group and in the titanium group respectively) (Table 1). Axial pain improved in both groups after surgery with statistical significance at discharge and at last follow-up ($p < 0.01$) (Table 2). In both groups neurological improvement was recorded after surgery and only 2 patients overall worsened at last follow-up (Table 3). A total number of 230 pedicle screws and 2 plates were used for CFR-PEEK, while a total number of 288 pedicle screws and 5 plates were implanted when titanium was used. Mean duration of procedures was longer in the CFR-PEEK group than in the titanium group (215 vs 168 min). Mean blood loss was higher in the CFR-PEEK group (586 vs 410 ml). Length of hospital stay was about 4 days in both groups (3.9 vs 4.2 respectively for CFR-PEEK vs titanium). In the CFR-PEEK group the majority of patients received a circumferential decompression (28/36), while in the titanium group 31 out of 42 patients underwent posterior or posterolateral decompression (Table 4). No significant differences were found between the two groups in terms of post-operative clinical complications and hardware-related complications. A single case of infection and screw loosening was recorded in the titanium group. Failure of

Table 1

Patients demographics, Histology, instability scores and epidural compression data.

	CFR-PEEK group	
Patients	36	42
Sex	M 23 F 13	M 25 F 17
Age	Mean 62.2 (46–78)	Mean 65.6 (42–74)
ASA	2 (81.2%) 3 (18.8%)	2 (85.7%) 3 (14.3%)
score		
Location	1 cervical spine (2.9%) 30 thoracic spine (83.3%) 5 lumbar spine (13.8%)	2 cervical spine (4.7%) 32 thoracic spine (76.2%) 8 lumbar spine (19.1%)
Histology	12 Lung NSCLC (33.3%) 6 Mieloma (16.7%) 4 Breast (11.1%) 4 Prostate (11.1%) 3 Renal Cell Cancer (8.3%) 3 Colon (8.3%) 2 Melanoma (5.6%) 2 Non-Hodgkin Lymphoma (5.6%)	11 Lung NSCLC (26.2%) 7 Mieloma (16.7%) 7 Breast (16.7%) 6 Prostate (14.3%) 4 Melanoma (9.5%) 3 Colon (7.1%) 2 Renal Cell Cancer (4.7%) 1 Hepatocellular carcinoma (2.4%) 1 Non-Hodgkin Lymphoma (2.4%)
SINS	0–6 pts (stable) – 1 (2.8%) 7–12 pts (potentially unstable) – 21 (58.3%) 13–18 pts (unstable) – 14 (38.9%)	0–6 pts (stable) – 1 (0%) 7–12 pts (potentially unstable) – 27 (64.3%) 13–18 pts (unstable) – 15 (35.7%)
ESSC	1a – 1 (2.8%) 1b – 4 (11.1%) 1c – 6 (16.7%) 2–17 (47.2%) 3–8 (22.2%)	1a – 0 (0%) 1b – 3 (7.1%) 1c – 8 (19%) 2–18 (42.9%) 3–13 (30.1%)

the instrumentation, such as breakage of screws, rods, or plates, were not recorded. Follow-up was longer in the titanium group but this difference did not reach a statistical significance (Table 5).

Table 2
Clinical data about axial pain. Both groups improved after surgery with statistical significance.

	NRS pre (mean ± SD/range)	NRS discharge (mean ± SD/range)	NRS last follow-up (mean ± SD/range)	Mean FU (Max/Min) (Months)	p
All patients	8.6 ± 1.3/7–10	4.2 ± 1.9/3–6	2.1 ± 0.9/1–3	14 (28/1)	<0.01
CFR - PEEK group	8.5 ± 1.5/7–10	4.1 ± 1.6/3–5	1.9 ± 1.1/1–3	8 (17/1)	<0.01
TITANIUM group	8.4 ± 1.4/7–9	4.2 ± 2.1/3–6	2.1 ± 1.0/1–3	14 (28/2)	<0.01

Table 3
Neurological improvement after surgery according to the AIS scale for both groups.

AIS scale	AIS pre-op	AIS discharge	AIS last FU
<i>CFR-PEEK group</i>			
A	0	0	0
B	0	0	1
C	3	0	0
D	9	5	4
E	24	31	31
<i>TITANIUM group</i>			
A	0	0	0
B	0	0	1
C	5	2	1
D	15	10	8
E	22	30	32

Table 4
Surgical data.

	CFR-PEEK Group	TITANIUM Group
Previous radiotherapy	7/36	8/42
Extent and type of decompression	28 Circumferential bilateral 3 Circumferential monolateral 2 Anterior 3 Posterior or Postero-lateral 29 Corpectomy 25 Partial 4 Total	31 Posterior or Postero-lateral 5 Circumferential monolateral 4 Circumferential bilateral 5 Anterior 9 Corpectomy 4 Partial 5 Total
Instrumentation	2 cervical plate 230 pedicle screws 70 rods	5 cervical plate 288 pedicle screws 80 rods
Body replacement	3 PEEK cages 6 bone grafts	3 Titanium cages 2 PEEK cages 1 bone graft
Duration of procedures (Mean/Minimum/Maximum)	215 min (80/360)	168 min (95/420)
Blood loss (Mean/Minimum/Maximum)	586 ml (170/1800)	410 ml (165/1450)
Intra-operative complications	1 Incidental durotomy	2 Incidental durotomy
Length of hospital stay (Mean ± SD/range)	3.9 days (±1.1/2–6)	4.2 days (±1.2/2–8)

4. Discussion

Post-operative radiation therapy is a well-established step in the treatment of spinal metastases. In the last decades, the development and integration of spine stereotactic radiosurgery (SSRS), together with the introduction of particle radiation therapy (protons and ions), has revolutionized the field of radiotherapy, dramatically improving control rates of the disease. The selectivity of radiation allows for delivery of a high dose to the target, sparing healthy tissues, thus enhancing local control, regardless of histology and size of the tumor [1,10,11].

Metallic hardware implanted for fixation has always constituted a limitation for postoperative radiotherapy. Density and composition of standard titanium implants are very different from normal tissues and produce perturbation effects [7]. Furthermore,

Table 5
Post-operative data about complications, recurrences and follow-up. CFR-PEEK implants showed a non inferior favorable profile compared to titanium.

	CFR-PEEK Group	TITANIUM Group	P
Post-operative complications	1 CSF leakage (2.7%) 1 Wound Dehiscence (2.7%)	1 CSF leakage (2.2%) 1 Neurological worsening (2.2%) 2 Wound Dehiscences (4.4%)	>0.01
Post-operative hardware-related complications	0 Breakage of screws, rods or plates, disconnection 0 Infections 0 Screw Loosening/Pullout/Failure 0 device misplacement requiring surgery	0 Breakage of screws, rods or plates 1 Infections (2.2%) 1 Screw Loosening (2.2%) 0 device misplacement requiring surgery	>0.01
Local recurrence	2/36 (5.5%)	5/45 (11.1)	>0.01
Mean Follow-up Months (Min/Max)	11 (3/19)	14 (2/28)	>0.01
Death	4/36	19/45	Not Applicable

dose distribution and calculation is negatively influenced by metallic hardware, which hampers the contouring precision. Metals are also responsible for radiation absorption, reducing the effectiveness of radiotherapy [6,7]. In the last few years CFR implants for spine surgery have been developed in order to reduce metal artifacts and absorption, thus strengthening radio-therapeutic planning and effects [12]. In an ex-vivo study [13], CFR-PEEK screws caused a very slight beam perturbation in comparison with titanium ones, therefore providing a lower degree of dose degradation in case of contouring or set-up uncertainties. Reduced artifacts on CT images also improved image quality and dose calculation accuracy.

Oncological results and concrete advantages in terms of local control validated by clinical studies are still lacking, given the very few years of experience with carbonaceous instrumentations. However, the evaluation of biomechanical properties and clinical/radiological outcomes of CFR fixations should represent the first step in this scenario, in order to validate the achievement of a proper primary and long-term stability. CFR composite implants represents a consolidated option in orthopedic surgery [14–17], but few studies described their use in spine surgery. Lindtner et al. performed a cadaveric biomechanical study evaluating screw loosening comparing carbon instrumentation vs titanium [18]. Left and right pedicles were instrumented randomly with either CFR-PEEK or titanium screws. Each pedicle was subjected to cyclic cranio-caudal loading with increasingly progressive forces until loosening or a maximum of 10,000 cycles. In the second part of the study, augmentation of screws with Polymethyl methacrylate (PMMA) was randomly performed with the same biomechanical examination. In their results, CFR-PEEK pedicle screws resisted a similar number of load cycles until loosening compared to titanium screws. The study also demonstrated an enhanced screw

anchorage after cement augmentation. Adler et al. evaluated the biomechanical data of vertebral body replacement (VBR) built in CFR-PEEK [19]. Six thoracolumbar specimens were tested and in all of them CFR-PEEK pedicle screws were used. Two different rods (CFR-PEEK versus titanium) with/without cross connectors and two different VBRs (CFR-PEEK prototype versus titanium) were tested. The authors found that range of motion was significantly reduced in all groups. Compared to titanium rods, the use of CFR-PEEK rods resulted in higher range of motion. The stiffness of the material of the rods was found to influence range of motion more than the stiffness of the material of vertebral body replacement. Ringel et al. described a case series of thirty-five patients with spinal tumors that underwent posterior stabilization with a CFR-PEEK pedicle-based posterior stabilization system [20]. Of 251 pedicle screws implanted, in only one patient with osteoblastic metastases, CFR implantation failed because of a single screw breakage; however, the same failure at the same level was registered with a standard titanium implant after having changed strategy. Apart from that, no other implant-related complications occurred or were registered. As for post-operative planning, a quantitative and qualitative comparison showed a more favorable profile of CFR implants: this instrumentation showed remarkably smaller values of assigned CT-Hounsfield Units (HU) values compared to titanium in the planning system and regions of image artifacts were reduced, improving the accuracy of computational dose calculations and decreasing dosimetric uncertainties. Boriani et al. described preliminary reports of CFR-PEEK in two consecutive studies [6,7] with a final cohort series of 34 tumor patients (14 metastases and 20 primaries). Out of 232 screws only one intraoperative screw breakage occurred. Two events of sacral screw loosening were found at 9 and 12 months in multilevel constructs performed on multirecurrent tumors. Six local recurrences were found early, thanks to the reduced artifacts. Radiation oncologists' opinion was favorable, because of better treatment planning on CT and lack of scattering effect. Clinical use of CFR-PEEK seemed safe and at least comparable with commonly used titanium implants in terms of intraoperative complications, stability, and functional recovery.

The results of the present study confirmed the preliminary reports published in the last few years. Considering axial mechanic pain, linked to spinal instability, a significant improvement was recorded in both groups (Table 2). Neurological recovery or preservation was consistent at last follow-up (Table 3) In the CFR-PEEK group the majority of patients underwent circumferential decompression, while in the titanium group a posterior or posterolateral decompression was performed in most cases (Table 4). This difference is due to a shift in the treatment paradigm through the years, after recent validated evidence supporting separation surgery [2]. Since circumferential decompression usually results in a higher rate of iatrogenic instability compared to a simple posterior decompression, presented clinical and radiological data of CFR-PEEK group confirm the value of the carbonaceous instrumentation. Duration of the procedures was longer in the CFR-PEEK group. This is due to the different and more complex closure system mechanism of the implant used in this series, as the heads of the screws have a small poliaxial range of motion and rods are not moldable. Surgeons are therefore forced to plan the entry points of the screws to allow for proper rod placement. It is clear that there is a learning curve in the handling of this system. Mean blood loss was higher in the CFR-PEEK group because of the higher number of surgeries involving debulking into the vertebral body and circumferential decompression [21]. This did not result in significative differences in the length of hospital stay. A certain disadvantage during surgery is caused by the reduced visibility of the screws during implantation because of their radiolucency on fluoroscopy. However, screw identification appeared to be sufficient

thanks to their titanium coat. Furthermore, intraoperative neuromonitoring constituted a reliable tool to prevent misplacement or cord damage as supported by other studies [22,23]. As for post-operative complications, no differences were found between the two groups. Above all, no hardware related complications were registered among CFR-PEEK fixations. Two recurrences were detected early although it is not possible to estimate to role of implant radiolucency in the timing of diagnosis. The rate of local recurrence and the duration of follow-up did not show significant differences among the two groups. No considerations could be made about the number of dead patients given the different periods of investigation (2015–2017 for Titanium, 2017–2019 for CFR-PEEK).

4.1. Limitations of the study

The relatively small number of patients constitutes a relative limitation of this study. Moreover, the two groups, however similar, were not matched. A bias of the study was the use of different materials for the reconstruction of the anterior column. This investigation does not provide any evidence about the real oncological advantage of carbon instrumentation, which would also allow a cost/benefit analysis. However, recurrences were detected early during follow-up and radiation oncologist' confirmed increased suitability of these composite implants for radiotherapy. Probably a longer follow-up would be needed. However, the mean follow-up of the two groups could be considered acceptable given the nature of the disease of these patients.

5. Conclusion

CFR-PEEK implants constitute a feasible and effective way to restore stability in cases of metastatic tumors to the spine. Compared to titanium, this study showed a non inferior favorable profile in terms of intraoperative and postoperative complications and functional recovery. Further prospective studies are needed to clarify the potentially enormous oncological advantages of their radiolucency for detection of recurrences and a more precise planning for radiotherapy.

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None.

Conflict of interest

The authors have no conflict of interest to disclose.

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Appendix A. Supplementary data

Supplementary data to this article can be found online at <https://doi.org/10.1016/j.jocn.2020.03.013>.

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