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Safety and effectiveness of reinforced carbon-fiber polyetheretherketone (CF-PEEK) in patients with musculoskeletal tumors: experience in a referral center

João Miguel Morgado Silva

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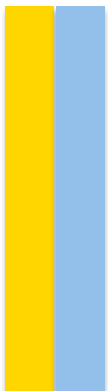

Safety and effectiveness of reinforced carbon-fiber polyetheretherketone (CF-PEEK) in patients with musculoskeletal tumors: experience in a referral center

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Dedicatória

Para ti, minha eterna Maria, que sempre acreditaste que um dia conseguiria aqui chegar e aqui estou. Partiste sem poderes testemunhar todo o meu percurso nesta prestigiada casa, mas onde estiveres, sei que o teu coração transborda de orgulho.

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List of Abbreviations

CF	Carbon-fiber
CF-PEEK	Carbon-fiber polyetheretherketone
CHUdSA	Centro Hospitalar Universitário de Santo António
PEEK	Polyetheretherketone
PTFE	Polytetrafluoroethulene
UHMWPE	Ultra-high molecular weight polyethylene

Abstract

Introduction: Bone is the third most frequent location for metastasis, after lung and liver. We are witnessing an improvement in the survival of patients, and because of that, we expect the number of patients with bone metastasis to grow. Carbon-fiber polyetheretherketone implants (CF-PEEK) have been used in other fields of medicine and in the future can be the *gold standart* in the treatment of pathological and impending fractures. This study evaluates the safety and the effectiveness of CF-PEEK in intramedullary fixation of the bone.

Methods: Between 2018 and 2023, 18-year-old and older patients treated with a CF-PEEK implant for a musculoskeletal tumor at long bones were included. The patients were then divided in groups regarding the type of implant used and were compared incidence and risk factors for mechanical and non-mechanical complications, using the Henderson classification and SPSS Statistics. The results were then compared to the available data in the literature about conventional materials such as titanium.

Results: Thirty-one patients were included in the study. The majority of patients had a malignant diagnosis. 67.7% of patients were treated with CF-PEEK nails and the most common location of surgery was the femur. Complications were found in four patients, and all were classified as non-mechanical with one infection in the surgical site and three tumor progressions. There was no statistical difference between the plate and nail groups regarding complications. Mean follow-up time was 14.08 months and during its period eleven patients have died.

Conclusion: In this study there was no associated mechanical complications, and by so, it shows that CF-PEEK implants are effective and safe in the treatment of musculoskeletal tumors. Despite this, there is the need to more prospective multicentric studies to evaluate the possible mechanical complications to leaping forward in the treatment of musculoskeletal tumors of long bones.

Author Keywords: *Carbon-fiber implants; bone tumors; pathologic fracture; internal fixation; mechanical complications.*

Resumo

Introdução: O osso é o terceiro local mais frequente de metástases, a seguir do pulmão e do fígado. Com os avanços no tratamento, temos testemunhado um aumento da sobrevida dos doentes, e por isso, esperamos que se verifique um aumento no número de doentes com metástases ósseas. Implantes de fibra de carbono reforçados com polieteretercetona (CF-PEEK) têm sido usados em várias valências da medicina e no futuro podem destacar-se como a terapêutica *gold-standard* no tratamento de fraturas patológicas. Este estudo avalia a segurança e a eficácia do CF-PEEK na fixação intramedular do osso.

Métodos: Entre 2018 e 2023, doentes com 18 anos ou mais, com tumor musculoesquelético, tratados com implantes de CF-PEEK foram incluídos. Posteriormente, foram divididos em grupos, tendo em conta o tipo de implante usado, e foi comparada a incidência, bem como fatores de risco, para complicações mecânicas e não mecânicas. Foi utilizada a Classificação de Henderson e o SPSS. Os resultados do estudo foram depois comparados com os dados disponíveis na literatura acerca de materiais em titânio usados previamente neste tipo de tratamento.

Resultados: Trinta e um doentes foram incluídos no estudo. A maioria tinha como diagnóstico um tumor maligno. 67.7% dos doentes tiveram encavilhamento endomedular com varetas de CF-PEEK e a localização mais comum foi o fémur. Verificaram-se quatro complicações, todas não mecânicas, com uma infeção do local cirúrgico e três progressões tumorais. Estatisticamente não houve diferença na incidência de complicações entre os grupos. O tempo médio de follow-up foi de 14.08 meses e durante este período foram registadas onze mortes.

Conclusão: Neste estudo não foram documentadas complicações mecânicas. Desta forma, podemos considerar que os implantes de CF-PEEK são eficazes e seguros no tratamento de metástases ósseas. Apesar disto, existe a necessidade de mais estudos prospetivos multicêntricos, no sentido de avaliar as possíveis complicações mecânicas deste material para cada vez mais, melhorar o tratamento dos tumores musculoesqueléticos nos ossos longos.

Author Keywords: *Carbon-fiber implants; bone tumors; pathologic fracture; internal fixation; mechanical complications.*

Introduction

Bone tumors treatment include intralesional techniques or wide resection with biological or endoprosthetic reconstruction, depending on it's a benign or malignant tumor, primary or metastatic lesion, and accordingly to histology.

Bone tumors are associated to pain, dysfunction, and pathological fractures. Mainly, aggressive benign bone tumors have indication for intralesional treatment with adjuvants and depending on location and size, followed by internal fixation.

Rarely, malignant soft tissue tumors also need segmental bone resection for free margin (wide resection) and those cases require reconstruction including internal fixation or even endoprosthesis if articular reconstruction is needed.

Malignant bone tumors in adults require wide resection and the reconstruction is most frequently made with an endoprosthesis. Nevertheless, depending on location, may have indication for biological reconstruction including allograft and/or vascularized autograft and internal fixation technique.

Bone is the third most frequent location for metastasis, after lung and liver. With the advance in cancer treatments, we are witnessing a significant improvement in overall survival of patients, and by consequence, the number of patients with bone metastases is expected to increase even further. Bone metastases are the main cause of cancer related pain, and are associated to pathological fractures, compression of the spinal cord or nerve roots, and conditions like hypercalcemia which can threaten the patient's life. Treatment depends on primary tumor and histology, response to previous treatments, number of metastases, patient characteristics, and location, articular and soft tissue involvement. In parallel to the systemic treatment, they may require different techniques (in association or not) for local tumor control such as radiotherapy, radiofrequency ablation, and surgery.[1]

Carbon-fiber polyetheretherketone implants (CF-PEEK) have been used in spinal cages, bone fixation screws, and cardiac and neurological leads.[2]

What is Polyetheretherketone?

Polyetheretherketone (PEEK) is a colorless organic thermoplastic polymer, and it belongs to a larger family of materials. It was invented by the ImperialChemical Industries in its laboratories in the UK back in 1978. Even though it was initially conceived as a tough cable-insulation material, capable of resisting to high temperatures, quickly, its characteristics allowed people to explore more fields in which it could be used. By 1981, PEEK was established as a general-purpose molding and extrusion material not only in its pure form or in combination with other materials for high performance applications.[3]

To produce PEEK polymers, a complete dyalkylation of bisphenolate salts is needed, using a step-growth polymerization. The reaction needs to be conducted around 300ºC in polar aprotic solvents, in this case, diphenyl sulfone. The process to produce PEEK is as follows: 4,4'-difluorobenzophenone with disodium salt of hydroquinone, which is generated in situ by deprotonation with sodium carbonate.[4]

After it is produced, PEEK has shown to be insoluble and chemically inert in all the solvents that we use in a daily basis, at room temperature, except for 98% sulfuric acid. PEEK has also shown to have high levels of toughness in tests such as, fracture mechanics, instrument falling weight impact and post-impact compression.[4]

Carbon Fiber

The use of carbon fiber (CF) materials is shared by many industries, and its physical properties have helped us to continuously develop new innovations in medicine. With advances in the production of CF, even more CF composites can be manufacture due to the increased experience that we have and the many more tests that can be done with carbon fiber. In the field of medicine CF is usually used in implants and devices, which range from complete limb prothesis to the smallest of dental implants. We reach a point where we can find almost everything we need from head-to-toe.

In addition, studies have shown that there are no cases of allergic reaction to CF implants throughout the years, not only in animal models but in clinical applications in humans as well, or hypersensitivity responses.[5]

A composite material

The use of composite materials by orthopedic surgeons was initially described in the late 1980s. In that time, these materials were used in joint replacements or fixation of fractures due to trauma. However, in the current practice, the use of composite materials for total joint replacement, has a high failure rate, which, can be assumed, by the formation of a fibrous capsule around the CF reinforced implants preventing their integration to bone. The use of materials like plastic or epoxy in the first composite plates to be produced had the massive disadvantage of their inability to be molded to the anatomy of the bone. In recent years and with the advances in the manufacture of composite materials with thermoplastic polymeric plates this property has been successfully maintained.[4]

To produce a composite material, two or more constituent material of different physical or chemical properties in the micro to macro size range are needed. Therefore, it is composite by one continuous phase, called the reinforcement (in this case the PEEK) and a discontinuous phase, the matrix (the CF in this case). One or more discontinuous phase can be embedded with a continuous phase. The discontinuous phase is harder and stronger than the continuous phase. CF-PEEK shows a high utilization of the fiber in stiffness and strength, and a similarly high utilization of the matrix ductility in toughness.[4]

Disadvantages

CF-PEEK has little to no disadvantages when compared to the conventional materials used. The major one, is undoubtfully, the incapacity to be manually bent to pair to the anatomy of the bone, and because of this, the medical team needs to be able to study preoperatively to guarantee that the implant will fit in the best way. And we know that making these personalized implants to each patient have a considerable cost in time.

Another thing that can be a theoretical disadvantage of using CF-PEEK is the inexperience of surgeons to the material. This can lead to an increased surgery time and consequently exposing the patient to more infections or complication. Of course, after the learning curve is surpassed, the surgical time is expected to be similar.

In addition, as it was said, one of the most important features of PEEK is its radiolucency, and to accomplish that, the surgeons team needs to find its optimal position in the bone and insert the proper screws.[6] CF-PEEK implants cannot be modulated locally. Per-op imaging is essential and radiation exposure and time for fixation may be increased during the learning curve.

Also, some studies have shown that PEEK surfaces are considerable inert and its ability to stimulate osteogenesis is somewhat poor.[7] Although this may not be a problem for oncologic orthopaedic surgeon.

By last, production and availability can bring some disadvantages as it is a somewhat recent material, and the production may not be optimal yet. Despite having higher cost than conventional materials, the difference is small and we know that CF reinforced materials are used across industries like, automotive and aerospace, or even communications, which allow these materials to be more competitive and, consequently, its production costs are decreasing. In addiction there are far more designs of plates made of titanium to match the anatomy of the bone when in comparison with CF-PEEK.[6] CF-PEEK implants may need to be ordered in advance as they are less readily available yet.[8,9] Currently we see that CF-PEEK plates and nails are competitive to conventional titanium plates.[6]

Advantages

Biomechanical Advantages (Elastic modulus closer to the bone)

When in comparison with the conventional metals used in intramedullary fixation of the bone, such as titanium and its alloys, PEEK and its composites show an elastic modulus closer to the bone. To be clear, we know that the elastic modulus of 100GPa which mismatches the human bones (18-25 GPa). This mismatching can lead to bone absorption when we use these materials. However, PEEK has proved to have elastic modulus of 3-4 GPa. This may reduce the concern of the medical team about the bone absorption and the possible osteoporosis that could be caused by stress shielding.[7,10]

Radiolucency

Radiation therapy is an important adjuvant therapy in orthopedic oncology. To plan the radiation therapy properly, we need a material that affects the minimum of the surrounding tissue. The literature shows that conventional metallic implants show a dose-modulating effect in radiotherapy and can complicate its planning. This is caused not only by backscattering, but also advertent dose increases because of the beam attenuation, compromising the efficacy of the treatment.[8,9] To show this comparison in numbers, in previous studies, titanium attenuated the radiation beam by 30% whereas CF-PEEK showed only 5%.[10–12] The follow-up of the patient is also affected, and some recurrences may not be detected earlier due to conventional metallic artefacts that can obscure the imaging results.[8,9]

However, CF-PEEK has shown to be a radiolucent material. It enhances the radiological follow-up of the affected bone regarding their healing, progression, or relapse. Because CF-PEEK has a density closer to that of the tissue to be irradiated the metallic artefacts are reduced during CT-based planning. This affects not only the radiological imaging but also the radiotherapy. These characteristics make CF-PEEK implants mostly valuable to patients that need postoperative radiotherapy. Nevertheless, is yet to be quantified the dose variations that occur within the bone and the implant-bone interface. In addition, in the cases where it is used a CF-PEEK plate and titanium screws, the dose-modulating effect, of those distant to the lesion is unknown and we can theoretically assume that it will depend on the orientation of the radiation beam. With the advances in radiation therapy, we could see a higher agreement of calculated and measured dose distributions.[8–10]

Also, for internal fixation of pathological fractures with articular involvement facilitates the anatomical reduction visualization during the surgical technique.

Creep resistance

PEEK is considered the best creep resistance in the field of thermoplastic polymer.[10]

Self-lubrification and abrasion resistance

PEEK has admirable self-lubricating properties. The wear amount of CF reinforced with PEEK is half of ultra-high molecular weight polyethylene (UHMWPE). PEEK

modified with CF, graphite and polytetrafluoroethulene (PTFE) have excellent abrasion endurance.[10]

Non-toxic

When compared to titanium and its alloys, PEEK has a close cell compatibility and the particles from its wear do not harm or damage body cells.[10]

Excellent sterilization performance

CF-PEEK can preserve its original properties despite being expose to radiation, hot high-pressure steam or ever ethylene oxide, for long periods of time.[10]

Easy to process

We can process PEEK in a lot of ways, and it is easy to combine this material with others. There are numerous processing methods used now to process PEEK such as compression molding, injection molding, extrusion molding, subtractive manufacturing, or even additive manufacturing.[10]

Allergies

CF-PEEK has shown to be the alternative to the conventional materials in patients with allergies to metal.[13]

Methods

Study Design and Setting

This is a retrospective study approved by the DEFI and the Ethics Commission of Centro Hospitalar Universitário de Santo António (CHUdSA), EPE. The information was gathered from a prospective registry that included patients receiving CF-PEEK implants for the treatment of a musculoskeletal tumor.

Participants/Study Subjects

Between 2018 and 2023, 18-year-old and older patients of CHUdSA treated with a CF-PEEK nail and plate for a musculoskeletal tumor at long bones (malignant and benign) were included.

The surgery

Patients were previously discussed by the CHUdSA multidisciplinary team of musculoskeletal tumors. The patient and the orthopaedic surgeon mutually agreed on the course of treatment and this type of procedure. All patients underwent postoperative clinical and imaging follow-up at the 2-week, 6-week, 3-month, 6-month, and 1-year. Subsequent annual follow-up was depending on the patients' oncological status and survival. When indicated, patients performed postop radiation therapy and/or chemotherapy.

Outcome measures

Incidence and risk factors for mechanical and non-mechanical complications were analyzed. Accordingly, to Henderson classification, the mechanical complications included: (Type 1) screw aseptic loosening, (Type 2) structural failures of the host bone, and (Type 3) structural failures of the carbon-fiber implant. Non-mechanical complications included: (Type 4) deep infection and (Type 5) tumor progression.[14] Other complications such as superficial wound dehiscence and/or superficial infection, and perioperative medical adverse events including deaths are also reported. Exclusion criteria included (1) patients younger than 18 years; and (2) oncological surgery. Implant failures were documented within a year and without a time limit.

The following clinical indicators were identified: age, sex, primary tumor, surgical side, pathological or impending fracture, anatomical location, implant type, and use of adjuvants.

Statistical analysis

For the statistical analysis, SPSS Statistics 29.0 was used. The variables are displayed as medians (interquartile range, for continuous variables as they were not normally distributed based on histograms inspection), and frequencies (percentages for categorical variables). Historical data, available in the literature, from patients who received conventional treatment were compared to mortality rates and sequelae, both mechanical and non-mechanical. The papers regarding other materials used for internal fixation were searched in *PubMed, Google Scholar,* and *UpToDate* from November 2022 to April 2023.

Results

Study population

There were 31 patients in this study. With a median age of 60.2 years, 51.6% were females and 48.4% were men (IQR,44.1-76.3; Table I). The majority of patients in the study (61.3%) had an ASA score of 3, and only one patient (3.2%) had an ASA score of 1. Multiple myeloma (32.3%), lung cancer (19.3%), benign tumors (giant cell tumor of bone and aneurysmal bone cyst) (Attachment 1.) (19.3%), and atypical cartilaginous tumor (low-grade chondrosarcoma) (12.9%) were the most common primary tumors (Table II).

The femur (67.7%) was the most common location of surgery, followed by the humerus (25.8%) and tibia (6.5%) (Figures 1-3). Except for one patient (3.2%) with the diagnosis of soft tissue sarcoma, all surgical margins were intralesional. CF-PEEK nails and plates were applied to 67.7% and 32.3% of the patients, respectively. Adjuvant treatment was performed in 51.8% of the patients, with fourteen patients (45.2%) needing postoperative chemotherapy and four (12.9%) needing postoperative radiotherapy. There was no need to autografts or allografts in any of the patients included in the study. PMMA was used in half of the patients, combination of cement and radiofrequency ablation was used in six patients (21.6%), and association of drill, phenol and cement as adjuvants to curettage were used in eight patients (30.8%).

Complications

Complications were found in 4 patients (12.9%), and all were classified as non-mechanical. Of these, one patient experienced infection within a year at the surgical site, and the remaining three experienced tumor progression, two of them within a year and another within two years. Revision was performed in all cases. Revisions were performed in two patients with benign tumors and in two patients with atypical cartilaginous tumor (ACT). In one ACT patient there was the need to transfemoral amputation due to local tumor up-grade recurrence (high-grade chondrosarcoma). In the other ACT patient, it was performed a total shoulder reverse endoprosthetic reconstruction subsequent to the diagnosis of chondrosarcoma grade 2, just after the initial intralesional treatment. A patient with a giant cell tumor of the distal femur was reviewed to an endoprosthesis (in 2-stages treatment), after being infected and attempt two times failed surgical treatment. Currently, there is no evidence of an active infection. In the revision of the patient with the Henderson 5A complication, there was no need to change the CF-PEEK plate, only resection of the soft tissue recurrence (GCT). There was no statistical difference between the nail and plate groups regarding complications. The mean follow-up time was 14.08 months (range 0-47). Patients with a follow-up time of 0 months were followed up at other institutions. Unfortunately, eleven patients (35.5%) died during follow-up (metastatic patients).

Discussion

As CF-PEEK is a relatively new material and few studies have been published. Despite this, multicenter studies on CF-PEEK implants in patients with musculoskeletal tumors are starting to come out.

For many years, titanium has been the preferred material for internal fixation of bone, as it has an edge over materials such as stainless steel, showing benefits in increased range of motion, general healing, and the ability to walk again.[15,16] Its use is relatively safe, and its clinical outcomes are good for most types of patients. However, in oncological patients, the use of titanium nails and plates may affect the general outcome.[6] However, the most important factor seems to be the capacity

to reduce the beam attenuation, facilitating postoperative radiotherapy and follow up, particularly for recurrence detection. With the use of a radiolucent material, we're able to see much better the recovery of the patient and the surgical site, through MRI or CT scans as the backscattering effect is reduced as *Zinel et al. (2015)* has shown.[17] This study has shown that CF-PEEK nails and plates cause a much less loss of signal in MRI than titanium alloys, especially as the angle increased with relation to direction of the static magnetic field.[17] *Ziran et al. (2020),* in one of the few studies comparing head-to-head CF-PEEK to titanium nails in trauma patients, showed that patients treated with CF-PEEK nails had accelerated healing times at 8, 12, 16, and 20 weeks post-op. This opens a discussion point, whereas the use of CF-PEEK can reduce the barometric pain of the patients by providing them with a quicker healing time, but evidently, more research in this field must be done.[18]

Steinberg et al. (2015) compared the use of CF-PEEK nails and plates to commercially available materials for wear/debris for trauma patients. For this purpose, they considered the amount of debris generated in the connection between the CF-PEEK tibial nails, dynamic compression plates, proximal humerus plates and titanium screws. In this study, the CF-PEEK nails performed equally in terms of four-point bending, static torsion of the nail, and bending fatigue. The authors showed a better performance of the CF-PEEK than the titanium alloys, as it created a lower weight of debris.[2]

Because CF-PEEK is a very durable material, its combination with less-invasive surgical techniques can be an option for patients to whom are particularly important to reduce the reoperation risk.[2]

Calleb et al. (2022) in a direct comparison between titanium and CF-PEEK nails in oncologic orthopaedics, showed a slightly higher complication rate in the group of patients treated with titanium ones. In that study, 36 patients were treated with conventional material and showed a 19% complication rate, whereas in the CF-PEEK group, the complication rate was 3%.[19]

In the present study, four complications were reported. All four patients experienced non-mechanical complications, mainly tumor progression. Compared to the available data in the literature, this percentage of complications was slightly lower than that reported by *Jansen et al. (2016).*[20] There may be many reasons that contribute to the lower complication rate of CF-PEEK compared to that of titanium alloys. The use of materials with improved stiffness and strength allows a more rigid fixation of the fracture without sacrificing the original benefits of CF-PEEK.[19]

Although we are using more and better materials in the treatment of our patients, we cannot ignore the fact that patients with advanced metastatic disease are in a late stage of illness and may not live long enough to experience the complications of this treatment and benefit from a local tumor control in combination to the systemic palliative treatment to improve their quality of life.[21] Advances in current medicine and the discovery of new ways to not only treat oncological diseases but also provide patients with a better quality of life have led to an increase in the overall survival rate of patients with cancer, in studies such as those by *Italiano et al*.[22] Despite this, it is well known that this battle is still very unbalanced, and there is still a lot to discover and study to ultimately come up with a cure for this type of disease.

There was one chronic infection case and 3 tumor progression cases that required revision surgery, preserving the implant in one case (25%).

Intramedullary nailing with CF-PEEK long nails for long bone metastases presenting impending or pathological fractures are expected to increase.[21] Concerning the long bone metastases, intramedullary nailing is frequently used to stabilize an impending or actual fracture because it is a minimally invasive procedure, minimizes complications risk, reliefs localized pain, allows for immediate weight bearing in femur, immediate mobilization, and rapid rehabilitation.[23,24] The use of a long nail also provides mechanical support and prophylactic treatment against future fractures in other regions of the long bone.[23] It should be assumed the minimal healing tendencies or non-union of pathological fractures, nevertheless, as a result of the limited survival of these patients, the load-sharing device may not exceed the fatigue life of the implant.[23,25–28]Long survival is an important risk factor for failure and for that is important to adequately estimate survival.[23]

Willeumier et al. reported a 5 centers retrospective study of 245 patients treated for impending or actual fracture of the femur and reported a local complications rate of 12% with 6-month cumulative incidence of 8%. Implant breakage occurred in 8% of patients and 6-month cumulative incidence was 4%. All the fractured nails (3%) occurred at the junction with the neck screw. Independent factors associated with increased risk of implant breakage were actual fracture and previous radiotherapy. Revision occurred in 5% of patients and 6-month cumulative incidence was 2.2%. An actual fracture was independently associated with a higher revision risk, and use of cement was independently associated with a lower risk of revision. Authors confirmed that the overall incidence of revision, implant

breakage, and local complications (lasting pain despite surgery and analgesics, or tumor progression, needing further adjuvant treatments such as radiotherapy or surgery) was low, also as a result of the short survival of patients.[23]

Intramedullary nailing for pathological humeral fractures demonstrated good overall results, although may present complications with longer survival. *Willeumier et al.* reported 12.6% of failures associated to intramedullary nailing of humerus. Nevertheless, the short survival of the metastatic patients may underestimate the complications rate. *Willeumier et al.* showed that cement association to intramedullary nailing of femur reduces the risk of revision, particularly important for actual fractures treatment.[23] In addition, studies on percutaneous cement augmentation while performing close intramedullary nailing of long bones demonstrate significant and rapid pain relief, and suppressed progression of the metastasis on PET-CT, CT scan or bone scintigraphy up to 15 months of follow-up.[21, 29, 30]

It is important to have conscience that any major complications and re-operations have a high impact on these patients' limited lifetime and on the quality of remaining life.[21]

Cappellari et al. concluded that intramedullary nailing is indicated in metaphyseal or diaphyseal metastases when the life expectancy of patients does not overcome the expected survival of the nail, avoiding the need for further surgery. Patients expected to live longer may benefit from resection and endoprosthetic reconstructions.[31]

Willeumier et al. conclude that decision should be based on the expected survival of the patient, the type and extent of the tumor, and the location of the fracture, on a referral centralized care.[32]

CF-PEEK nails presented no mechanical complications in our study comparing to the published rate of titanium implants. Nevertheless, *Rijs et al.* published a multicenter study with a complication rate, with 9,8% of the complications occurring in the first year postoperatively.[6]

The reported fractures of the titanium nails occurred at the junction with the neck screw. At the CF-PEEK nails, the titanium screws present a potential risk of failure due the previously described biomechanical characteristics of the CF-PEEK compared to the titanium. Actually, in that study fracture of the titanium screws was already reported in a few cases of intramedullary nailing, occurring in 2.9% of the patients, with the femoral nail being the most common to fracture (2.1% of

patients), followed by the humerus' (0.8% of patients). No fracture of the tibial nail was observed.[6] Maybe it will be possible to improve the fixation technique of CF-PEEK implants in the future, especially when applied for longer survival patients. For that, it is important to more accurately analyze these implants outcome in larger studies with longer follow-up.
Nevertheless, the advantages and effectiveness of CF-PEEK implants are already prevalent and started to came out. This present study also contributes to show their effectiveness.

This study has some limitations. First, the study's retrospective approach and inherent flaws should be considered when interpreting the results. Nevertheless, the impact of the retrospective nature was thought to be small because the results of success and failure are undeniable. Second, there was no direct comparison of the results and clinical outcomes of patients treated with titanium nails and plates. Our results are compared with those of published papers, and a direct comparison of these two types of materials in our patients would be a better fit. However, this was not possible due to the small number of patients included with femur, tibia, or humerus lesions. Besides that, there are heterogeneity inherent to the tumor type, its biological behavior, and subsequent bone-tumor microenvironment. In addition, these patients' survival, particularly the metastatic patients, may limit the follow-up.

Conclusion

This study shows that CF-PEEK implants are safe and effective for the treatment of musculoskeletal tumors. For oncological patients these implants provide known advantages. In this study there was no associated mechanical complications.
Larger, prospective multicentric studies are important to better analyze the possible mechanical complications and if there is something to improve in order to leaping forward in the treatment of musculoskeletal tumors of long bones.

References

1. Tsukamoto S, Kido A, Tanaka Y, et al. Current Overview of Treatment for Metastatic Bone Disease. *Curr Oncol*. 2021;28(5):3347-3372. doi:https://doi.org/10.3390/curroncol28050290
2. Li CS, Vannabouathong C, Sprague S, Bhandari M. The Use of Carbon-Fiber-Reinforced (CFR) PEEK Material in Orthopedic Implants: A Systematic Review. *Clin Med Insights Arthritis Musculoskelet Disord*. 2015;8:33-45. doi:10.4137/CMAMD.S20354
3. May R. Polyetheretherketones. *Encycl Polym Sci Technol*. Published online 2008. doi:https://doi.org/10.1002/0471440264.pst266
4. Steinberg EL, Rath E, Shlaifer A, Chechik O, Maman E, Salai M. Carbon fiber reinforced PEEK Optima—A composite material biomechanical properties and wear/debris characteristics of CF-PEEK composites for orthopedic trauma implants. *J Mech Behav Biomed Mater*. 2013;17:221-228.
5. Hillock R, Howard S. Utility of Carbon Fiber Implants in Orthopedic Surgery: Literature Review. 2014;4(1). doi:https://doi.org/10.15438/rr.v4i1.55
6. Rijs Z, Weekhout A, Lozano-Calderon SA, et al. Complications of patients with bone tumors treated with carbon-fiber plates: an international multicenter study. *Sci Rep*. 2022;12(18969). doi:https://doi.org/10.1038/s41598-022-23519-9
7. Qin W, Li Y, Ma J, et al. Osseointegration and biosafety of graphene oxide wrapped porous CF/PEEK composites as implantable materials: The role of surface structure and chemistry. *Dent Mater*. 2020;36:1289-1302. doi:https://doi.org/10.1016/j.dental.2020.06.004
8. Christoph J. Laux, Hodel SM, Farshad MD, Müller A. Carbon fibre/polyether ether ketone (CF/PEEK) implants in orthopaedic oncology. *World J Surg Oncol*. 2018;16(1):241. doi:10.1186/s12957-018-1545-9
9. Fleege1 C, Makowski M, Rauschmann M, et al. Carbon fiber-reinforced pedicle screws reduce artifacts in magnetic resonance imaging of patients with lumbar spondylodesis. *Sci Rep*. 2020;10. doi:https://doi.org/10.1038/s41598-020-73386-5
10. Ma H, Suonan A, Zhou J, et al. PEEK (Polyether-ether-ketone) and its composite materials in orthopedic implantation. *Arab J Chem*. 2021;14(3). doi:https://doi.org/10.1016/j.arabjc.2020.102977
11. Laux CJ, Hodel SM, Farshad M, Müller DA. Carbon fibre/polyether ether

ketone (CF/ PEEK) implants in orthopaedic oncology. *World J Surg Oncol*. 2018;16(241). doi:https://doi.org/10.1186/s12957-018-1545-9

12. K. A. Jockisch, S. A. Brown, T. W. Bauer KM. Biological response to chopped-carbon-fiber-reinforced peek. *J Biomed Mater Res*. 1992;26(2):133-146. https://doi.org/10.1002/jbm.820260202
13. Vles GF, Brodermann MH, Roussot MA, Youngman J. Carbon-Fiber-Reinforced PEEK Intramedullary Nails Defining the Niche. *Case Rep Orthop*. 2019;2019:1-6. doi:10.1155/2019/1538158
14. Henderson ER, O'Connor MI, Ruggieri P, et al. Classification of failure of limb salvage after reconstructive surgery for bone tumours: A modified system including biological and expandable reconstructions. *Bone Jt J*. 2014;96B(11):1436-1440. doi:10.1302/0301-620X.96B11.34747
15. Greco T, Fulchignoni C, Cianni L, Maccauro G, Perisano C. Surgical management of tibial metastases: a systematic review. *Acta Biomed*. 2021;92. doi:10.23750/abm.v92iS3.12540
16. Barber CC, Burnham M, Ojameruaye O, McKee MD. A systematic review of the use of titanium versus stainless steel implants for fracture fixation. *OTA Int Open Access J Orthop Trauma*. 2021;4(3):e138. doi:10.1097/oi9.0000000000000138
17. Zimel MN, Hwang S, Riedel ER, Healey JH. Carbon fiber intramedullary nails reduce artifact in postoperative advanced imaging. *Skeletal Radiol*. 2015;44(9):1317-1325. doi:10.1007/s00256-015-2158-9
18. Ziran BH, O'Pry EK, Harris RM. Carbon fiber-reinforced PEEK versus titanium tibial intramedullary nailing: A preliminary analysis and results. *J Orthop Trauma*. 2020;34(8):429-433. doi:10.1097/BOT.0000000000001756
19. Yeung CM, Bhashyam AR, Groot OQ, et al. Comparison of carbon fibre and titanium intramedullary nails in orthopaedic oncology. *Bone Jt Open*. 2022;3(8):648-655. doi:10.1302/2633-1462.38.bjo-2022-0092.r1
20. Janssen SJ, Kortlever JTP, Ready JE, et al. Complications after surgical management of proximal femoral metastasis: A retrospective study of 417 patients. *J Am Acad Orthop Surg*. 2016;24(7):483-494. doi:10.5435/JAAOS-D-16-00043
21. Oliveira VCC. Innovative Treatment for Bone Metastases. Doctoral Thesis in Medical Sciences, ICBAS – University of Porto. Vânia Oliveira (Ed). ISBN 978-989-33-1712-9
22. Italiano A, Mathoulin-Pelissier S, Cesne A Le, et al. Trends in survival for

patients with metastatic soft-tissue sarcoma. *ACS Journals*. 2011;117(5):1049-1054. doi:10.1002/cncr.25538

23. Willeumier JJ, Kaynak M, Van Der Zwaal P, et al. What factors are associated with implant breakage and revision after intramedullary nailing for femoral metastases? *Clin Orthop Relat Res*. 2018;476(9):1823-1833. doi:10.1007/s11999.0000000000000201
24. Tanaka T, Imanishi J, Charoenlap C, Choong PFM. Intramedullary nailing has sufficient durability for metastatic femoral fractures. *World J Surg Oncol*. 2016;14(1). doi:10.1186/s12957-016-0836-2
25. Shemesh S, Kosashvili Y, Sidon E, Yaari L, Cohen N, Velkes S. Intramedullary nailing without curettage and cement augmentation for the treatment of impending and complete pathological fractures of the proximal or midshaft femur. *Acta Orthop Belg*. 2014;80(1):144-150.
26. Gainor BJ, Buchert P. Fracture healing in metastatic bone disease. *Clin Orthop Relat Res*. 1983;178:297-302. doi:10.1097/00003086-198309000-00041
27. Maes M, Deboer Y, Brabants K. Failure of the titanium trochanteric Gamma nail in ununited metastatic fractures. *Acta Orthop Belg*. 2012;78(4):552-557.
28. Beauchamp CP. Surgical treatment of skeletal metastatic lesions of the proximal femur: Endoprosthesis or reconstruction nail? *Yearb Orthop*. 2007;2007:282-283. doi:10.1016/s0276-1092(08)70268-2
29. Y.-I. K, H.G. K, J.H. K, S.-K. K, P.P. L, H.S. K. Closed intramedullary nailing with percutaneous cement augmentation for long bone metastases. *Bone Jt J*. 2016;98(5):703-709. http://www.embase.com/search/results?subaction=viewrecord&from=export&id=L611038242%0Ahttp://dx.doi.org/10.1302/0301620X.98B5.35312
30. Oliveira V, Leite XF, Ribau A, Cardoso P, Araujo A (2021) Rapid Pain Relief and Functional Improvement after Local Radiofrequency Ablation and Cementing Combined with Internal Fixation for Long Bone Metastases: A Prospective Study. J Orthop Oncol 7: 145.
31. Cappellari A, Trovarelli G, Crimì A, et al. New concepts in the surgical treatment of actual and impending pathological fractures in metastatic disease. *Injury*. Published online 2020. doi:10.1016/j.injury.2020.11.025
32. J.J. W, M.A.J. VDS, R.J.P. VDW, P.D.S. D. Trends in the surgical treatment of pathological fractures of the long bones: Based on a questionnaire among

members of the Dutch orthopaedic society and the European musculo-skeletal oncology society (EMSOS). *Bone Jt J*. 2018;100B(10):1392-1398. http://www.embase.com/search/results?subaction=viewrecord&from=export&id=L624277473%0Ahttp://dx.doi.org/10.1302/0301-620X.100B10.BJJ-2018-0239.R1

Attachments

Table I. Characteristics of patients treated surgically with CF-PEEK implants (n=31)	
Variables	***% (n)***
Age (years) - median (IQR)	60.2 (44.1-76.3)
Female	51.6 (16)
ASA score	
1	3.2 (1)
2	25.8 (8)
3	61.3 (19)
4	9.7 (3)
Tumor grade[a]	
Low	65.4 (17)
High	34.6 (9)
Preoperative chemotheraphy	38.7 (12)
Preoperative radiotheraphy	3.2 (1)
Postoperative chemoteraphy	45.2 (14)
Postoperative radiotherapy	12.9 (4)
Surgical variables	
Surgical side	
Left	54.8 (17)
Right	45.2 (14)
Pathological fracture	32.3 (10)
Impending Fracture	51.6 (16)
Anatomical location	
Femur	67.7 (21)
Humerus	25.8 (8)
Tibia	6.5 (2)
Location of bone	
Diaphyseal	45.2 (14)
Metaphyseal (or meta-epiphyseal)	54.8 (17)
Type of implant	
Nails	67.7 (21)
Plates	32.3 (10)
Margins	
Intralesional	96.8 (30)
Wide	3.2 (1)
Complications[b]	
Henderson 4A	3.0 (1)
Henderson 5A	3.0 (1)
Henderson 5B	6.0 (2)
Cement (PMMA)[c]	50.0 (13)
Cement + RFA[c]	23.1 (6)
Adjuvants[c]	
None	69.2 (18)
Drill + phenol + cement	30.8 (8)
Revision Surgery	
Yes[d]	12.9 (4)

IQR – interquartile range; ASA – American Society of Anesthesiologists; PMMA - Polymethyl methacrylate; RFA – Radiofrequency Ablation.
a Missing data was present in 6 patients.
b Missing data was present in 1 patient.
c Missing data was present in 6 patients.
d All revisions were made in patients with complications.
Source: Made by the authors.

Table II. Characteristics of tumors (n=31)

Tumor	***% (n)***
Breast (bone metastasis)	6.5 (2)
Lung (bone metastasis)	19.3 (6)
Multiple Myeloma	32.3 (10)
Atypical Cartilaginous Tumor	12.9 (4)
Soft Tissue Sarcoma	6.5 (2)
Benign	19.3 (6)
Gastrointestinal (bone metastasis)	3.2 (1)

Source: Made by the authors.

Figure 1. Giant cell tumor of distal femur treated with curettage, drill, phenol and cement filling. A CF-PEEK plate was used for internal fixation.

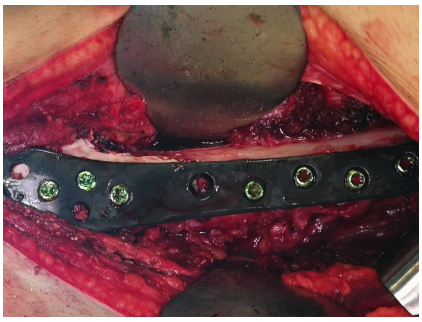

Figure 2. Conventional radiographs showing a proximal tibia osteolytic metastasis (a-b) submitted to radiofrequency ablation (c), cement and intramedullary fixation of the right tibia using a CF-PEEK nail (d). The CF-PEEK nail is radiolucent and the fixation screws are radiopaque in titanium.

Figure 3. Atypical cartilaginous tumor of the left humerus after curettage, drill, phenol, cement filling and internal fixation with a CF-PEEK plate of the proximal humerus.