

The advantages of carbon fiber-based orthopedic devices in patients who have to undergo radiotherapy: an experimental evidence

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Summary. *Background and Objectives:* The modern approach to primary and secondary muscular skeletal tumors is multidisciplinary. The right combination of chemotherapy, surgery and radiotherapy (RT) makes obtaining local and distant disease control more likely. When surgery is indicated, radiotherapy often has a fundamental role as an adjuvant treatment; however, the titanium alloy instrumentations interfere with Radiotherapy setting, decreasing its effectiveness. It is common opinion that carbon fiber-reinforced devices are convenient in case of adjuvant RT in muscular skeletal oncology. The aim of the study is to support this intuition with experimental data, verifying the more accurate estimation of the delivered dose during RT, comparing Carbon Fiber-Reinforced PEEK (CFRP) plates with titanium-alloy orthopedic devices in order to evaluate their effects on target volume identification and dose distribution for radiation treatment. *Methods:* Phantoms were then irradiated with a linear accelerator Varian 2100 C/D with photon beams of 6 and 15 MV energies. Absorbed dose in the point of interest was verified by EBT3 gafchromic films above and below the two materials. Images from CT simulations were also analyzed in terms of Hounsfield numbers in patients with titanium and carbon fiber orthopedic implants in the spine or in the femur. *Results:* For a 6 MV photon beam, the doses measured just under the titanium-alloy plate were less than approximately 20% of the value calculated by the TPS. For a 15 MV beam energy, these differences were slightly lower. Using CFRP plate, the difference between measured and calculated doses was within $\pm 3\%$ for both energies, which was comparable with the statistical uncertainties. In the cases of simulated treatment of humerus titanium implants, the difference varies in range $\pm 10\%$ with hot spot of + 10% and cold spot of -15%. *Conclusions:* The use of CFRP for orthopedic devices and implants provides a valuable advantage in identifying the target due to the reduction of artifacts. Clear imaging of the soft tissues surrounding the bone is useful and reduces the discrepancies between calculated/delivered and measured doses, generating a more homogeneous dose distribution. Furthermore, there is a significant benefit in detecting the state of disease in CT imaging during the follow-up of treated patients. In-vivo studies are encouraged to verify whether a more effective radiotherapy leads to a decrease in local recurrence and local progression. (www.actabiomedica.com)

Key words: Metastatic bone disease, Radiochromic film, Orthopaedic implant, Carbon fiber, Radiotherapy

Introduction

The modern approach to primary and secondary muscular skeletal tumors is multidisciplinary. The right combination of chemotherapy, surgery and radiotherapy (RT) makes obtaining local and distant disease more likely. When surgery is indicated, radiotherapy often has a fundamental role as an adjuvant treatment [1,2].

After tumor resection or in cases of osteolysis or fracture, long bones are fixed with intramedullary nails or plates and screws. Unfortunately, osteosynthesis limits the feasibility and efficacy of adjuvant radiation therapy. Indeed, ferromagnetic materials such as titanium alloy or stainless steel, generally used in these types of implants, cause artifacts in imaging, making target identification and the assessment of the amount of radiation dose actually administered to the tissues difficult. In literature, this is a well-known issue for patients with pelvic tumors who previously underwent hip replacement; several authors have evaluated the dosimetric uncertainties and have tried to propose practical solutions to improve treatment [3,4].

New carbon-based materials could represent a possible solution because they generate fewer artifacts at CT and MRI scans, in addition to being chemically and biologically stable.

In order to increase their biomechanical qualities, carbon fibers are wound in a double helix on a plastic support giving rise to a new composite material, named Carbon Fiber-Reinforced Poly-Ether-Ether-Ketone (CFRP). Mechanical properties related to clinical applications such as strength and elasticity have been extensively studied [5].

The radiation properties of this material are similar to those of biological tissues and therefore it is more suitable for patients who have to undergo radiotherapy, or rather in patients with bone metastases for whom surgery only has a mechanical intent while radiotherapy is mandatory to improve local disease control.

The clinical applications and relative imaging of CFRP implants were already described in literature [6-9].

The use of intramedullary nails, plates, rods and screws made of carbon alloy permits to enhance imaging, to reduce artifacts and plan an optimal radiation strategy [10,11].

Ringel et al. [12] evaluated the differences in Hounsfield units in 35 patients with spinal tumors who underwent stabilization with CFRP or titanium, in order to perform a qualitative comparison of the effect of artifacts in dose distribution obtained with photons and protons.

Nevelesky et al. [13] calculated the perturbation in the dose distribution calculated with Monte Carlo simulation at different distances from the CFRP screw.

However, to the best of our knowledge, there are no studies investigating the accuracy of dose distribution obtained with clinical treatment planning systems (TPSs) reporting quantitative data. This is a critical issue because Monte Carlo simulations are not generally used in clinical practice so the assessment of the accuracy of TPSs and measurements is of paramount importance.

The aim of this study is to value the predictability of the actual radiation dose distributed to tissues in the presence of CFRP orthopedic devices and in the presence of titanium-alloy orthopedic devices when irradiated with photon beams of 6 and 15 MV energies, and to value their effects on target volume identification and dose distribution in bone cancer patients.

Materials and Methods

Design of the study: The basic idea of this study is to simulate two identical radiotherapy treatments performed on two patients, one with a titanium prosthesis and one with a carbon prosthesis.

In clinical practice, the preparation for radiotherapy treatment begins with the CT images, continues with the treatment planning set up and ends with the irradiation.

To reproduce these "artificial" patients, the titanium and carbon nails were inserted in human tissue-equivalent materials. The procedures performed during the experimental processes are the same as for real patients.



Fig.1 Photo of setup #1, carbon plate on the left and titanium alloy on the right.



Fig.2 Carbon nail right before being wrapped in water equivalent bolus.

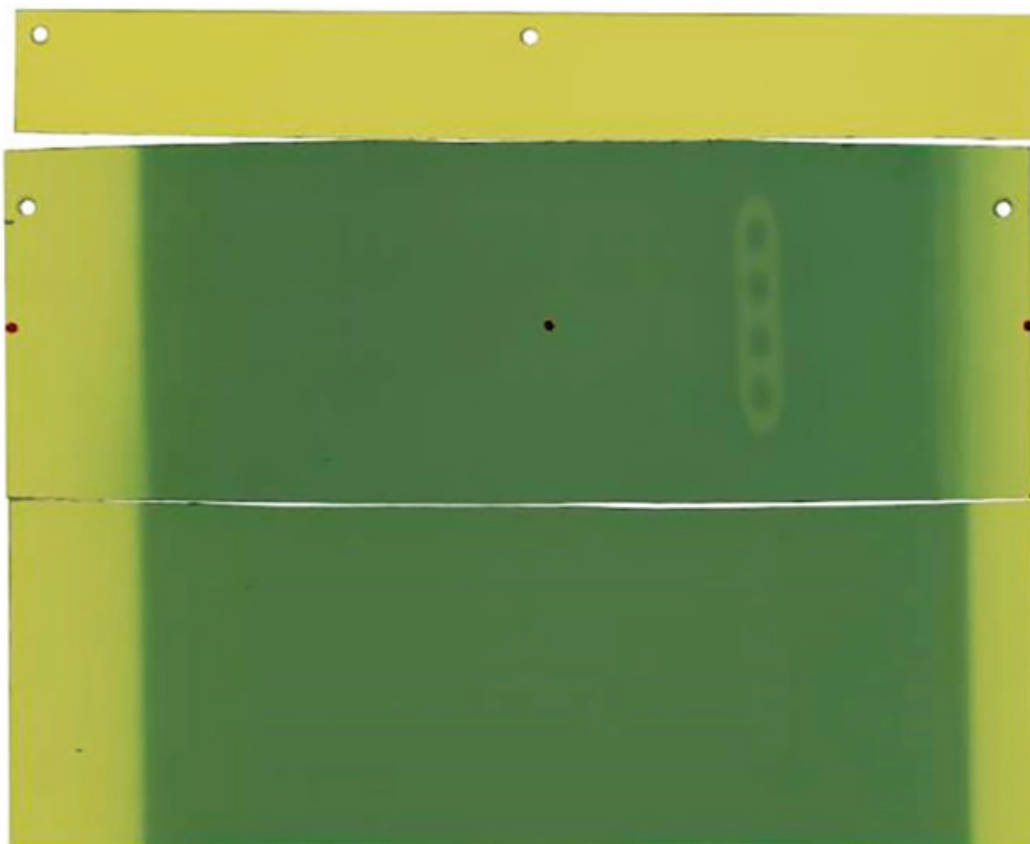


Fig.3 Gafchromics image of setup #1 after irradiation

This made it possible to highlight the critical issues and qualitatively and quantitatively evaluate the treatments carried out .

Orthopedic implants investigated and phantom to simulate patients: Two measurement setups were used with the intent to simulate irradiation in patients who had undergone surgery during which the hardware was implanted.

The simulation was done by including both the carbon and the titanium alloy in order to value the difference in terms of relapsed dose and imaging.

Setup n.1: A 6 cm carbon plate (Carbofix™) and a 6 cm titanium plate, generally used for fracture and osteotomy fixation, were positioned in a solid water phantom to simulate a homogeneous human tissue (Fig.1). The phantom consists in 30x30 cm² slabs of different thicknesses overlapping for a total height of about 20 cm.

Setup n.2: a flexible sheet of 5 mm and/or 10 mm thick water equivalent material was wrapped around a titanium nail and around a carbon nail (Carbofix™) (2) to simulate the implant in a long bone.

CT scans were performed for both set-ups.

Dosimetry: EBT3 Gafchromic films were used to measure the dose delivered around the orthopedic devices. These are self-developing dosimetry films composed by different layers of active material. They are nearly tissue equivalent and can be immersed in water. EBT3 are available as sheets of 0.25 mm of thickness so that, cut in the desired shape, they were particularly suitable for this experiment. Before irradiation, EBT3 films are yellow, and change to green after irradiation because the active layer undergoes a polymerization process causing a peak in the absorption spectra at 636 nm. These effects are used for dose determination.

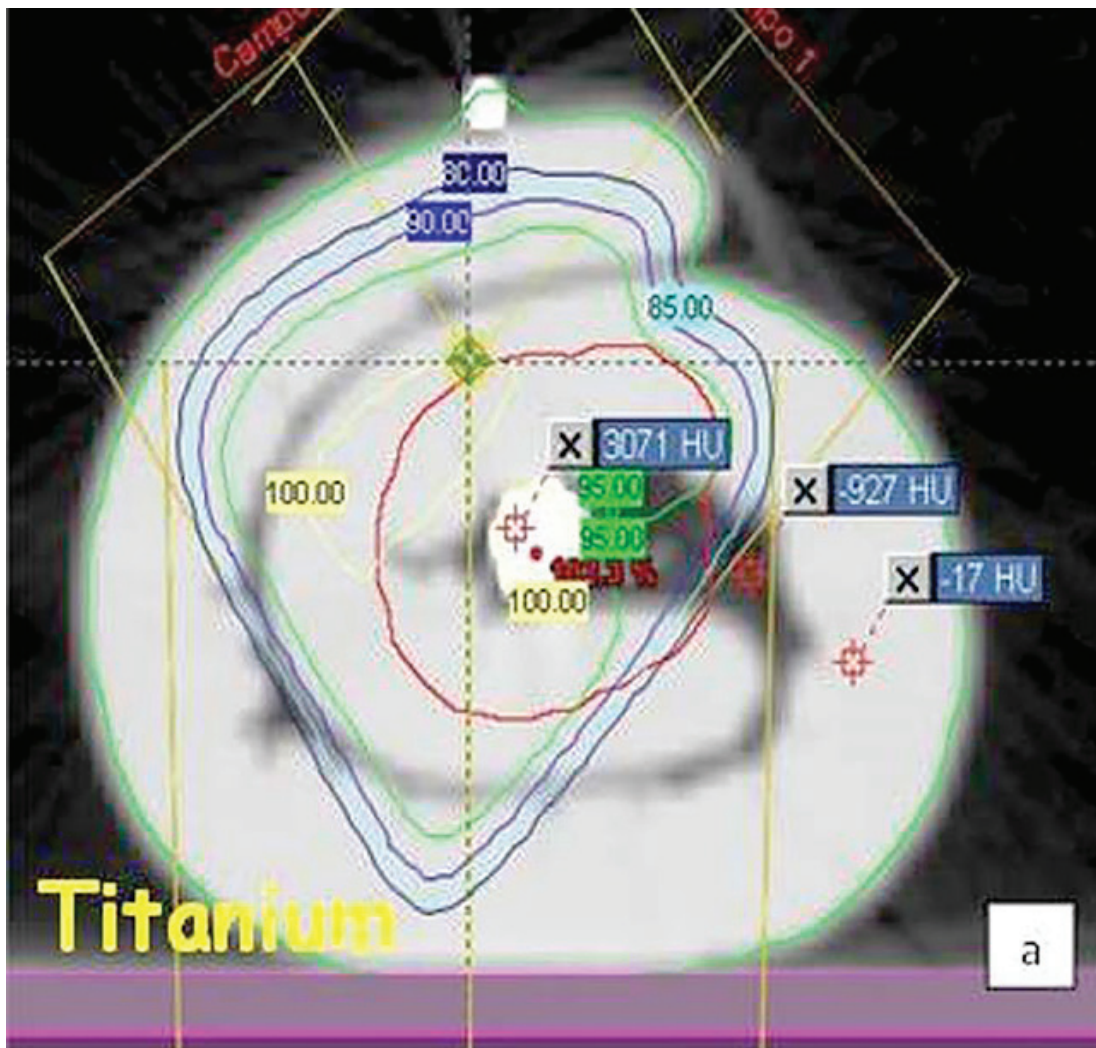


Fig.4 a) image from TPS: HU and dose calculation for setup #2 with the titanium nail;

For calibration, film samples were cut ($2 \times 3 \text{ cm}^2$) and irradiated with a 6 MV photon beam with a Varian Clinac 2100C/D accelerator. Samples were placed at the build-up in a solid water phantom positioned on the beam axis, $20 \times 20 \text{ cm}^2$ field size at a Source to Surface Distance (SSD) 100cm. The absorbed dose was determined in the point of measurement by a PTW ionization chamber, calibrated at a Standard

Laboratory, according to the IAEA protocol (TRS 398). Dose range was from 0 to 8 Gy. A commercial Epson Expression 10000XL color flatbed scanner was used to digitalize the film samples in landscape orientation. The scanner had a high spatial resolution and the acquisition was performed in the red channel. In order to minimize errors all film pieces were positioned in a well identified area of the scanner, in

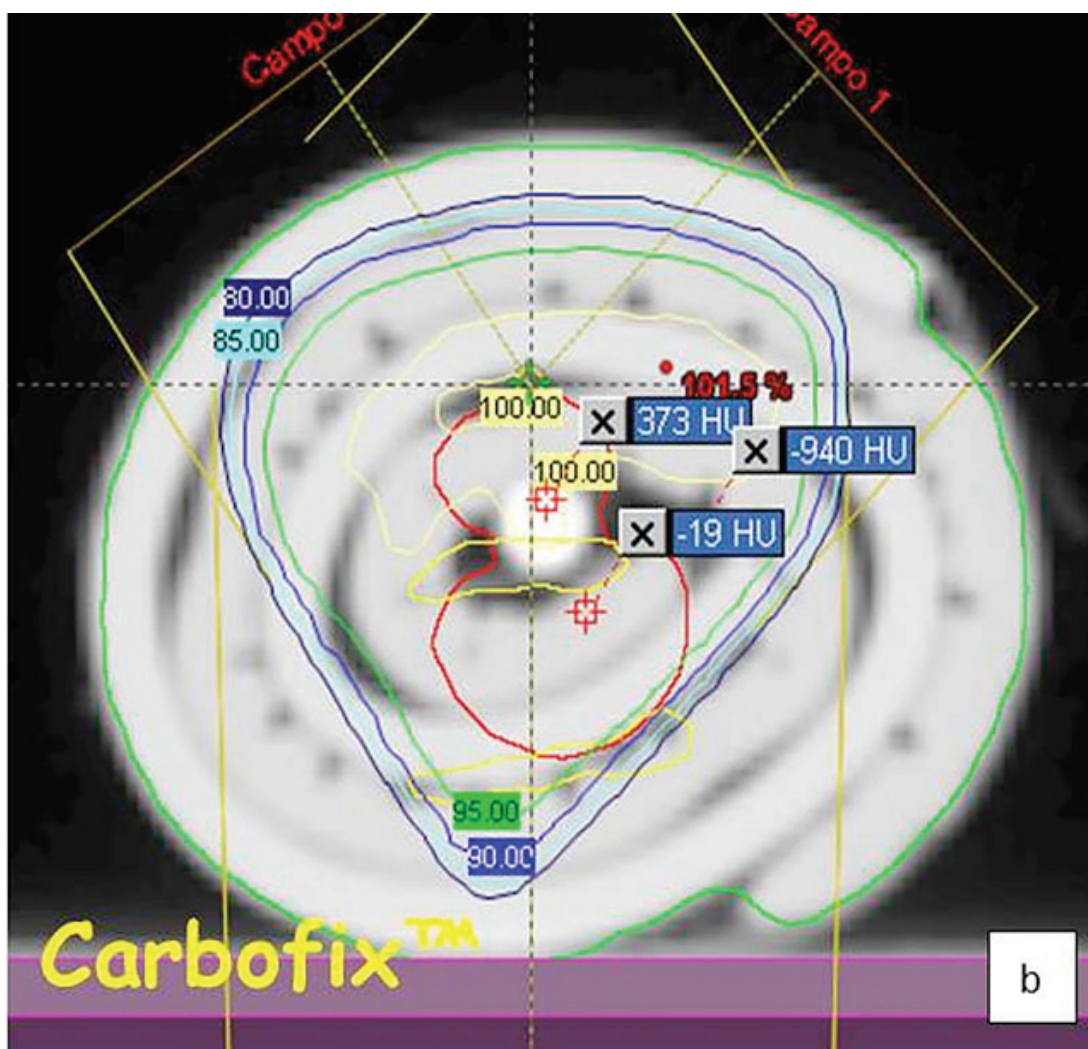


Fig.4 b) image from TPS: HU and dose calculation for setup #2 with the carbon nail.

landscape orientation. Films were scanned 24h after the irradiation. Images were analyzed with Picodose X PRO software. For each dosimeter, a rectangular central area with an appropriate standard deviation was selected and the corresponding mean grey level value (GL) was obtained. The Net Optical Density (NOD) was calculated by $NOD = -\log_{10} (GL/GL_0)$ where GL_0 was the grey level for non-irradiated film and GL was the grey level corresponding to the delivered absorbed dose. Dose calibration curves, such as the function of NOD were plotted; data were fitted using a fourth order polynomial function. The overall uncertainty was about $\pm 3\%$. Data were fitted with a four-degree

polynomial function to obtain the calibration curve of grey level versus absorbed dose.

For setup 1, large sheets of radiochromic films were positioned before, behind (2mm) and in contact with the carbon and titanium plates, a further film was positioned 1 cm further back.

For setup 2, 5cm x 25cm rectangular films were placed between the bolus sheet and the carbon or titanium nails during the wrapping to identify a number of verification points.

Treatment planning, dose calculation and irradiation: In the Radiation Oncology Department, Computed Tomography (CT) images were used with the

Table 1. Differences between TPS normalized and measured dose for setup 1 and setup 2

Setup 1	TPS Normalized Dose (%)	Gafchromic Measured Dose (%)
single field 6MV photon beam		
2 mm depth Under Ti plate	100	80 ± 3
2 mm depth Under whole of Ti plate	100	110± 3
At the interface immediately above Ti plate	100	120± 3
2 mm depth Under CFRP plate	100	97± 3
2 mm depth Under whole of CFRP plate	100	103± 3
At the interface immediately above CFRP plate	100	100± 3
single field 15MV photon beam		
2 mm depth Under Ti plate	100	75± 3
2 mm depth Under whole of Ti plate	100	118± 3
At the interface immediately above Ti plate	100	125± 3
2 mm depth Under CFRP plate	100	97± 3
2 mm depth Under whole of CFRP plate	100	103± 3
At the interface immediately above CFRP plate	100	100± 3

Setup 2	TPS Normalized Dose (%)	Gafchromic Measured Dose (%)
three fields 6MV photon beam		
near Ti nail (average of 5 points)	100	110± 3
5mm depth Under Ti nail	100	90± 3
At the interface immediately above Ti nail	100	115± 3
near Ti CFRP (average of 5 points)	100	100± 3
5mm depth Under CFRP nail	100	100± 3
At the interface immediately above CFRP nail	100	100± 3

Treatment Plans System (TPS) software to calculate monitor units (MU) in order to provide the desired absorbed dose in the volumes of interest, selecting the geometry of beams similar to those used in limb sarcoma patients. We tested two levels of photon beam energies. First, we studied dose perturbation from a single direct beam on setup n.1. For setup n.2, three fields in a similar arrangement to clinical irradiation with 3DCRT (3-Dimensional Conformal Radiotherapy) were investigated.

For treatment plan preparation, the TPS Eclipse (Varian) was used with the analytical anisotropic algorithm (AAA). A calibration curve was used in terms of

Hounsfield Unit (HU) versus electronics density with a maximum value of 3100 HU.

Phantoms were then irradiated with a linear accelerator Varian 2100 C/D with photon beams of 6 and 15 MV energies. Absorbed dose in the point of interest was verified by EBT3 gafchromic films above and below the two materials.

Images from CT simulation in patients with titanium and carbon fiber orthopedic implants used both in the spine and in the femur were also analyzed in terms of Hounsfield numbers.

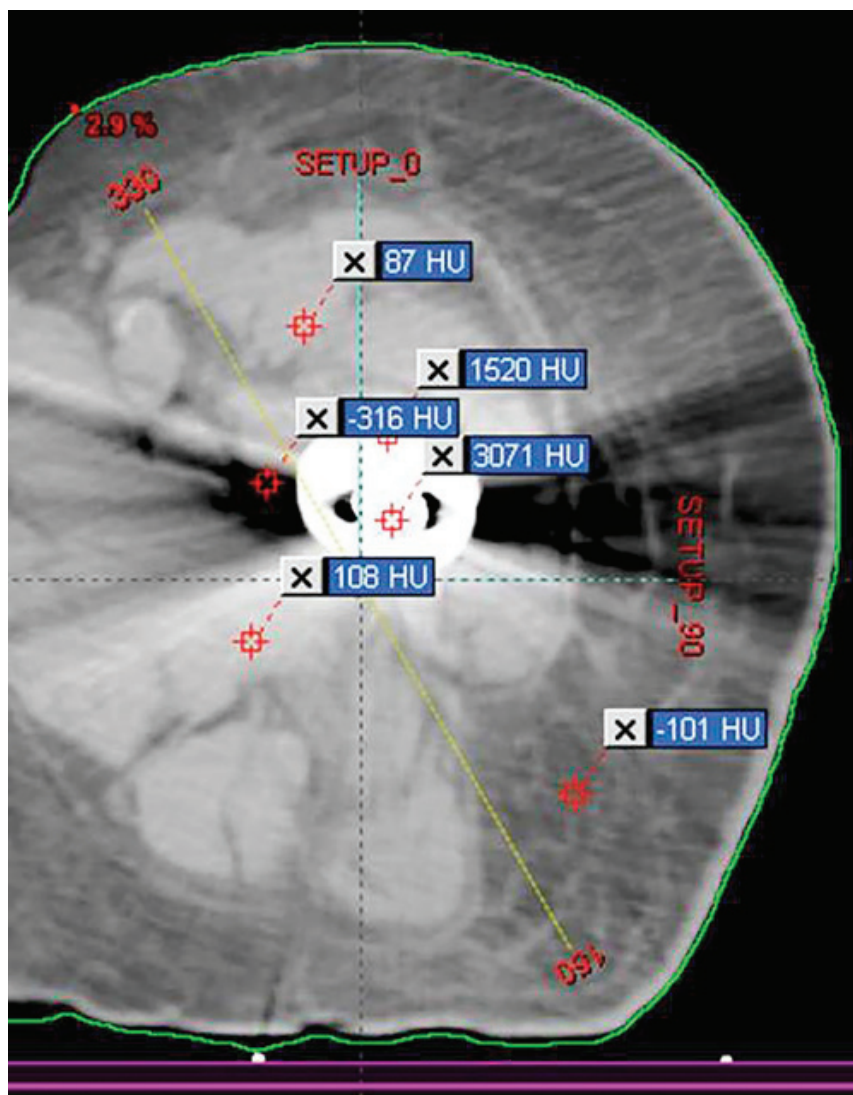


Fig.5 a) titanium alloy implant artifacts in a CT slice;

Results

For a single 20x20 cm 6 MV photon beam, the doses recorded just under the titanium-alloy plate were less than approximately 20% of the value calculated by the TPS, while doses under the whole region of the plate were 10% higher (Tab.1 – Setup 1). Doses at the interface immediately above the titanium-alloy plate increased 20% compared to those in the solid water phantom without implants, due to the backscatter of electrons from the metal implant. Differences are reduced to the 3% values at a distance greater than

1 cm. For 15 MV beam energy these differences were slightly higher.

Using the CFRP plate, the differences between measured and calculated doses were within $\pm 3\%$ for both energies, which is comparable with the statistical uncertainties of gafchromic dosimetry (Tab.1 – Setup 1). This difference rose up to 5% in some points just under the carbon fiber plate, due to the radiopaque tantalum marker at the plate contour used for fluoroscopic visualization (Fig.3).

In case of simulated treatment of humerus titanium implants (Fig.4a), when three fields of 6 MV

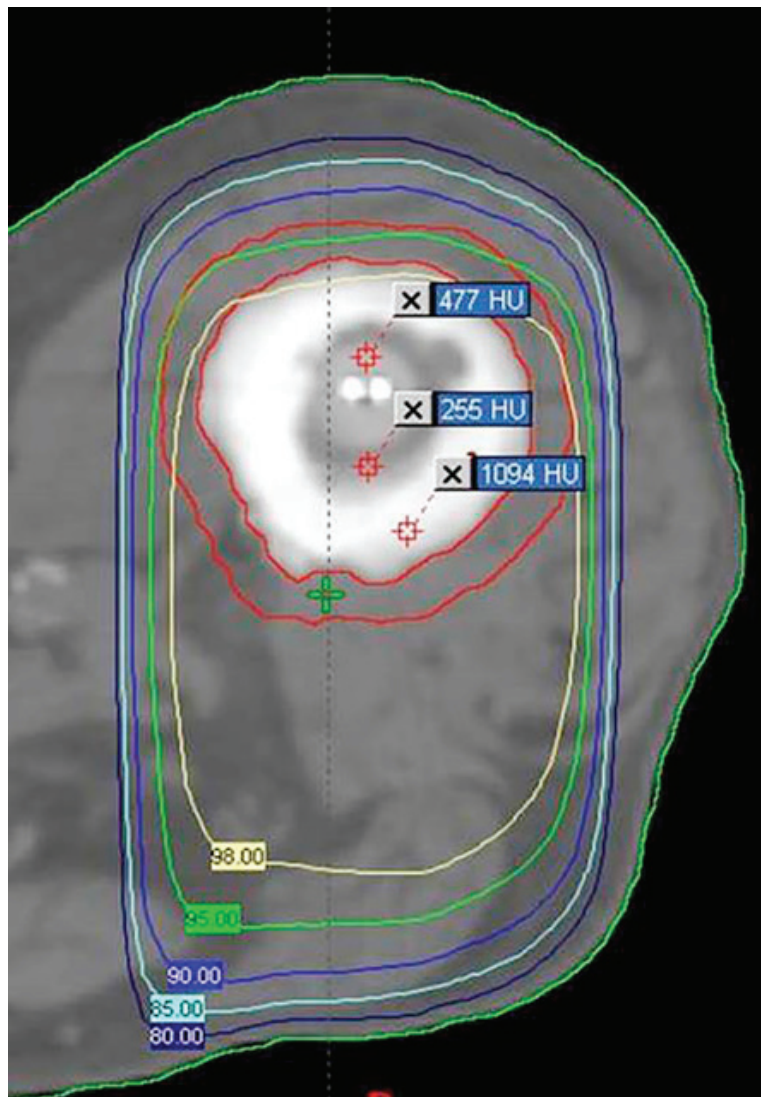


Fig.5 b) CT slice image of a carbon nail implant

energy were used, the differences between point doses measured with gafchromics calculated by TPS varied in the range of $\pm 10\%$ with hot spot of $+10\%$ and cold spot of -15% (Tab.1 - Setup 2). The presence of CFRP generates a more homogeneous dose distribution than titanium nails. The carbon fiber implant has almost no effect on the dose distribution (Fig.4b).

The specific differences between normalized TPS and measured doses according to different field setups and energies are reported in Table 1.

The difference of Hounsfield numbers evaluated for each material on phantom and patients CT images confirmed that the introduction of visual artifacts due to the titanium electron density made identifying the target volume a real challenge since part of information on the surrounding tissues was lost.

During treatment planning, before the dose calculation with TPS software, these areas were retrieved by replacing the missing parts with tissue that had the same density as water or bone, depending on the

position of the artifacts on imaging (Fig.5a). This procedure introduced some errors in dose calculation because the electron densities derived from Hounsfield numbers were not real, but arbitrarily estimated. When using carbon fiber-reinforced polymer orthopedic implants, we did not have artifacts and thus these problems were completely overcome. The carbon fiber implant does not influence the quality of the CT image, as shown in Fig.5b.

Discussion

It is well known in literature and in clinical practice that the presence of titanium or more generally of metal components within the CT field introduces artifacts that make it difficult to identify the target volume [14]. These artifacts, typically seen as starburst streaking, reduce the capability of CT image scans to provide the correct information on the electron density of surrounding structures as well as a correlated loss of information and an impossibility to correctly identify tissues.

The importance of a low level of artifacts in post-operative radiotherapy has been widely demonstrated in literature for spine tumor where the correct identification of the target is fundamental in order to decrease the risk of spinal cord damage and provide more effective treatment.

Several efforts have been made to try to decrease the interference between ferromagnetic implants and CT scans; modern CT systems present several protocols which can decrease the artifact level in the final imaging. The single energy metal artifact reduction technique should be able to reduce the artifacts of 57.4% compared to traditional CT protocols [16].

Dual-energy computed tomography images should be more adequate in reducing the artifact level in the spine [17,18]. However, this technology is not available in most radiotherapy departments.

In addition, the residual associated uncertainties can be considered critical when artifacts concern the spinal area and where the spinal cord is considered an organ at risk for the generation of permanent radiation-induced effects.

Nevertheless, despite progress, radiation oncologists are forced to manually contour the CTV (Clinical Target Volume) on the geometric extension criteria of the disease.

CFRP partially resolves this problem but unfortunately it can only be used in selected cases as it is not malleable and the plates are not available for all anatomic sites. Moreover, prostheses are made of titanium alloy which undergoes osseointegration.

Metastatic spine patients could probably benefit from a safer and more effective radiotherapy. Indeed, Tedesco et al. [19], recently demonstrated a low rate of local progression in a series of patients affected by primary spine tumors who had undergone surgery, stabilization with CFRP devices and postoperative radiotherapy but no comparative studies are present in literature valuing the impact on prognosis.

Ringel et al. recently published a series of 35 patients mainly affected by spinal metastasis who underwent spinal stabilization with Carbon Fiber-Reinforced Pedicle Screws and reported a low level of artifacts in MRI and CT-scans. Indeed, our work confirms their results, that the Hounsfield units from images of patients with spinal tumors who underwent stabilization with CFRP or titanium differ greatly. [11]

During the first planning step, before dose calculation, black artifact areas on CT slices which the system erroneously reads as "air" are often filled with "virtual tissue" having water or bone density. This procedure, introducing further factors of uncertainty, causes the difference between planned and actual radiation dose. Moreover, the value of electronic density of metals used by the TPS in the dose calculation is not correct. This study quantitatively showed the extent of indeterminacy of the provided dose using titanium and highlighted how the use of new carbon fiber materials overcomes these problems, making adjuvant radiotherapy more effective and safer.

Moreover, dose calculation uncertainties can be reduced by increasing the number of fields, so Volumetric Modulated Arc Therapy (VMAT) approaches are recommended in order to decrease the differences between calculated and measured doses in

clinical plans. The variances are more relevant using a single field, as reported in the Monte Carlo simulation at different distances from the CFRP screw [13]. However, this approach should be avoided in clinical practice.

The attention towards the use of these new materials in oncological orthopedic surgery is gradually increasing, considering their numerous benefits over conventional implants made of metal alloys but industries have to support the clinical effort to provide tools for all anatomic sites.

CFRP can guarantee a safer and more effective postoperative radiotherapy with less side-effects and may decrease the local recurrence rate for primary and secondary tumors.

Conclusions

Traditional orthopedic implant materials are usually made of stainless steel or titanium-alloy whose atomic numbers are larger than those of human body tissues.

The use of innovative carbonaceous materials for orthopedic devices and implants in bone cancer patients waiting to undergo radiotherapy gives the radiation oncologist a valuable advantage in the identification of the target volume, especially in case of extensive implants. Clear imaging of the soft tissues surrounding the bone is useful; dose calculation results are more accurate and dose distribution is more homogeneous.

In addition, there will also be a significant benefit in the definition of the state of disease, detectable in CT imaging follow-up of treated patients.

Further human studies are necessary to value the effect of this new technology on the percentage of local recurrences and of local progressions.

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