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Metallic implants and CT-artefacts in the CTV area: where are we in 2020?

Comment aborder en 2020 la question des artefacts tomодensitométriques dus aux implants métalliques dans le volume cible anatomoclinique (CTV) ?

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Abstract

Radiation therapy (RT) is one of the main modalities of cancer treatment worldwide with computed tomography (CT), as the most commonly used imaging method for treatment planning system (TPS). Image reconstruction errors may greatly affect all the radiation therapy planning process, such as target delineation, dose calculation and delivery, particularly with particle therapy. Metallic implants, such as hip and spinal implants, and dental filling significantly deteriorate image quality. These hardware structures are often very complex in geometry leading to geometric complex artefacts in the clinical target volume (CTV) area, rendering the delineation of CTV challenging. In our review, we focus on the methods to overcome artefact consequences on CTV delineation: 1 - medical approaches anticipating issues associated with imaging artefacts during preoperative multidisciplinary discussions while following standard recommendations; 2 - common metal artefact reduction (MAR) methods such as manually override artefact regions, ballistics avoiding beam paths through implanted materials, megavoltage-CT (MVCT); 3 - prospects with radiolucent implants, MAR algorithms and various methods of dual energy computed tomography (DECT). Despite substantial and broad evidence for their benefits, there is still no universal solution for cases involving implanted metallic devices. There is still a high need for research efforts to adapt technologies to our issue: "how do I accurately delineate the ideal CTV in a metal artefact area?"

Résumé

La radiothérapie est l'une des principales techniques de traitement du cancer dans le monde. La scanographie) est la méthode d'imagerie la plus couramment utilisée pour le système de planification des traitements (TPS). Les altérations de l'imagerie, telles qu'induites par des artefacts, peuvent considérablement affecter toutes les étapes de planification de la radiothérapie, telles que la délinéation de la cible, le calcul de la dose et la délivrance de la dose, et ceci plus particulièrement avec les traitements par particules. Les implants métalliques, comme les prothèses de hanche, les matériaux de fixation rachidiens, et les matériaux dentaires, dégradent fréquemment la qualité de l'imagerie en radiothérapie. Ces matériaux ont souvent une géométrie très complexe, ce qui entraîne une géométrie

d'artefacts complexe dans la zone du volume cible anatomoclinique (CTV), rendant sa délimitation difficile. Nous avons évalué l'impact des artefacts sur les indications de radiothérapie et les méthodes existantes permettant de prendre en compte leurs conséquences sur la délimitation du volume clinique cible : 1 - approches médicales lors de discussions multidisciplinaires préchirurgicales anticipant le problème de l'image de planification de radiothérapie artéfactée tout en suivant les recommandations médicales actuelles ; 2 - méthodes communes de réduction des artefacts métalliques (MAR) telles que la délinéation manuelle avec correction de densité des régions artéfactées, le choix d'une balistique évitant les trajectoires de faisceau à travers les matériaux implantés, la scanographie en mégavoltage (MVCT) ; 3 - perspectives avec des implants radiotransparents, des algorithmes MAR et diverses méthodes de scanographie double énergie (DECT) ou multi-énergie ou spectrale. Malgré des preuves substantielles et étendues de leurs avantages, il n'existe toujours pas de solution universelle pour les situations comportant des dispositifs métalliques implantés en radiothérapie. Des efforts technologiques et physiques restent indispensables pour définir de façon optimale un CTV dans une zone proche de matériaux métalliques.

Keywords:

CT-artefacts

Radiation therapy

Particle therapy

Metallic Implants

Metallic Hardware

Metallic artefact reduction

Dual energy CT

Mots clés

Artefacts

Scanner

Radiothérapie

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Implants métalliques

Réduction des artéfacts métalliques

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Implants métalliques et artéfacts tomodensitométriques

INTRODUCTION

Radiation therapy (RT) is one of the main modalities of cancer treatment worldwide with computed tomography (CT), as the most commonly used imaging method for treatment planning system (TPS). The accuracy and resolution of the CT image set integrated for dose calculation in TPS is crucial. Imaging errors may greatly affect all of the radiation therapy planning steps, such as target delineation, dose calculation and dose delivery; and may lead to tumor underdosage and overdosage of organs at risk in the treatment area. These uncertainties are of greater relevance for proton therapy (PT) compared to photon RT. Although advances in image-guided radiation therapy (IGRT) have increased the accuracy of dose delivery and decreased the need for large planning target volumes (PTV), metallic implants, such as hip and spinal implants, and dental filling significantly deteriorate image quality. They cause streaking and beam hardening artefacts responsible for imaging reconstruction errors.

Advances in orthopedic surgery have resulted in significant increase in the number of patients receiving metallic implants. Prostate cancer is a very frequent malignancy in men over 65 years old (1). As radiation therapy is one of the major treatments, the number of patients affected by CT metal artefacts due to hip implants is expected to increase significantly in the near future.

Spinal metastases and primary tumors together represent 20-40% of cancer patients during the course of their disease (2). A combination of stainless steel or titanium rods, plats, screws and/or spinal fusion cage is frequently necessary for spinal stabilisation after surgical removal of spinal tumors. These hardware structures are often very complex in geometry leading to complex artefacts geometry in the vicinity of clinical target volume (CTV) area, rendering the delineation of target and organs at risk (OAR), i.e. spinal cord, extremely challenging.

Dental fillings or implants in the oral cavity are often present in patients with head & neck cancers and cause image-degrading metal artefacts leading to challenging TPS processes as well.

This literature review focuses mainly on these three metallic devices with respect to CTV delineation.

ORIGINS OF ARTEFACTS

Metallic objects in the field of view are a well-known problem in medical imaging because of their negative impact on image quality. Standard CT scan acquires projection data of an object at different angles and reconstructs the measurements into an image using filtered back projection (FBP) or an iterative method of reconstruction. A metallic object in the imaging region causes errors in the projection data mainly due to photon starvation, beam hardening, noise, scatter, or non-linear partial volume effects. Reconstruction using corrupted or incomplete data will result in an image with artifacts. Their radiological aspects on CT-scan images are often observed as bright and dark streaks. First, beam hardening and scatter are due to the change in the attenuation processes in high atomic number (Z) materials. Indeed, lower-energy photons are more easily absorbed and consequently the effective energy of the polychromatic imaging beam is shifted towards higher values, so called the beam hardening effect. Second, at kV energies, Compton scattering dominates the attenuation of the remaining photons (i.e. with a higher average energy). They will be scattered and measured by the detector off the central axis of the incident beam. Therefore, the combination of beam hardening and scatter leads to an underestimation of the attenuation coefficient because of the photons reaching area of the detector where they normally would not be. Moreover, as there is photon starvation next to the metallic part due to increased absorption of photons, the noise in the image increases contributing to metallic artefacts. Indeed, this lack of photons modifies the photon flux's statistic and creates random errors at the detector level, which are responsible for dark and bright streaks in the image. Furthermore, when the edge of a metallic objects is in the projection line, there is a variation in the attenuation coefficient perpendicular to the X-ray axis resulting in density estimation errors in the image. Metallic artefacts managing is a well-known issue for physicists in radiation therapy departments. Indeed, these artefacts have an impact on a major part of the treatment chain: CT image quality, delineation and dose calculation.

MEDICAL DATA

1. Unresolved common uncertainties

Although several common metal artefact reduction (MAR) methods are commonly used, the lack of *a priori* knowledge of the type of implants (shape, size, metal or alloy composition and metal's effective atomic number) seriously hampered the process accuracy of CTV delineation and dose calculation. Radiation therapy teams face this unresolved situation to reach these data due to two main reasons: unknown composition of old-fashioned devices and trade secret regarding the composition of the current implants. Homogeneous surgical practice in using metallic devices, a close collaboration with industry, *a priori* knowledge of metal exact composition, and a traceability of products could lead to overcome this main issue.

2. What do we know about metallic implants and their oncologic clinical consequences?

Methods to overcome metal artefacts in CT imaging have been investigated and developed for nearly 40 years. The first study on the CT MAR methods was published in 1995, i.e. 20 years after CT introduction. Nowadays, several hundred papers enrich the physics and dosimetric literature.

This contrasts with the lack of data about direct effects of metallic hardware on local tumor control and normal tissue side effect rates in cancer patients with a metallic implant.

In a prostate cancer patient with bilateral hip implants, MVCT-image-based treatment planning was used for a helical tomotherapy unit (HiArt) (3). The authors pointed out the sufficient morphological information of the pelvic anatomy for CTV delineation and radical prostate treatment planning.

Sources of uncertainty present in conventional radiation therapy apply even more to PT.

However, an important and fundamental difference exists in proton therapy—the proton range. The Hounsfield units (HU) are converted into relative proton-stopping powers so dose calculations can be made. However, range calculation inaccuracy arises from the planning CT due to noise, CT artefacts and beam hardening affecting the target coverage and sparing of the OARs. Two clinical studies of proton therapy as spinal chordoma treatment showed significant reduced tumor control rate when metallic spinal hardware stabilization was required. In 2018, Snider *et al* reported the results from the Paul Scherrer Institute in Switzerland with surgery and spot-scanned protons (median dose 74.0 GyRBE) for the treatment of 100 spine chordomas (4). They showed that the presence of metallic surgical stabilisation prognosticates for worsened local outcomes (46% versus 75% at 5 years, $p=0.01$).

Similarly, from Massachusetts General Hospital Cancer Center in Boston, Delaney *et al* noted slightly more local failure in patients with hardware stabilization (35% versus 22% at 8 years) but the difference was not statistically significant ($p=0.277$) (5). Their proposed explanation included artefacts in CT and MRI datasets, with difficulties to plan and deliver radiation treatment, including target definition and dose inhomogeneities.

In a theoretical model based on the EUD algorithm, Tomé and Fowler showed a dose deficit to 1% volume of the target that is larger than 20% of the prescription dose may lead to serious loss of tumor control probability (TCP) with intensity modulated radiation therapy (IMRT). This reflects indirectly the potential clinical consequences of metal imaging artefacts causing under dosage of the target volumes. They reported boosting could not compensate for this underdosage (6).

3 Which common medical approaches could override imaging artefacts and their consequences before radiation therapy process?

The definition of GTV and CTV for each patient could be anticipated during *a priori* multidisciplinary discussions between surgeons, radiologists, radiation oncologists and medical oncologists. Hence, before starting radiation therapy process itself, more specifically particle therapy, physicians could discuss medical strategies to override the imaging-artefact issue while following the current medical recommendations.

Removing metallic implants from the patient or opting for non-metallic implants in the first place appears as an obvious option. In practice, these options are often not realistic due to the invasive surgery required and inadequate metallic alternatives (mechanical constraints, versatility, cost of the implant materials, etc).

Removing hip implants in pelvic cancer patients sounds unethical due to the risks of a second surgery. Therefore, minimisation of CT-artefact algorithms and metal-carbon fiber composite femoral stems have been assessed in hip replacements (7).

Removing dental amalgams is at risk for release of mercury but may be done if this device contraindicates PT for example. Removing dentals crowns can be discussed on a case-by-case scenario while implants, in general, cannot be removed if already integrated to the bone unless the teeth are mobile. In head and neck cancer patients, a potential solution involves replacing the components of the dental fillings of amalgams with composite before PT planning to improve tumor visualization and dosimetry. Indeed, Richard *et al* showed the PTV

was underdosed with the metallic amalgam compared with the composite filling in a phantom model (8).

Spinal and paraspinal tumor patients appear as the best candidates for *a priori* multidisciplinary discussion because they are treatment naive. Indeed, treatment paradigms for patients with spine tumors have evolved significantly over the past decade leading to close collaboration between these specialists. For instance, integration of several advances has changed current treatment paradigms for metastatic spine tumors. The validated Spinal Instability Neoplastic Score (SINS) criteria serve as an independent surgical indication guideline (9). The introduction of less invasive surgical techniques including percutaneous pedicle screw instrumentation and cement augmentation has shortened recovery periods and allowed earlier return (around 1 week) to irradiation. *Spine stereotactic body radiation therapy* (SBRT) has dramatically improved tumor local control rates. The trend toward less invasive surgery is illustrated by the concept of *Hybrid Therapy* (HT) and *Minimal Access Surgery* (MAS). The HT refers to the combination of spine SBRT and *separation surgery* (SS). SS is a procedure in which tumor resection is limited to the spinal cord decompression to create a gap between the tumor and normal tissues and provide a safe target for SBRT. The MAS technique refers to the use of percutaneous instrumentation, mini-open approaches for decompression (10). Both HT and MAS allow the use of different metallic hardware to reduce artefacts and helps to facilitate the delivery of an ablative dose to the residual tumor while sparing the spinal cord or cauda equina (11).

In spinal chordomas, current consensus is that a regimen incorporating surgery and high dose PT reaches the best tumor local control. However, consensus is lacking on what materials to use in patients needing spinal stabilisation and, therefore, how to manage PT, given the high local failure rates in patients with metallic devices, as reported in two PT series (4,5). An option could be to use a minimal surgical device associated with a halo brace during radiation therapy. Sanpakit *et al* have proposed to implant a smaller metal quantity in the CTV area using halo brace (12). Long-term observations of patients who underwent occipital cervical fusions using only bone graft and wiring, with postoperative halo vest immobilisation during postoperative radiation therapy revealed high fusion rates and reasonable intraoperative or postoperative complications. An optimal stabilisation could be planned in a second step after radiotherapy leading to remove the halo immobilisation. An optimal geographic set up of

stabilisation devices is described as cross-links between rods placed at levels above and below the affected spine level allowing more radiation proton beam incidences. Lewandrowski *et al* proposed chordoma maximal resection was followed by spine reconstruction with allografts or cages minimising the use of metallic rods (13). In case of spinal chordoma recurrence, the presence of metallic implants may be a main cause contraindicating curative PT or to decide to deliver photon radiation therapy, which is less sensitive to artefacts. If a debulking or separating surgery is planned, the possibility of modifying, removing or substituting metallic implants with carbon fiber devices should be considered to enable radiation therapy with potentially curative intent. Finally, physicians may offer the best practice of spinal radiation therapy to all patients with spinal tumors through a multidisciplinary approach. All of these medical approaches do not totally overcome imaging artefacts and difficulty of CTV delineation. However, they are the first step towards an artefact minimisation in the CTV area.

Metal artefacts in radiation therapy: a clinical issue

Nowadays, we have achieved a high level in delivery accuracy with static IMRT, Volumetric Modulated Arc Therapy (VMAT), SBRT or PT that have increased the requirements in delineation accuracy. Metallic artefacts are significant clinical issue in radiation and particle therapy. They hide or modify the aspect of the structures of interest for the treatment planning. This degradation of the image quality leads to large uncertainties in the delineation of target volumes and surrounding OARs and decreases the dose calculation accuracy. Artefacts are responsible of errors in CT numbers, which propagate to density assignment errors and consequently to dose calculation errors. The HU values acquired from CT images range from -1024 to 3071 (depending on the CT-scan), which usually covers the range of the patient's tissues. However, metallic implants (titanium, stainless steel) have estimated densities that are outside the HU range of the CT scanner and saturate CT numbers scale. This degradation of CT numbers accuracy has an impact on the dose calculation. Indeed, to calculate dose distribution, TPSs need a calibration curve relating CT numbers and electron densities. Consequently, if the HU value is wrong, the TPS does not correctly calculate the attenuation for metals and the dose distribution. Kilby *et al* showed the importance of the accuracy of electron density in photon and electron dose calculation and established

tolerance levels for water, bone and lungs (14). Chu *et al* reported that a variation of 20 HU in soft tissues leads to 2% uncertainty in electron density and a variation of 250 HU in cortical bone up to 5% (15). They noticed an impact on dose calculation accuracy for a 6MV beam inferior to 2% up to 20 cm depth in soft tissues. In addition to calculation errors associated with imaging artefacts, errors also result from the limited ability of modern dose calculation algorithms to accurately model radiation transport in and near metallic implants. Indeed, type A algorithms like pencil-beam are not appropriate in presence of high Z materials. Pencil-beam algorithms result in dose calculation errors near the metal/tissue interfaces, underestimating the backscatter dose enhancement at the proximal interface and overestimating the dose directly downstream of the implant. Although these errors are typically confined to the local region near metal/tissue interfaces (within a few centimeters of the interfaces), local errors can be high, depending on the photon energy and the type of metal. Collapsed-Cone is another type of convolution/superposition algorithm, which takes into account the lateral heterogeneities. Several studies showed the reliability of Collapsed-Cone methods in inhomogeneous media in comparison with Monte Carlo (MC) calculations (16). Indeed, MC dose calculation is more accurate in presence of metallic implants compared to the superposition/convolution process because it models the photon fluence attenuation and electron transport within and around the metal media, yielding accurate dose estimates. The American Association of Physicists in Medicine (AAPM) Task Group 63 published a report to inform the Radiation Oncology community of the problems associated with metallic implants in the treatment field, and provide recommendations related to the treatment planning and delivery in patients with hip prostheses (17). Concerning dose calculation, when the metallic implant is in or near the target volume, they recommend to avoid type A algorithms (pencil beam) and choose more accurate ones, like AAA, collapsed-cone or Monte Carlo. Kim *et al* described the presence of hot and cold spots in OAR and CTV for IMRT head and neck treatments due to the presence of dental metal artefacts (18). In another study, Kim *et al* also demonstrated that the TCP decreases as well as Normal Tissues Complication Probability (NTCP) increases in regions where metal artefacts have a relevant impact on image quality (19). Spadea *et al* assessed the dosimetric impact of titanium, platinum and gold on IMRT treatment plans (20). They showed that the atomic number (Z) of the metal influences the severity of the artefacts. Without any correction, the uncertainties regarding the dose calculation and measurement are not acceptable near high-Z materials. Indeed, the

difference between calculated and delivered dose should be less than 2% or 3% according to the complexity of the field. In the case of particle therapy, metal artifacts in CT simulation images also have a clinical impact like tumor underdosage volume or OAR overdosage. Indeed, Andersson *et al* assessed the role of a MAR algorithm for applications in treatment planning in PT (21). They showed some water equivalent thicknesses (WET) differences up to 2 cm and recommended to use proton beams with caution in presence of artefacts. Moreover, in a MR-based MAR method study, Park *et al* noticed differences of 2.4 cm on average in brain in presence of metal implants (22).

Current routine methods to limit artefact's influence on CTV delineation and dose distribution

Currently, some usual MAR methods are implanted in most of radiotherapy departments. As regards the CTV delineation, multi-modality imaging (MRI and TEP) is the most widespread method to limit artefacts' impact. Megavoltage CT (MVCT) is already a solution to help in reducing uncertainties in delineation step. About dose distribution, a common technique is to affect manually a density to artefacts and to optimise the treatment ballistic.

1 Could multimodal imaging approaches override CT-imaging artefacts and their consequences?

The CT images are commonly combined to other imaging modalities (MRI, TEP) in order to obtain more information to delineate target volumes and surrounding OARs. However, metallic objects induce MRI and TEP-degrading metal artefacts with large areas of signal loss around the hardware and overestimation and/or underestimation of the tracer uptake in regions adjacent to metallic implants, respectively.

MRI

On MR imaging, delineation of target structures is challenging as ferromagnetic contents of the hardware are a significant source of image degradation. These ferromagnetic materials cause significant local magnetic field inhomogeneities, resulting in a geometric distortion referred to as a susceptibility artefact. These artefacts appear as large areas of signal loss around the hardware. Susceptibility artefacts cannot be totally eliminated, but can be minimized using several different techniques. The use of titanium-made hardware produces much less severe artefacts than do ferromagnetic implants made of stainless steel. The use of

lower magnetic field strengths at MR imaging produces less obtrusive artifacts than does the use of higher field strengths (23). When the direction of the main magnetic field is aligned parallel with the longitudinal axis of the hardware device, there is a significant relative reduction in artefacts. Reduction of artefacts can be made by choosing relevant MR imaging parameters. Fast Spin Echo (FSE) sequences with short echo spacing (short time intervals between echoes) are less sensitive to magnetic susceptibility effects than are fast SE sequences with longer echo spacing or conventional SE sequences. Short inversion time inversion recovery (STIR) imaging is an effective alternative method of fat signal suppression and less dependent on the homogeneity of the main magnetic field). Hence, the use of a small field of view, high-resolution matrix (eg, 256 x 256 or 512 x 512), thin section, and high gradient strength can help reduce metal-related artifacts (23,24). Suh *et al* showed their consequences on alteration of artefact magnitude with a 3.5-mm-thick titanium screw when the long axis of the screw is parallel or perpendicular to the main magnetic field (25). The artefact size range was 6.5-10 mm at the 90° angle depending on aforementioned MR parameters and exclusively 4 mm at the 0° angle whatever the parameters. An interesting combination has been developed with a MRI-based CT artefact correction method to improve CT image quality and proton range calculation accuracy for patients with severe CT artefacts (22).

TEP

PET/CT has been integrated as a powerful tool in Radiation Oncology, with multiple roles ((26). PET/CT images are suited to the RT planning process, fused with the RT planning CT scans. CT images are used to derive an attenuation correction map for the PET reconstruction, which means that CT influences the PET image in combined PET/CT imaging. If the ROI is located near the implant, the metal not only distorts the CT image but also influences the quantification of radiotracer uptake and can reduce the quality of the interpretation of the scan (27). Hence, metallic implants should hamper diagnosis and therapy planning in prostate and head & neck cancer patients with metallic implants. In recent years, different metal artefact reduction (MAR) methods have been developed for CT. Nevertheless, the use of MAR of CT for attenuation correction in combined PET/CT is still emerging. Two studies reported the MAR tool is as a promising approach to improve image quality and PET

quantification and the enhanced diagnostic value depended on the location and size of the metallic devices (28,29).

2. Mega-voltage CT

Simulation images acquired with kVCT system can be associated to MVCT images that are not as susceptible as metal artefacts. These methods could be very useful in case of serious imaging artefacts due to bilateral hip prostheses or dental implants in the CTV area. Aubin et al used MVCT to complement the planning kVCT (30), as well as De Marzi et al. in proton therapy to evaluate relative proton stopping power in various high density implants (31). Both sets of images were acquired and co-registered. Non-viewable data on the kVCT were shown on the MVCT because metallic implants have little impact on MVCT image quality. Indeed, they showed a change of only 3% in the HU between MVCT images with and without metal. Son et al noticed that MVCT allowed calculation error reduction compared to manual density assignment (32). However, target and OAR delineation may be more challenging because of the low contrast resolution. Indeed, the drawbacks of this method are the uncertainty of the accuracy of the registration with kVCT, the lack of soft tissue contrast, the small field-of-view (40cm) or large slice thickness and the additional dose for the patient. It however seems MVCT could be a common and relatively safe option to improve CTV delineation for metallic implant patients.

3. Manual density overriding and dosimetric optimization

One of the methods to reduce the dosimetric impact of metallic implants on CTV is to delineate the artefact regions manually and assign a CT number corresponding to the relative electron density of water or surrounding tissue. Several limitations are reported: the delineation of streaking artifacts is operator-dependent; the process is time-consuming; the arbitrary choice of the CT number may introduce systematic uncertainty; and not all of TPS provide this option. A study of Son et al confirmed these limitations about time and accuracy but this method seems to be the most widespread in radiation therapy departments (32). The previous method is commonly applied with of a treatment ballistic avoiding beam paths directly through the material. In three-dimensional radiation therapy (3DRT), dosimetrists set up the beams as necessary. In contrary, in more advanced treatment techniques using inverse

planning methods, sector avoiding allows cutting off the beam where it is supposed to go through metallic implants. This ballistic optimisation is achievable in case of hip prostheses for prostate irradiation but more challenging in head and neck treatment tumor where the CTV is often located near metallic implants. AAPM recommended beam arrangements avoiding prostheses but with a risk to increase OAR's dose (17). Furthermore, a study of Maerz *et al* advised to use VMAT technique in presence of metallic implant (33). They showed a higher accuracy of dose calculation for VMAT than for static IMRT thanks to the fact that the dose is delivered by multiple segments from different directions whereas in static IMRT it is from one beam direction.

MAR prospects in radiotherapy and particle therapy.

In addition to the previous methods developed before, other MAR methods can be used in order to improve CTV delineation. From a medical point-of-view, the use of carbonaceous materials could be promising. Moreover, some recent technological tools may help to limit the impact of metallic implants. Indeed, nowadays, most CT vendors provide MAR algorithms, which could be used in radiotherapy department. Dual Energy CT (DECT) imaging is another technology with potential applications in radiotherapy and particularly in metal artefact reduction. However, even if they generally increase image quality and help to delineate the CTV and OARs, they could have an impact on dose calculation step or other drawbacks.

1. Are radiolucent implants a promising means to override artefacts and theirs consequences?

In the surgical treatment of spinal and para-spinal tumors, poly-methyl-methacrylate (PMMA) bone cement is very commonly used, allowing custom shaping of supports and constructs at the time of surgery for anterior column support. A report demonstrated safety and efficacy of radiation therapy using PMMA materials (34).

Associated to PMMA, permanent metallic hardware is often required. Spinal fixation, using pedicle screws, cages and implant rods are responsible for rigid connections in the vertebrae of the spine. Traditional orthopedic implant materials are usually stainless steel or titanium and their use poses a major obstacle for accurate radiation therapy planning and delivery. The high-density stainless steel or titanium implants (stainless steel $\rho \approx 8 \text{ g/cm}^3$; titanium $\rho \approx 4.5 \text{ g/cm}^3$ and $Z=22$) are not properly accounted for in the dose calculation algorithms of the TPS.

Unlike metals, carbonaceous materials have low atomic numbers (carbon $Z=6$ and ρ between 1.7 and 1.9 g/cm^3), good biocompatibility, chemical stability, good mechanical properties, and modulus of elasticity similar to human bones. The use of carbon fiber reinforced polyether ether ketone (CF/PEEK) has been proposed in the spine, hip and maxillofacial surgery several years ago (35–37). Using CF/PEEK implants, the problem of imaging artefacts, as well as the problem of dose perturbation in post-implantation radiation therapy can be minimized (38). Poel *et al* showed the CF/PEEK implant had a 90% reduction of artefacts on CT and subsequently severely reduced the time for artefact correction with respect to the titanium only implant. Furthermore, the CFR-PEEK as opposed to titanium did not influence the robustness of the PT plan (39). These materials are accepted as a radiolucent alternative to metallic biomaterials in the surgical community; therefore facilitating adjuvant radiation therapy, specifically PT, and follow-up imaging of bone lesions. Some limitations need to be considered when choosing CF/PEEK implants. They currently are ten times more expensive than titanium implants and French Health system repay CF/PEEK implants at titanium implant price, meaning a shortfall for producers. Depending on the desired implant design, CF/PEEK implants are less readily available and need to be ordered well in advance. CARBON/PEEK implant would not be considered as deformable to match with anatomic structure shape. If during application, it reaches a point the fibers cannot bear, the matrix could be heavily damaged or cracked. Thus, the multidisciplinary team would usually discuss patients who may benefit from surgical management with the use of PEEK and carbon-fiber-reinforced PEEK implants.

The positioning of the carbon screws is more difficult due to the radiolucency and the set-up cannot be verified using standard intraoperative radiograms. However, some producers provide both screws covered by a thin layer of titanium or with a small reference point at the tip to override the intraoperative radiolucency (icotec AG Black Armor® pedicle system, Switzerland). Moreover, surgeons cannot model the rod contour to fit the screws on the operative field and a dedicated device is required to connect a small component fixed on the rod into the screw collar. All of these advancements require a learning curve and require additional training, due to the relatively narrow working channels or approaches, longer working distances, and challenges posed by excessive bleeding or CSF leakage (37). Some screw breakages have been reported supporting that resistance of the screws in CFR-PEEK to

rotational forces is lower than those in titanium (40). In contrary, Hak *et al* reported CF/PEEK implants provide fatigue strength similar to titanium devices (41).

A randomised controlled parallel-group study concluded metal-carbon fiber composite femoral stems in hip replacements showed promising results at the time of early follow-up, and the clinical outcomes at ten-year follow-up were similar to those of an all-metal stem (7). Although CF/PEEK implants sound to be promising, their above-mentioned limitations explain low using of them in current Surgical Oncology. Experimental and comparative clinical studies need to quantify their clinical benefits.

2. Dedicated metal artefact reduction algorithms

Commercial metal artefact reduction algorithms are available for CT imaging of patients in radiation therapy. To eliminate these artefacts, many MAR algorithms modify the process by which the image is reconstructed. The widespread approach is to directly correct or replace the corrupt projection data in the sinogram by synthesizing new projection data. This is achievable by interpolating replacement values, either from neighbouring projections or from a mathematical model. Another method to complete the sinogram is to incorporate prior information and back-project it to generate projection data for sinogram completion. Iterative methods can reduce the impact of artefacts by ignoring or statistically down-weighting data affected by the metallic object and use an iterative procedure to arrive at an image considering the more reliable features. For example, O-MAR (Philips Medical Systems, The Netherlands) algorithm is the first metal reduction function designed for radiation therapy. O-MAR combines sinogram completion and iterative reconstruction method.

From a practical point of view, Andersson *et al* evaluated four MAR algorithm' performances in presence of bilateral hip prostheses (42). With each algorithm, they noticed that CT number accuracy was improved and noise reduced near and between the two prostheses which may help for delineating CTV and OAR in radiotherapy treatment. Shen *et al* studied the O-MAR algorithm in five patients treated for spine SBRT with metallic implants (43). Image quality improvements were shown, which could be useful for delineation and patient positioning for image-guided radiation therapy (IGRT). However, a lower efficacy was described with small metallic implants than with larger ones. Li *et al* studied the clinical applications in treatment planning of O-MAR algorithm (44). In corrected images, they noticed an important reduction of metal artefacts; CT numbers were also more accurate and anatomy visualisation better

than in uncorrected data. They noticed no clinical impact on dose calculation. Huang *et al* studied the impact of three commercial MAR methods on dose calculation near metallic implants (O-MAR algorithm (Philips), GSI (Gemstone Spectral Imaging, General Electric) and MARS (Metal Artefact Software Reduction, General Electric) (45). O-MAR was the most consistent method for reducing calculation errors, by decreasing errors for dental case and having little effect on calculation accuracy in a context of spine tumor. Besides, they recommended using the MARS algorithm with caution because it was developed for diagnostic imaging purposes and causes calculations errors in modifying the size and shape of titanium implants, large implants and implants near other heterogeneities. Indeed, in case of spinal irradiation close to the lungs with metallic implants the use of this algorithm may have a negative impact on the CTV delineation and coverage.

Some authors do not recommend the common application of MAR algorithms for dose calculations in particle therapy because these algorithms can also alter the quantitative image information in regions that were not initially affected by metallic artefacts (46).

3. Dual energy CT

Another approach to reduce the impact of artefacts in radiation therapy workflow is the use of Dual Energy CT (DECT) scanner and particularly a post-processing technique allowing calculation of virtual monoenergetic images. This technology is nowadays widely used in Imaging departments. Indeed, in DECT, a high-energy and a low-energy dataset are acquired using polyenergetic X-ray spectra. A linear combination of these two datasets is calculated in order to create an effective image as if it were measured using a monoenergetic beam. These virtual monoenergetic images reflect the attenuation as if it was only caused by the respective linear attenuation coefficient for the specific energy. Because of the higher attenuation of soft X-rays, low-energy virtual monoenergetic images result in higher low-contrast resolution. On the other hand, hard X-rays are less attenuated by dense materials, therefore it can be expected that the corresponding virtual monoenergetic images display less artefacts from metallic implants. Various technical approaches have been developed for acquiring dual-energy data set focused either on X-ray tube output or on X-ray detection. Nowadays, four tube-based systems are clinically implemented. The first one is the realisation of two temporally sequential scans to acquire the data at each of the two tube potentials. The main advantage of this method is its ability to be performed on any CT scan. The significant

disadvantages are the unacceptable risk of patient motion and the radiation dose increasing. The second one is to use two orthogonal X-ray tubes and detectors combinations operating with two different kV settings. The use of separate tubes enables independent adjustment of the tube voltage to optimise separation of the low and high-energy spectra. One weakness of this dual-energy technique is the simultaneous use of both X-ray sources requires a specific scatter correction. Indeed, one of the two detectors can detect scattered radiation whose original primary photon comes from the other tube. Third, rapid kV switching (usually in less than 0.5 ms) of the X-ray tube is another dual-energy method. Since the delay between high and low projections is very short, there is an excellent spatiotemporal registration. Last, the tube-based method is the TwinBeam DECT scanner. The beam is pre-filtered at the output of the tube resulting in separation of the beam into a low-energy side and a high-energy one, which exposes different parts of the detector.

Alternatively, the only commercially available detector-based solution is dual layer systems. It uses a single X-ray source and measures the lower part of the spectrum in the surface layer whereas the photons of higher energies are detected in the layer below. Unique to the dual-layer approach is the simultaneous measurement of low and high-energy projection data at the exact same spatial and angular location, which allows for a raw-data based dual-energy post-processing. Moreover, this system always operates in dual energy mode, which allows retrospective processing for all acquisition.

Several studies have been published assessing different technical approaches. Bamberg *et al* evaluated the performance of a dual source CT (with 100 and 140 kVp) with virtual monoenergetic images reconstruction on 31 patients with metallic implants (47). An improved image quality of the metal surface and surrounding regions were noted for 29/31 patients and artefacts were reduced by 48.6%. The 105keV energy was optimal to reach a significant artefact reduction. Zhou *et al* used the same type of DECT with other energies, 80 and 140 kVp on 47 patients with fractures (48). They also noticed a reduction of metal artefacts and an enhancement of the image quality allowing an improved diagnostic value. In contrary, Bamberg *et al* defined an optimal energy of 130 keV (47). In 2019, Petterson *et al* studied the potential of DECT with kV-switching to reduce the metal artefacts and their impact on the structure delineation (49). They showed an improvement of delineation with DECT depending of the location of the structure relative to metals. However, some studies showed DECT approach needs improvement. Kovacs *et al* studied the impact on tumor

delineation in radiation therapy of a MAR algorithm and DECT virtual monochromatic images (DECT VM) for several implant sites (50). Both techniques improved the accuracy of HU value representation, significantly increased delineation accuracy and decreased delineation variability between operators. They showed that the combination of DECT VM and MAR algorithm was the most effective method for dental filling, and DECT VM only for spinal implants. No significant difference was reported between MAR only and the combination of DECT VM and MAR for hip prostheses. In agreement with several other studies, Kovacs *et al* noticed that strong metal artefacts are not removable with DECT (50–53). Schwahofer *et al* studied the impact on dose calculation of DECT and found an improvement of only 1% with remaining uncertainties of 10 to 20% (53). Huang *et al* also noticed no significant improvement in dose calculation accuracy by using only DECT VM solutions proposed by General Electric (45).

Furthermore, the implementation of DECT technology in radiation therapy is not widespread despite its capacity to improve image quality and consequently CTV delineation. Indeed, DECT presents some limitations for radiation therapy purposes. Concerning dual-source scanners because of the limited size of the gantry there is only space for a smaller second detector allowing only a usable field of view up to 35 cm which could be too small for some radiation therapy set-ups. There could be a solution of these limitations. However, because of the delay between low and high-energy any patient motion between the two sequences could produce unacceptable distortion for radiation therapy planning. Another limitation is the use of contrast enhancement. The delay between the two energies acquisitions changes the enhancement of the structures in the different images. Moreover, for dose calculation on DECT VM images, treatment planning system image value-electron density curves must be calibrated for each desired VM energy. DECT methods are more cumbersome to implement in radiation therapy workflow in order to decrease streaking artefacts than dedicated algorithms. To conclude about the potential use of DECT in order to reduce metal artefacts, the results are mitigated. Indeed, dual-energy method could not remove strong artefact alone and show no significant improvement of dose calculation accuracy near implants. In addition, DECT is more difficult to implement in daily practice than dedicated MAR algorithm. Contrary to multi-modal imaging, MVCT or MAR algorithms, DECT still needs an improvement to reduce the impact of metal artefacts on CTV delineation.

A special case : arteriovenous malformations (AVM) following embolization with Onyx

A therapeutic option of AVM may include embolization using Onyx. This is a biocompatible liquid embolic agent including suspended micronized tantalum powder. This metal has a high-Z element ($Z = 73$) causing streaking artefacts. Depending on the size of Shtraus *et al* suggested a modified heterogeneity corrections method, by assigning individual electron densities to the normal brain, bone and Onyx if embolization is followed by stereotactic radiosurgery (54).

Conclusion

The first step in the treatment planning is the CTV delineation. Artefacts due to metallic implants make challenging the delineation of CTV in the artefact area. Treatment paradigms for tumor patients have evolved significantly over the past decade leading to a deep collaboration between numerous specialists and physicists, resulting optimal using metallic devices to minimise imaging artefacts. The *a priori* discussion about the use of metallic implants during the multidisciplinary meetings for each patient appears as the first way to minimise the metal artefacts' consequences in the dosimetric imaging.

In current physics routine, three methods are reliable to reach the goal of a relevant delineation of the CTV (Table 1). *The CT images* are commonly combined to other imaging modalities (MRI, TEP) overcoming CT-artefacts; *the MVCT* is considered as a common and relative safe option to improve the CTV delineation for metallic implant patients; *the delineation of the artefact regions manually* and the assignation of a CT number corresponding to the water or surrounding tissues' relative electron density is the most widespread in radiation therapy departments if the mass density or atomic composition of the selected tissues is known.

Moreover, research and development have produced new methods for reducing metal artefacts (PEEK/Carbon implants, MAR algorithms, DECT). Despite substantial evidence highlighting their benefits, there is still a high need for research efforts to adapt technologies and assess their specific benefits for the application field of radiation therapy including the CTV delineation and dose calculation accuracy.

However, it exists a serious lack of medical data about direct effects of metallic hardware on local tumor control and normal tissue side effect rates in cancer patients harbouring metallic implant. Only two studies are published and they showed a negative effect of spinal implants

on tumor local control. Overall, research efforts addressing these metal artefact questions are encouraged and may call attention to the use of MAR methods to define the CTV. According to this review, it should be obvious that the benefits of each MAR method should be prospectively assessed in terms of tumor local control and toxicity in patients with metallic implants.

Table 1: Options of Treatment planning optimisation methods

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Options	Hip prostheses	Dental filling	Spinal metallic implants
Medical strategy	Removing Minimal metal amount using Radiolucent implants	Dental extraction Minimal metal amount using Radiolucent implants	Removing Hybrid therapy Minimal metal amount using Optimal geographic set up of metallic implants Radiolucent implants
Common Imaging Strategy	CT, MRI, TEP		
Physics Strategy	Ballistics avoiding beam paths through implanted materials Mega Voltage CT (MVCT) Metal artefact reduction (MAR) - Manual method - Algorithms Dual energy computed tomography (DECT)		