Australasian Physical & Engineering Sciences in Medicine (2019) 42:415–425
https://doi.org/10.1007/s13246-019-00751-8

REVIEW PAPER

A review and analysis of stereotactic body radiotherapy and radiosurgery of patients with cardiac implantable electronic devices

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Received: 23 May 2018 / Accepted: 27 March 2019 / Published online: 4 April 2019

Abstract

The implementation of stereotactic body radiation therapy (SBRT) and stereotactic radiosurgery (SRS) has greatly increased due to its convenience and advantages from perspectives ranging from radiobiology to radio physics. Because SBRT/SRS delivers high doses in few fractions, precise dose delivery to target volumes and sufficient sparing of adjacent organs at risk (OARs) are required. Achieving these conflicting objectives is challenging for all patients receiving SBRT/SRS and may be particularly challenging when SBRT/SRS is adopted for treating patients with cardiac implantable electronic devices (CIEDs) because cumulative doses in CIEDs must be limited. Published research considering the different aspects of stereotactic treatment in patients with CIEDs was reviewed to summarise their findings in the following sections: (I) conventional linear accelerator (linac)-based SBRT and SRS; (II) CyberKnife, Gamma-Knife, VERO and helical tomotherapy SBRT and SRS; and (III) proton therapy. A total of 65 patients who had CIEDs and underwent SRS, SBRT, or SABR treatments were identified in the reviewed studies. The functionality of the CIEDs was assessed for 58 patients. Of those, CIED malfunctions (such as data loss, mode change, and inappropriate shock) were reported in four patients (6.89%). This review highlights the available sparse information in the literature by posing questions for future research.

Keywords Stereotactic body radiotherapy (SBRT) · Stereotactic radiosurgery (SRS) · CyberKnife · Gamma-knife · Tomotherapy · Pacemaker · Implantable cardioverter defibrillator

Introduction

Stereotactic body radiotherapy (SBRT), which was more recently defined as stereotactic ablative body radiotherapy (SABR), is increasingly used in the treatment of different malignancies, including both primary and metastatic lung, liver, brain, vertebral, kidney and pancreatic tumours [1]. The increased use of SBRT is due to the possibility of achieving a highly localised dose distribution facilitated by the common use of non-coplanar beam deliveries, the explicit inclusion of motion management and the use of image guidance [2].

Although a higher dose per fraction can provide high rates of tumour control, it can increase the risk of long-term toxicity to normal tissues. Therefore, SBRT requires precise delivery of the dose to target volumes and sufficient sparing of adjacent organs at risk (OARs) [1, 2]. Achieving these conflicting objectives is challenging when planning radiotherapy for patients receiving SBRT/SRS and may be particularly challenging when SBRT/SRS is adopted for treating patients with cardiac implantable electronic devices (CIEDs).

The American Association of Physicists in Medicine (AAPM) report (TG34) was the earliest guideline published for the management of patients with CIEDs receiving general radiotherapy (RT) in 1994 [3]. Since

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the publication of the AAPM (TG34) report, technologies pertaining to all elements of the chain of RT have progressed. These developments, coupled with advancements in CIED technology, have led to a need for more research on this topic. Many aspects of how radiotherapy dose affects the CIED have been investigated in the literature, including how to measure dose to the device [4], the effect of direct and indirect exposure (reported in in vivo [5, 6] and in vitro [7–9] studies), and the assessment of risk [10], mechanism [8], and source [11, 12] of CIED malfunctions. Treatment planning techniques for CIED avoidance have also been reported [13]. Consequently, the number of guidelines [14–17] and review papers [18, 19] has increased. These guidelines and reviews mainly address the management of patients with CIEDs undergoing conventionally fractionated RT (e.g., 2 Gy/fraction).

Today, as the clinical use of advanced RT technologies and techniques increases, the need to consider the different challenges of these techniques when managing patients with CIEDs has arisen [14]. SBRT/SRS is a modern technique with widespread use in clinics. However, compared to conventional radiation therapy, SBRT/SRS has unique characteristics that might demand special considerations for the safety of patients with CIEDs. The following are some of these characteristics:

(a) *High dose per fraction*. One of the significant features that differentiates SBRT/SRS from conventional RT is the delivery of higher doses per fraction delivered in 1-8 treatments. A higher dose per fraction in SBRT/SRS might result in a higher dose per fraction for a CIED.
(b) *SBRT/SRS-dedicated Treatment Technologies.* As conventional RT, SBRT/SRS can be delivered by conventional linacs. Recently, SBRT/SRS-dedicated treatment units have become available commercially, such as CyberKnife, Gamma-Knife and VERO.
(c) *Techniques to achieve conformal doses*. SBRT/SRS can be delivered using different methods, such as multiple static fields or arcs, often employing multi-leaf collimator (MLC) fluence modulation and non-coplanar geometries to achieve dose conformity. Different challenges may be involved [20] compared to those associated with conventional radiotherapy.
(d) *Out-of-field doses (outside primary beam)*. Different delivery devices and beam modifiers used in SBRT/SRS can lead to different out-of-field doses [21]. Additionally, more leakage and higher collimator scatter occur due to higher monitor units (MUs) in modulated techniques (such as intensity modulated radiotherapy (IMRT)-SBRT and volumetric modulated arc therapy (VMAT)-SBRT) and higher monitor units associated with higher dose per fraction.
(e) *Flattening-filter-free (FFF) beam modes*. The use of FFF beams in conventional RT is less common because FFF beams are advantageous for small fields (e.g., SBRT/SRS) and conventional RT of large targets, may not benefit from FFF beams [22]. Compared with conventional FF photon beams, FFF beams have several unique features, such as different beam profiles, different head scatter properties, and a higher dose rate [22, 23].
(f) Electromagnetic Interference (EMI). In SBRT/SRS, electromagnetic field fluctuations are specific to repeated beam hold states (e.g., step-and-shoot IMRT and gating techniques) or non-conventional linac-based technologies (e.g., continuous motion of couch and gantry in tomotherapy with a shorter source-to-axis distance (SAD = 85 cm) instead of the usual 100 cm in conventional accelerators or the proximity/motion of CyberKnife linac relative to patients compared to conventional linac treatments).
(g) Extensive use of image-guided radiotherapy (IGRT).

For SBRT/SRS, the use of IGRT is essential compared with conventional RT. Accordingly, it is possible that the potential contribution of the imaging dose from kV [24, 25] and/or MV X-rays from repeated image guidance procedures to the CIED cumulative dose is sometimes not negligible.

The purpose of this paper is to review and analyse the effect of stereotactic treatment (including conventional linac, CyberKnife, Gamma-Knife, VERO and helical tomotherapy SBRT and SRS) on CIED. This review also attempts to demonstrate the sparsely available information scattered throughout the literature and ends with questions for future research.

Methods

A literature search was performed using the following search engines: PubMed, Science Direct and Google Scholar. Search keywords included the following terms: 'Stereotactic & Pacemaker', 'Stereotactic & Defibrillator', 'Radiosurgery & Pacemaker', 'Radiosurgery & Defibrillator', 'Tomotherapy & Pacemaker', 'Tomotherapy & Defibrillator', 'CyberKnife & Pacemaker', 'CyberKnife & Defibrillator', 'Gamma-Knife & Pacemaker', 'Gamma-Knife & Defibrillator', 'Pacemaker & Flattening Filter Free', 'Defibrillator & Flattening Filter Free', 'Imaging Dose & Pacemaker' and 'Imaging Dose & Defibrillator'. Only citations written in English after the year 2000 were considered (with the exception of a Turkish paper with an abstract written in English; the body of the text was translated by a native Turkish-speaking consultant). The literature search in Google Scholar was limited to the title of scholarly works

but without any filtration in PubMed and Science Direct. The second step was to examine the citations, regardless of their type (journal paper, conference paper and/or abstract, etc.), that met the following objectives:

(a) Scholarly works investigating SBRT/SRS features that may influence CIED operation/functionality.
(b) Scholarly works providing dosimetric data for patients with CIEDs undergoing SBRT/SRS.
(c) Instances (or lack thereof) of CIED failures reported during or after a course of SBRT/SRS.

The final step was to classify these citations into the following sections: (I) conventional linac-based SBRT and SRS; (II) CyberKnife, Gamma-Knife, VERO and helical tomotherapy SBRT and SRS; and (III) proton therapy. The classification was performed based on the aforementioned objectives as well as the number, type and methodology of research studies conducted on each radiation modality and technology. The Mendeley desktop and online versions, which are free bibliographic software, were used to capture, catalogue and analyse the results.

Results

A total of 1692 references (PubMed: 41, Science Direct: 658 and Google Scholar: 993) were identified. After deleting duplicates and non-relevant publications, 12 articles remained. These articles are summarised in Table 1.

It should be noted that scholarly works such as those addressing accelerated partial breast irradiation (APBI) and CIEDs or case studies reporting cancer patients with CIEDs undergoing conventional fractionated helical tomotherapy were considered non-relevant citations.

Conventional linac-based SBRT and SRS

Patient studies

Prisciandaro et al. [26] performed a retrospective dosimetry study on patients with CIEDs receiving RT over a 6-year period. Of the 69 patients treated with different techniques, 6 patients received at least one course of SBRT (8–18 Gy/fx), and one patient was treated with two intracranial stereotactic radiosurgery (SRS) plans (single 16 and 21 Gy treatments). The authors estimated the CIED dose prior to treatment based on published out-of-field dose data. Dose measurements were made with a thermoluminescence dosimeter (TLD) during the first treatment if doses to pacemakers (PMs) and implantable cardioverter defibrillators (ICDs) exceeded 2 and 1 Gy, respectively, or if the distance between the radiation field and CIED was less than 10 cm. The highest and lowest reported CIED doses measured by TLD for patients treated with SBRT were 0.75 Gy and 0.19 Gy, respectively. Two failures (ICD partial resets) occurred, and both were associated with a higher energy (16 MV), but it is not clear whether these beams were associated with the SBRT/SRS treatments.

A single-patient case report of a lung cancer patient whose CIED received a total cumulative dose of 69.6 Gy over three phases using different RT techniques was reported by Ahmed et al. [27]. The patient was first treated with three-dimensional conformal radiotherapy (3DCRT) to 30.6 Gy [1.8 Gy*17 fractions] (both 6-MV and 15-MV photons), followed by IMRT to 27 Gy [1.8 Gy*15 fractions] (6-MV photons). Finally, the patient received a boost of 12 Gy [3 Gy*4 fractions] (15-MV photons) delivered via stereotactic body RT. The maximum and mean doses to the CIED were 52.4 and 29.3 Gy, respectively. However, whether the reported dose was based on a treatment planning system (TPS) dose calculation or dosimetry measurement is unclear. No malfunctions or defects were reported during or after treatment.

In a Japanese prospective study by Soejima et al. [28], patients with CIEDs from 29 centres were treated using different RT techniques. The patients were monitored before, during and after RT. In this cohort study of 62 patients, four lung cancer patients received SBRT, and two patients received CyberKnife radiosurgery. Maximum doses of devices determined by a dose-volume histogram (20.96 Gy), diode and TLD (2.29 Gy) were reported, but they were not correlated with the type of treatment. No malfunctions were reported due to SBRT.

Out-of-field dose from the primary treatment beam and treatment planning system calculations

Although conventional linac-based stereotactic techniques produce relatively lower out-of-field doses than other stereotactic modalities, such as CyberKnife and Gamma-Knife [21, 29], these out-of-field doses have the potential to cause CIED malfunctions [21]. Some TPSs exhibit dose calculation inaccuracies in the out-of-field region exceeding 50–55% [30, 31], particularly in areas greater than 11.25 cm from the field edge [30]. This issue must be considered when assessing the calculated cumulative dose to the CIED in these regions [21, 30].

Prisciandaro et al. [26] also performed dose calculations in three TPSs, namely, UMPlan (an in-house TPS), Varian Eclipse with an anisotropic analytical algorithm (AAA, version 11.031) and Varian Eclipse with the Acuros algorithm (version 11.031). The summary of their results, including SBRT cases, demonstrated that compared to TLD measurements, the investigated TPSs underestimated the CIED dose in most cases. In this study, the three TPSs combined demonstrated an average underdosage of 0.69 Gy [0.06–1.61].

Table 1 A summary of studies considering stereotactic radiotherapy for patients with CIEDs

Author (Ref)/year	Number of patients and delivery technique	Total prescription dose (Gy)	Location	PM or ICD and model	Position of device relative to treatment fields	CIED dose	Malfunction and number of failures due to SBRT/SRS
Prisciandaro et al. [26] / 2015	N = 6 Conventional linac-based SBRT N = 1 Conventional linac-based SRS	40–54 16 and 21	Lung n/a	PM and ICD models were mentioned but without classification based on treatment techniques	Outside distance from edge field ranged from 1.5 to 40 cm	Reported for only three patients using TLD (0.19, 0.5, and 0.75 Gy), and the range of the calculated dose by TPSs for one patient was 0.54–1.81 Gy	Functionality of the CIEDs during RT was reported, and 2 failures (ICD partial-resets) occurred; both were associated with a higher energy (16 MV), but it is not clear whether these beams were associated with the SBRT/SRS treatments
Ahmed et al. [27] / 2014	(A case study) 3D-CRT + IMRT + Conventional linac-based SBRT	30.6 [1.8 Gy*17 fractions] + 27 [1.8 Gy*15fractions] + 12 [3 Gy*4 fractions]	Lung	AICD St. Jude Medical Fortify Assura VR 1257-40Q ICD	Inside	D_{min} = 13.5 Gy, D_{mean} = 29.3 Gy D_{max} = 52.4 Gy.	Functionality of the AICD during and after RT was assessed, and no failures occurred
Soejima et al. [28] / 2011	N = 4 Conventional linac-based SBRT N = 2 SRS CyberKnife	n/a	Lung Brain	PM & ICD All investigated models were mentioned but without classification based on treatment techniques	Outside	n/a	Functionality of the CIEDs during and after RT was reported, and no failures occurred due to SBRT/SRS
Scobioala et al. [33] / 2015	(A case study) 3DCRT and SBRT using tomotherapy	25.2 [1.8 Gy*14 fractions] and 35 [7 Gy*5 fractions]	Left main bronchus	PM St. Jude Medical GmbH ICD Atlas II VR SN CPS	Outside for 3DRT Inside for SBRT	Calculated by TPS ICD: D_{max} = 15.58 Gy D_{mean} = 5.55 Gy PM: D_{max} = 2.74 Gy D_{mean} = 1.13 Gy	Functionality of CIEDs during and after RT was assessed, and no failures occurred due to SBRT/SRS

Table 1 (continued)

Author (Ref)/year	Number of patients and delivery technique	Total prescription dose (Gy)	Location	PM or ICD and model	Position of device relative to treatment fields	CIED dose	Malfunction and number of failures due to SBRT/SRS
Bianchi et al. [34] / 2008	N = 2 CyberKnife	21 [7 Gy*3 fractions] 60 [20 Gy*3 fractions]	Thymus Lung	PM SORIN ELECT XS PLUS ICD Medtronic Maximo DR 7278	n/a	n/a	Functionality of PM during and after RT was assessed, and no failures occurred Functionality of ICD during and after RT was assessed, and a malfunction during the first fraction (defibrillator was triggered) occurred
Grant et al. [35] / 2015	N = 10 Gamma-Knife	n/a	n/a	n/a	n/a	n/a	Functionality of CIEDs during and after RT was assessed, and no failures occurred due to SBRT/SRS
Çakmak et al. [38] / 2012	A case study CyberKnife	55 [11 Gy*5 fractions]	Lung metastases from colorectal cancer	ICD EnTrust D154ATG, Medtronic	Outside	n/a	Functionality of ICD after RT was assessed, and it was found that 5 ICD inappropriate shocks during treatment had occurred
Riva et al. [36] / 2018	N = 35 CyberKnife VERO System	Total and median doses were mentioned but without classification based on treatment techniques	Chest and head and neck (N = 26), abdomen and pelvis (N = 9)	n/a	n/a	n/a	Functionality of CIED during and after (only for 73% of all patients) RT was assessed, and no failures occurred due to SBRT/SRS
Westover et al. [39] / 2012	N = 1 Proton SBRT	42 to 50 GyE [3 to 5 fractions]	Lung	PM *Model was not mentioned	Outside	n/a	Functionality of CIED during and after RT was not reported at all

Table 1 (continued)

Author (Ref)/year	Number of patients and delivery technique	Total prescription dose (Gy)	Location	PM or ICD and model	Position of device relative to treatment fields	CIED dose	Malfunction and number of failures due to SBRT/SRS
Ueyama et al. [40] / 2016	N = 2 Proton Therapy	66 GyE [11 GyE*6 fractions] 50 GyE [2 GyE*25 fractions]	Lung Pancreas	PM Medtronic PM IDENTITY® ADx; St. Jude Medical	Outside Distance from the edge field was 24 cm Outside Distance from the edge field was 30 cm	D_{max} = negligible The measured neutron dose = 154.6 mSv D_{max}: n/a The measured neutron dose = 96.4 mSv	Functionality of CIEDs during and after RT was assessed, and a change in the PM mode for patient 1 on treatment day 8 and a PM reset for patient 2 after treatment day 13 occurred

PM Pacemaker, *ICD* Implantable cardioverter defibrillator, *AICD* Automated implantable cardioverter defibrillator, *CPS* Cardiopulmonary support device, *CIED* Cardiac implantable electronic device, *SBRT* Stereotactic body radiotherapy, *SRS* Stereotactic radiosurgery, *n/a* not available

Plan optimisation studies

A conference proceeding paper by Chow and Jiang [32] described the investigation of a treatment planning strategy for patients with PMs undergoing lung VMAT-SBRT. The authors aimed to determine whether the PM dose could be reduced by considering the PM as an OAR in the VMAT plan. The prescription was 48 Gy [12 Gy*4 fractions], and the TPS was Varian Eclipse (version 10) using the progressive resolution optimizer (PRO) and AAA (version 10.0.28). The DVH of the planning target volume (PTV) and OARs was compared with and without consideration of the PM as an OAR in plan optimisation. The PTV coverages and OAR sparing were satisfied by considering the PM an OAR in both cases.

Tomotherapy, CyberKnife, VERO, and Gamma-Knife

Patient studies

A patient with a complicated case of RT with a PM, ICD as well as cardiopulmonary support (CPS) device who underwent a combination of SBRT using helical tomotherapy along with conventional RT was reported by Scobioala et al. [33]. Based on the treatment plans, the PM was not included in the PTV in conformal therapy, but the ICD was partially located in the SBRT treatment field. Conformal RT (with a prescription dose of 25.2 Gy [1.8 Gy*14 fractions] using two fields prescribed to the 95% isodose with 6-/15-MV photon beams) and SBRT (with a prescription dose of 35 Gy [7 Gy*5 fractions] with 6-MV photon beams prescribed to the 65% isodose) were applied. The dose for all implanted devices was determined using phantom measurements prior to treatment and during the first three fractions of RT using TLDs. However, the authors reported only the measured max ICD dose (15.85 Gy). The TPS calculated max and mean ICD doses were 15.58 and 5.55 Gy, and the maximum and mean PM doses were 2.74 and 1.13 Gy, respectively. Although high radiation exposure was used and the active part of the ICD was in the SBRT field, no PM and ICD malfunctions were reported during RT or 12 months post-treatment.

CIED dysfunction during CyberKnife treatment was investigated by Bianchi et al. [34]. Of the two patients investigated in this study, one lung cancer patient who received 60 Gy [20 Gy*3 fractions] prescribed to an 82% isodose experienced an ICD malfunction. During the first fraction, the directly irradiated defibrillator was triggered, and a specialist was asked to disable the defibrillator in the first fraction and during other sessions accordingly. No other malfunctions occurred during the remaining two fractions or 11 months after irradiation.

Additionally, patients with CIEDs were treated with CyberKnife radiosurgery in a prospective study by Soejima et al. [28], and the authors did not report any CIED malfunctions due to the CyberKnife treatment.

A large retrospective study of patients with CIEDs by Grant et al. [35] was the only study that considered Gamma-Knife treatment in patients with CIEDs. In their large cohort of 247 patients, ten patients with CIEDs were treated with a Gamma-Knife. No PM/defibrillator device malfunction was detected during the Gamma-Knife treatment. The range of the median incident doses on CIEDs for the non-neutron producing RT group (electron, Gamma-Knife and 6-MV photons) was generally reported. However, the authors did not specify the correlated CIED doses due to the Gamma-Knife treatment.

A recently published retrospective cohort study was conducted by Riva et al. [36] over a 6-year period from January 2010 to December 2016. This study was also the largest, with 35 out of 63 patients with CIEDs treated with SBRT. Radiation delivery of SBRT was performed using either a VERO system or a CyberKnife. No SBRT-related malfunctions were observed in the patient cohort, even though 26 (out of 35) patients received head and neck and chest SBRT treatments.

Blamek et al. [37] published a "mini-review" on stereotactic body radiosurgery and tomotherapy in patients with CIEDs. This paper first summarised the impact of certain general related factors in RT on patients with CIEDs, such as the effect of direct irradiation and scattered radiation. The authors identified potential factors that can influence the operation of the CIED during RT. For instance, the possible perturbation of CIEDs due to irradiation of either pacing or defibrillator leads when they are included in the beam and the possibility of receiving external electromagnetic impulses when electromagnetic field sources are close to patients (e.g., CyberKnife). Additionally, scholarly works indirectly and directly related to radiosurgery in patients with CIEDs were reviewed. In particular, a Turkish study by Çakmak et al. [38] reported oversensing due to EMI and several inappropriate ICD shocks during CyberKnife use on a lung metastasis patient.

Proton therapy

Patient studies

In a study on proton SBRT in lung cancer patients by Westover et al. [39], 1 patient among 15 who were treated with proton SBRT had a PM at the same level as the lung lesion. No detailed information was provided regarding this case, but the authors noted that they used two proton fields arranged such that they avoided the PM.

In another study by Ueyama et al., two cases of PM malfunction associated with proton beam therapy were reported [40]. The first patient received 66 Gray equivalent (GyE) [6.6 Gy*10 fractions] at three different angles in 210-MeV proton beams. The second patient was treated with standard fractionation and received 50 GyE [2 Gy*25 fractions] from two different angles. The proton beam energies were 210 and 150 MeV. Although the authors did not find any PM malfunctions during a phantom simulation measurement with the same PM model before treatment for the first patient, a PM malfunction occurred during treatment day 8. For the second patient, a PM malfunction occurred in the simulation, and accordingly, a PM reset was revealed after treatment day 13.

Discussion

Assay of search results

As patient age and comorbidities increase, the number of studies focusing on the management of patients with CIEDs undergoing RT with conventional RT has also increased. However, the number of publications that specifically address the issue of SBRT/SRS and CIEDs is not high. This paper highlights the case studies, treatment techniques, and CIED dose mitigation strategies for SBRT/SRS patients who have CIEDs.

Since 2000, only 12 related scholarly works related to patients with CIEDs undergoing SBRT/SRS have been reported; these citations include only three case studies, two abstracts and one conference paper directly focused on this topic. The remaining articles are general studies addressing different numbers of patients with CIEDs who received stereotactic RT in their total datasets without reporting detailed information regarding these patients.

Available data regarding SBRT and SRS in patients with CIED are limited with respect to delivery systems and techniques, as well as patient datasets. According to our review, only one study reported on the use of a Gamma-Knife to treat patients with CIEDs (ten out of 215 patients with CIEDs), with no additional details about these patients [35]. Additionally, only one case study reported the use of tomotherapy SBRT [33], and four studies reported the use of a CyberKnife to treat patients with CIEDs [28, 34, 36, 38]. Similarly, clinical data regarding conventional linac-based SBRT and SRS are scarce [26–28]. The only study found for this review regarding SBRT treatment plans and/or plan optimisation for patients with CIEDs was a conference proceeding paper [32].

Other considerations, questions and further research

High dose-per-fraction and SBRT/SRS-dedicated treatment technologies

Although several in vitro studies of CIED irradiation using conventional linacs have been conducted, no specific in vitro or in vivo data on irradiation of different ICDs and PMs and dose fractionations using CyberKnife and Gamma-Knife units are available. In two in vitro studies performed by Mouton et al. [10] and Hurkmans et al. [41], CIEDs were exposed to high dose fractions. However, CIED irradiation was conducted with incremental dose deliveries (from 0.05 and 0.5 Gy up to 20 Gy). Although no adverse effects were expected as a result of the increased doses per fraction in SBRT/SRS treatments, more clinical/epidemiological and in vitro studies are required to investigate the risks associated with different stereotactic systems and techniques in larger study populations and to provide more reliable data.

Techniques to achieve conformal doses

Berlach et al. [20] described an issue they faced during a non-isocentric robotic SBRT using a CyberKnife. This concern is particular to SABR planning/treatments due to the overlapping entrance of non-coplanar beam paths. This issue can cause "fingers of death", which is a streak of unexpectedly high doses in unexpected places. The dose delivered to the entire patient volume should be calculated to ensure that no unexpected regions of high doses are encountered, particularly if the high dose overlaps with a CIED. This finding highlights the challenges related to delivery techniques for SBRT when managing patients with CIEDs that may exist and must be addressed.

Flattening-filter-free beam modes

Flattening filter-free SBRT has become established in many cancer centres. Because of several unique features of FFF beams compared with flattened beams, including a lower out-of-field dose, sharper penumbra, less head scatter, and especially higher dose rates [22, 23], the effects of these distinct and possibly advantageous characteristics should be considered for patients with CIEDs.

According to Hurkmans et al. [14], a high dose rate may cause possible abnormal functionalities in some parts of CIEDs. The authors concluded that for conventional FF beams, the dose rate effect (e.g., ranging from 1 Gy/min to 6 Gy/min at depth of maximum dose at reference distance) on CIEDs is not significant because the dose rate at the CIED location is lower than the recommended maximum acceptable value (0.2 Gy/min) [10]. Hurkmans and colleagues further added that for FFF beams, the dose rate would be lower than 1 Gy/min, provided that the CIED is located outside of the treatment field. Thus, dose rate effects might not be frequent. In modern linear accelerators, the dose rate for flattening filter-free SBRT can reach up to 24 Gy/min. For this dose rate, the question arises as to whether the effects of such high dose rates on CIEDs are still rare.

Gauter-Fleckenstein et al. [42] investigated the effect of pelvic and thoracic FFF-VMAT on 76 ICDs. Irradiation [10 Gy*3 fractions] in five sets with a cumulative dose of up to 150 Gy in the isocentre was performed with 6-, 10- and 18-MV beams and a dose rate of up to 2500 cGy/min. The authors observed different unpredictable incidents, including inadequate defibrillation, reset and data loss at 10 MV and 15 MV. However, the authors found no incidents with 6-MV FFF-VMAT even at dose rates of 2500 cGy/min, provided that the ICD was not positioned in the direct radiation beam.

Rodriguez et al. [43] found that a transient effect on CIED can occur due to radiation-induced photocurrents generated by a high dose rate. This effect can become appreciable with a pulse dose rate greater than 10^4 Gy/s. In that case, the effect of the pulse dose rate might be much more significant [43]. Although the usual range of the pulse dose rate used is much less than this value [14], questions regarding whether one needs to consider dose/min, dose/s, and dose/pulse and their effect on CIEDs may arise.

Regarding out-of-field doses for FFF photon beams, Covington et al. [44] developed a comprehensive out-of-field dose dataset for various field sizes and distances from the field edge for 6 FFF and 10 FFF beams. In this study, the clinical implementation of this dataset was demonstrated by taking a patient with CIED treated with a 6 FFF beam as an example. However, the out-of-field dose values estimated using this dataset are mainly applicable to static field sizes, and applying this model to the use of modulated fields could result in greater uncertainty.

Electromagnetic interference (EMI)

Magnetic resonance imaging (MRI) is considered the non-invasive modality of choice for characterising soft tissue tumours [45] and accurate delineation of target volumes and organs at risk during radiotherapy treatment planning procedures [46]. However, EMI might result in CIED system malfunction [47]. As such, the evaluation of EMI and strategies for minimising the associated risks are highly recommended for cancer patients with CIEDs.

The role of MRI in the SBRT technique for lung cancer has recently gained increasing attention [48]. However, for cancer patients with CIEDs, the EMI due to the application of each or combination of the therapeutic and diagnostic interventions may pose more challenges [49–51]. The recent advancements in the technology of MR-conditional CIEDs

mitigate the hazards associated with EMI and minimise the risk of device malfunction, as well as the clinically significant adverse events to some extent. These advancements mainly include magnetic protection by reduction of the ferromagnetic components, utilising optimal device shielding, modification of device electronic circuitry (particularly the filters and sensors), and design modifications of the coil and electrodes on the bipolar leads [52, 53]. In particular, over the course of cancer treatment for patients with CIEDs, more frequent exposures of the CIED to EMI could increase the probability of a device malfunction. The identified common hazards from external electromagnetic sources in radiation therapy and diagnostic modalities include but are not limited to pacing inhibition and permanent damage to the electronic circuitry of the device [54]. To mitigate the risk of EMI affecting CIED functionality, device program-change protocols have been employed to minimise inappropriate activation or inhibition of brady-/tachyarrhythmia therapies [55].

Integrated MRI-linacs provide high precision and accurate dose delivery, and the use of this system is increasing [48]. Considering the significant advantages of this system, there is a growing interest in clinically implementing lung SBRT [48, 56]. Due to concerns of the interaction between MRI fields and CIEDs, patients with these devices may be restricted from taking advantage of this technology [57].

Although there are no reported instances of clinically significant adverse events as a result of EMI induced by the conventional linac system from previous studies [55], some evidence of transient complications such as pacing inhibition and inappropriate detection of ventricular arrhythmia during the treatment has been reported [35, 55]. Therefore, the restrictions on the electromagnetic exposure of cancer patients with CIEDs might be justifiable.

In stereotactic treatment, the electromagnetic field fluctuations are specific to repeated beam hold states (e.g., step-and-shoot IMRT and gating techniques) or non-conventional linac-based technologies (e.g., continuous motion of couch and gantry in tomotherapy with a shorter source-to-axis distance [SAD = 85 cm] instead of the usual 100 cm in conventional accelerators or the proximity/motion of CyberKnife linac relative to patients compared to that of conventional linac treatments).

The recent advancements in CIED technology and the introduction of clinical safety protocols during RT (such as accessing special programming modes via the CIED clinic or with the application of a vendor-supplied external static magnet) can potentially minimise the risk of an EMI-related malfunctions [47, 55].

Extensive use of image-guided radiotherapy (IGRT)

Another specific feature of stereotactic RT is the extensive use of IGRT. In previous studies [24, 25] on the imaging dose from Elekta XVI and Varian OBI kV-CBCT Systems to CIEDs, the maximum overall imaging dose delivered from a 30 fraction, daily, 4D kV-CBCT lung protocol could reach as high as 50 cGy. Wronski et al. [58] reported that the imaging dose for each fraction ranged from 2.2 to 4.3 cGy for PM and from 0.8 to 1.9 cGy for ICD. Ming et al. [59] reported Monte Carlo (EGS4)-simulated CIED doses of 1.5 cGy (low-dose thorax) and 0.9 cGy (high-quality HN) per fraction. In the case of CyberKnife imaging dose, Maffei et al. [60] evaluated the potential contribution of the corresponding imaging dose to the CIED cumulative dose. The therapeutic dose to the CIED was 1.4 Gy, and the imaging dose was 0.4 Gy. In some cases, this additional imaging dose to CIEDs is not negligible. Hence, the following questions must be addressed. How could this additional imaging dose be managed? What about the portal imaging dose from MV X-rays to CIEDs?

Conclusion

We identified a total of 65 patients who had CIEDs and underwent SRS, SBRT, or SABR treatments in the reviewed studies. The functionality of the CIEDs was assessed for 58 patients. CIED malfunctions (such as data loss, mode change, and inappropriate shock) were reported in 4 of those patients (6.89%). The result demonstrates the potential risk of CIED malfunctions during stereotactic RT treatment.

With the ever-increasing use of advanced RT technologies and techniques, the different characteristics of such techniques should be considered when managing patients with CIEDs. More studies are needed to enrich existing data and address the challenges of stereotactic treatment in relation to patients with CIEDs, such as managing additional imaging doses, potential EMI, overlapping non-conformal beams, and the possible effect of the dose rate in SBRT-FFF.

Acknowledgment We would like to extend our gratitude to the director, coordinator, and board members in the Department of Medical Physics at the International Centre for Theoretical Physics (ICTP) for providing access to ICTP resources and databases. Sincere thanks to Dr. Recep Kandemir, medical physicist at Dokuz Eylul University, for his outstanding work in translation of reference#38. Also, special thanks go to the editor, and anonymous reviewers for their constructive comments and suggestions. The first author would like to acknowledge the financial support from University of Trieste and European Fund (FSE-S3/2, Project Code: FP1683026001) to perform this study.

Compliance with ethical standards

Conflict of interest All the authors declare no conflict of interest.

Informed consent Not applicable.

Research involving human participants and/or animals This article does not contain any studies with human participants or animals performed by any of the authors.

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