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CASE REPORT

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Case study with dosimetric analysis: Total body irradiation to a patient with a left ventricular assist device

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Key Clinical Message

A patient presented with cardiogenic shock, requiring the implantation of a left ventricular assist device (LVAD), and acute myeloblastic leukemia. This necessitated total body irradiation (TBI) while balancing dose reduction to the LVAD components to avoid potential radiation damage. Here we outline our treatment approach and dose estimates to the LVAD.

Abstract

This case report discusses the delivery of TBI to a patient with an LVAD. This treatment required radiation-dose determinations and consequential reductions for the heart, LVAD, and an external controller connected to the LVAD. The patient was treated using a traditional 16MV anterior posterior (AP)/posterior anterior (PA) technique at a source-to-surface-distance of 515 cm for 400 cGy in two fractions. A 3 cm thick Cerrobend block was placed on the beam spoiler to reduce dose to the heart and LVAD to 150 cGy. The external controller was placed in a 1 cm thick acrylic box to reduce neutron dose and positioned as far from the treatment fields as achievable. In vivo measurements were made using optically stimulated luminescence dosimeters (OSLDs) placed inside the box at distances of 2 cm, 8.5 cm, and 14 cm from the field edge, and on the patient along the central axis and centered behind the LVAD block. Further ion chamber measurements were made using a solid water phantom to more accurately estimate the dose delivered to the LVAD. Neutron dose measurements were also conducted. The total estimated dose to the controller ranged from 135.3 cGy to 91.5 cGy. The LVAD block reduced the surface dose to the patient to 271.6 cGy (68.1%). The block transmission factors of the 3 cm Cerrobend block measured in the phantom were 45% at 1 cm depth and decreased asymptotically to around 30% at 3 cm depth. Applying these transmission factors to the in vivo measurements yielded a dose of 120 cGy to the implanted device. The neutron dose the LVAD region is estimated around 0.46 cGy. Physical limitations of the controller made it impossible to completely avoid dose. Shielding is recommended. The block had limited dose reduction to the surface, due to secondary particles, but appropriately

reduced the dose at 3 cm and beyond. More research on LVADs dose limits would be beneficial.

KEYWORDS

cardio-oncology, heart-assist devices, leukemia, neutrons, radiation dosage, radiation protection

1 | INTRODUCTION

There is no cure for end-stage heart failure. Currently, the only viable long-term treatment is a heart transplant. Among the absolute contraindications for a heart transplant is the presence or history of most types of cancer within the previous 5 years due. This is due to concerns about active disease. A further complicating issue is the known cardiotoxicities of cancer therapies, including radiation, chemotherapy, and immunobiologics, all exacerbated by pre-existing cardiac morbidities.[1,2] Left ventricular assist devices (LVADs) help to improve survival rates in cases of heart failure and can be used as a bridge to transplant candidacy and ultimately receiving a transplant. An LVAD is an implanted mechanical pump which is directly attached to the left ventricle of the heart. The pump continuously pushes blood out of the ventricle to the aorta and the rest of the body. The LVAD consists of the mechanical pump as well as an external controller attached by a short driveline cable, 100 cm in total length. Generally, the pump is powered by batteries located externally to the patient. The device can also be directly plugged into an electric outlet, if needed. As LVAD technology improves, more patients are having them implanted and survival rates with them are increasing. This leads to a growing number of patients concomitantly afflicted with cancer. To bridge patients to transplant candidacy, radiation is frequently used as part of the multidisciplinary approach to treatment.

Radiation is well known to damage electronics. While the effect of radiation on other cardiac implantable electrical devices (CIEDs), including pacemakers and defibrillators, has been well studied, there remains limited data on radiation to LVAD.[3–7] Much of the existing radiation data is in the form of in-vitro studies and case reports.[8–15] None of these studies considered the radiation sensitivity of the LVAD external controller. Here, we report the first case of dose delivered to the controller and the first reported case of total body irradiation (TBI) to a patient with an LVAD.

The nature of TBI treatments makes this an especially challenging case. The goal of the TBI is to eliminate the leukemia cells within the bone marrow, as well as to suppress the immune system in order to decrease the potential for transplanted hematopoietic stem cell rejection. By requiring that all the bone marrow cells are sufficiently irradiated, it is necessary to treat the entire body, including the bones proximal to the LVAD and heart, such as the ribs and sternum. This eliminates the diseased cells while simultaneously temporarily reducing the immune response which would otherwise likely lead to rejection of the marrow transplant.[16] Traditional TBI techniques use opposing fields, AP/PA or laterals, to deliver a therapeutic dose. This does not allow for the same level of precise dose delivery as more advanced treatment techniques for localized cancers. This creates a tradeoff between limiting dose to the LVAD while ensuring sufficient dose to the surrounding bone marrow. There are existing techniques such as VMAT TBI and total marrow irradiation that would allow for more precise dose delivery, but those technologies were not available to the clinic at the time of treatment.[17]

In addition, these TBI treatments utilize large open radiation fields with sufficient flash to cover the entire patient. This is quite different from the majority of case reports in localized radiotherapy, where the LVAD controller is usually far away from the radiation field. Even outside of the direct radiation field, there is out-of-field dose to consider from scatter and linear accelerator leakage. As a result, the external controller cannot be completely removed from all radiation. This report details the treatment approach used to manage this complex patient.

Accurately assessing the dose delivered to the LVAD poses unique challenges. The use of Cerrobend blocks to partially shield the LVAD creates electron contamination, which complicates the interpretation of in vivo measurements.[18] In-scatter and back-scatter contribute to further uncertainty in the dose at depth in this situation.[19] Furthermore, there is a lack of information on out-of-field doses in treatments with extended SSDs and TBI treatments.[20] To quantify the dose delivered to the LVAD, in vitro measurements were made with the TBI setup and delivery to quantify the dosimetric effects of the beam spoiler and Cerrobend blocks used in the treatment of the patient.

2 | METHODS AND MATERIALS

2.1 | Patient background

The patient in this case study is a 36-year-old male, with a history of acute myeloblastic leukemia. Chemotherapy

is believed to have caused cardiomyopathy leading to cardiogenic shock with an ejection fraction of 18% and the subsequent need for an LVAD. To bridge the gap to transplant candidacy, the patient was implanted with an Abbot HeartMate 3 LVAD approximately 5 months prior to radiation treatment.[21,22]

2.2 | TBI simulation

The patient was simulated and treated using a traditional technique using opposing 16MV anterior–posterior and posterior–anterior (AP/PA) beams. High-energy x-rays (>10MV) produce less dose variation form the central axis.[19] However, known neutron contamination in high-energy x-rays is detrimental to electronics.[7,23] At the time of treatment, alternative TBI treatments using 6MV were not commissioned in our clinic. As such, the patient was classified as high-risk and associated recommendations made in the report of AAPM Task Group 203 were followed, including having members of the cardiology team present for every treatment.[4]

During simulation, the patient laid on their left side facing the treatment machine. A 2.54 cm thick acrylic beam spoiler was placed between the patient and the LINAC at a source-to-surface distance of 500 cm. The beam spoiler is used to increase scatter and surface dose in the buildup region of the patient. The patient was then positioned such that the distance from the beam spoiler to their umbilicus was 15 cm. Measurements of the patient's thickness were acquired at the umbilicus, head, neck, shoulder, mediastinum, hip, mid-thigh, knee, and ankle. The midline separation was measured to be 26 cm. Off-axis distances and the beam spoiler-to-patient separation were also measured for each anatomical landmark. Planar imaging was done with 16MV beams and film in this position to ascertain the position of the heart and LVAD within the patient. This entire process was repeated with the patient on their right side facing away from the machine to simulate the PA treatment. The PA simulation setup of the patient is shown in Figure 1A.

The patient was prescribed 400 cGy to the midline in two daily fractions of 200 cGy, with the AP and PA fields equally weighted. After careful discussion about the patient's safety, the area encompassing the LVAD and heart was prescribed a reduced total dose of 150 cGy (37.5% prescription). The size and shape of the Cerrobend were determined by the physician based on the planar imaging acquired during the simulation.

The necessary number of monitor units (MU) for each beam was calculated to be 2951. An in-house TBI calculator was used to calculate the necessary thickness of lead compensators to optimize dose homogeneity at each anatomical site. Using the patient separation and off

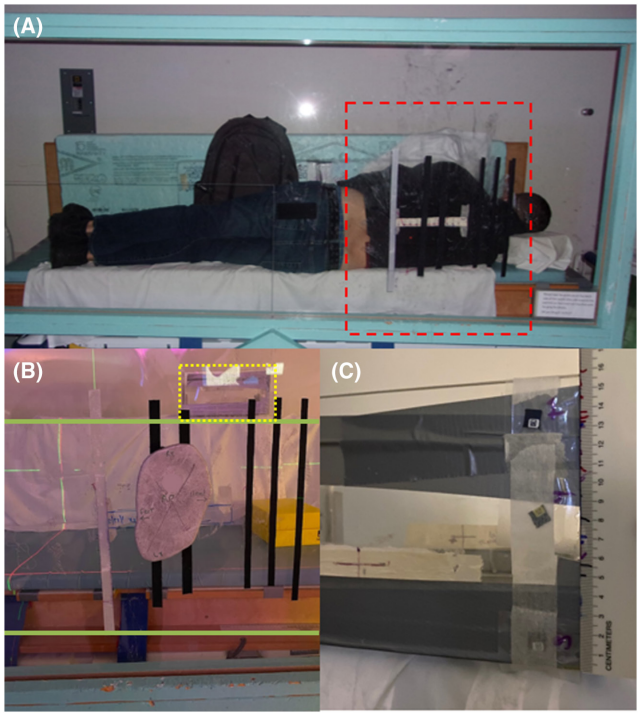

FIGURE 1 Patient Simulation and Recreation of the treatment setup. (A) Patient setup for simulation in the posterior–anterior position, with the spoiler located in front of the patient. The dashed red line indicates the area shown in (B), which shows the Cerrobend LVAD block attached to the spoiler. The box used to contain the LVAD controller, highlighted by the dotted yellow rectangle can be seen in the upper right. The solid horizontal lines indicate the region of the treatment field. (C) The location of the OSLDs on the box in which the LVAD controller was placed. The OSLDs are placed on the outside of the box in this image for easier visualization of the OSLD placement. During the treatment, they were located inside the box.

axis-values measured at simulation, the thickness was optimized to deliver a dose within 5% of the prescribed dose to the midline and midpoint of each anatomical region. Lead compensators were fabricated out of 1.69 mm thick lead sheets to be attached to an acrylic mount which is placed in the gantry mount. A transmission factor of 0.919 per sheet was used. The size of each lead compensator was calculated by backprojecting the patient separations to the head of the LINAC. The in-house TBI calculator was also used to determine the desired thickness of Cerrobend to block the heart and LVAD (LVAD block) based on a half-value layer of 1.83. From this, the LVAD block was calculated to be 3 cm thick. The size and shape of the LVAD block were determined by the physician to optimally balance the dose reduction to the LVAD and heart while ensuring sufficient dose to the surrounding bone marrow. To fabricate the LVAD block, this outline was back projected from the patient midline to the beam spoiler, where the LVAD block was mounted for treatment.

2.3 | Treatment

Both treatment fields were $40 \times 12 cm^2$ at isocenter with the collimator set to 90 degrees. The LVAD was switched from battery power to external power to minimize the chance of power disruption during the treatment. As shown in Figure 1B, the external controller for the LVAD was placed inside a 1 cm thick acrylic box to reduce neutron dose and positioned outside the treatment field above the patient as far as possible. The controller could not be moved any further out of the field due to the finite length of the 100 cm driveline cable connecting it to the rest of the LVAD. As a result, the field edge was approximately coincident with bottom of the box. High-Z shielding was not used due to the concern of creating secondary particles. The appropriate LVAD block was placed on the beam spoiler for each treatment field. Figure 1B shows the placement of the AP block. Planar film imaging was used to confirm the position of the block. If necessary, the position of the block was adjusted, and imaging was repeated. For the first fraction, in vivo measurements were obtained by placing two optically stimulated luminescent dosimeter (OSLD; nanoDot®, Landauer, Glenwood, IL, USA) on the patient for each treatment field. The first OSLD was placed directly along central axis, in line with the patient's umbilicus. The second OSLD was placed in the center of the area blocked by the LVAD block, as determined by the shadow cast by the treatment field projected onto the patient with the LVAD block in place on the beam spoiler.

In addition, OSLDs were placed inside the box with the controller at distances of 2 cm, 8.5 cm, and 14 cm from the field edge, as shown in Figure 1C. In the figure, the OSLDs are placed on the outside of the box for ease of visualization. The OSLDs were not placed directly on the controller to minimize the handling of the controller and to help expedite the treatment process. Before, during, and after each treatment, the LVAD was interrogated by the cardiology team to monitor the operational parameters of the LVAD.

2.4 | Dose estimation

In addition to the in vivo measurements taken during treatment, a series of phantom-based measurements were acquired to estimate the dose more accurately to the LVAD at depth. First, ion chamber measurements in Virtual Water® (Model number 457, Standard Imaging, Middleton, WI) were made to estimate the depth dose behind the LVAD block. An Exradin A12 ion chamber (Standard Imaging, Middleton, WI), with a radius of 0.61 was used for all measurements. The Virtual Water® used has been shown to alter the dose measurement by no more that 1.5% beyond the dose buildup region.[24] The ion chamber used was ADCL accredited with a maximum uncertainty of 1.5%.[25]

The overall size of the Solid Water® phantom was kept constant at $30 \times 30 cm^2$ and a 24 cm thickness. The thickness of the phantom was chosen to match the patient thickness, while the height and width were limited by the size of the Virtual Water® available. However, the size was deemed sufficiently large to account for scatter. The phantom was placed 15 cm from the beam spoiler, centered behind the LVAD block location. To acquire a depth dose curve, ion chamber measurements were taken at depths of 1, 2, 3, 4, 6, 9, 12, and 15 cm. The effective point of measurement for each of these points was shifted upstream by 0.6 multiplied by the chamber radius upstream, as recommended for cylindrical ion chamber dosimetry.[26,27] These measurements were first taken with the LVAD block placed on the beam spoiler identical to the treatment setup, and the process was repeated with no LVAD block in place. The ratios of these two measurements determined a depth-dependent transmission factor of the LVAD block. To estimate the transmission factor at the surface, an OSLD was placed on the surface of the phantom to measure the dose with and without the LVAD block present. The OSLDs have a reported uncertainty of 1.3%.[28]

The final dose estimate to the LVAD motor was based on CT imaging taken subsequently to the TBI treatment. This imaging was used to ascertain the depth of the LVAD motor from the AP and PA directions.

Neutron dose was estimated using a neutron dose survey meter (Model 12–4, Ludlum Measurements Inc, Sweetwater, Tx). These measurements were taken with the survey meter centered along the central axis at 515 SSD. To assess the neutron dose contribution from each component of the delivery setup, all measurements were made with all possible combinations of including or omitting the lead compensators, LVAD block, and acrylic beam spoiler.

3 | RESULTS

The imaging from the AP and PA simulation and treatment of the patient's chest can be seen in Figure 2. The treatment images include the LVAD blocks. Daily interrogation of the LVAD showed no transient effects during or immediately after radiation. A 15-month follow-up reported no ill adverse effects from his TBI conditioning regimen from a cardiac perspective. Periodic integration of the LVAD during the 15 months since treatment have detected no abnormalities, and all components have continued to operate as intended. In fact, the ejection fraction had recovered to 65%, and LVAD team is considering removal and disconnection of LVAD.

It appears the risk of damage or injury to the LVAD device, and heart radiation exposure were well reduced. As shown in Table 1, the in vivo OSLD measurements showed good agreement between the expected dose of 100 cGy and measured dose to the central axis. The AP and PA doses were 103.45 and 102.20 cGy, respectively. The OSLDs behind the LVAD block measured 66.49 and 73.61 cGy for the same treatment fields. This equates to an average surface dose of 70.05 cGy behind the block and a relative transmission factor of 68.1%.

Figure 3 shows the amount of radiation to the controller box and the percentage of the prescribed dose to the central axis, excluding imaging dose. In this region, the out-of-field dose dropped perfectly linearly ($R^2 = 1.000$), ranging from 33.83% (135.30 cGy) to 22.87% (91.46 cGy) at 2 cm and 14.5 cm, respectively. Extrapolating the results, the dose at the field edge is estimated to be 35.6% of the prescription (142.5 cGy). The dose decreased away from the field edge at 0.91% (3.65 cGy) per centimeter. Based on the location of the controller, average dose to the controller is estimated to be 27.5% (110 cGy) for the course of the entire treatment.

The result of the transmission factor measurements can be seen in Figure 4. The OSLD-based transmission factor at the surface is 67.9%. This agrees very well with the in vivo measurements taken. Below the surface, the relative transmission drops until leveling out around 30% at a depth around three centimeters. Starting at a depth of 8 cm, the dose ratio slowly increased, reaching 31% at a depth of 15 cm. The higher values in the region upstream of 3 cm can be attributed to a couple factors: in-scatter from the beam spoiler and secondary particles from the LVAD block. The slight increase at the distal edge of the measurements is likely a result of backscatter from the wall beyond the phantom setup and in-scatter from other surfaces in the treatment room. Beam hardening beyond the block may also have contributed to this increase.

The chest CT of the treated patient was used to localize the LVAD motor within the patient. Based on this imaging, the motor, including the housing, was estimated to have a width of 5.7 cm. From the AP direction, the motor had a depth ranging from 6.3 to 12.0 cm. From the PA direction, the depth was 7.1–12.8 cm. These values fall within the flat region of Figure 4, where the LVAD block transmission was measured around 30%. Based on the estimated total of 200 cGy delivered by each field, the final estimated dose to the LVAD motor is 120 cGy. However, this estimate has some caveats, as noted in the Section 4.

The neutron dose was not affected by the lead compensators, which were attached to an acrylic mount. All measurements with and without the acrylic mounted lead were identical. The results of the neutron measurements with and without the LVAD block and acrylic beam spoiler are shown in Table 2. The Cerrobend LVAD block had a minimal effect on the neutron dose; <1%. The acrylic beam spoiler reduced the neutron dose from 44.4 μrem/MU to 38.8 μrem/MU, a 12.5% decrease. This equates to a total of approximately 0.23 cGy per fraction and 0.46 cGy for the entire treatment due to neutron contamination.

4 | DISCUSSION

Based on the measurements acquired, much of the LVAD pump within the patient is estimated to have received a total of around 120 cGy with 0.23 cGy from Neutrons. However, a couple factors complicate this estimate. The high-Z titanium shell of the LVAD pump causes attenuation and backscatter. The amount of dose penetrating the titanium to the distal end of the pump itself is likely less than the estimated 30%. The dose deposition to the proximal region would have been slightly elevated. These elements would slightly offset, the extent of which is challenging to determine. It is worth noting that the dose estimates presented here are only applicable to this patient and subsequent cases may require their own investigations.

The neutron contamination resulting from each component in the TBI setup match well with expectations. The

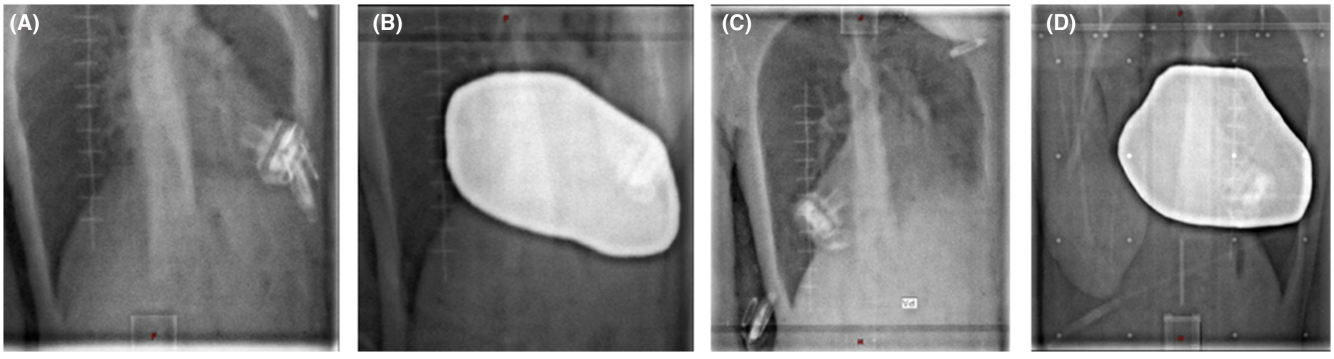

FIGURE 2 (A) AP simulation imaging, (B) AP treatment imaging, (C) PA simulation imaging, and (D) PA treatment. Treatment imaging includes the Cerrobend block to shield the LVAD and heart.

Treatment fields	Prescribed dose to CAX [cGy]	Measured dose to CAX [cGy]	Measured blocked dose [cGy]
AP	100	103.45	66.49
PA	100	102.20	73.61
Average	100	102.825	70.05

TABLE 1 In vivo OSLD dose measurements along the central axis (CAX) and directly behind the LVAD block (blocked). The OSLDs were placed directly on the patient.

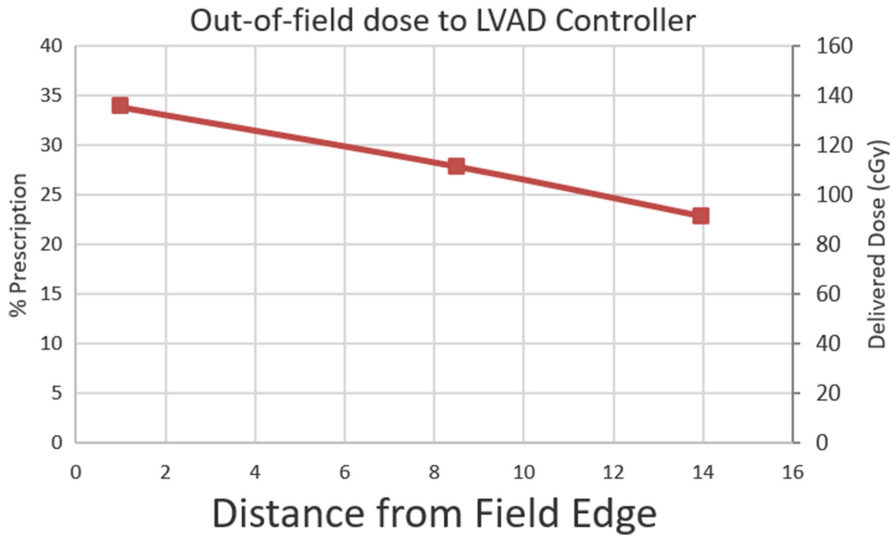

FIGURE 3 In Vivo dose measurements to the LVAD controller based on distance from the field edge. All measurements were taken with Landauer nanoDot OSLDs.

high-Z nature of lead causes it to have photoneutron interactions with high-energy photons (>10 MeV).[29] However, the relative thinness of the compensators plus the potential moderating effect of the acrylic mount on which they were mounted on would lead to little measurable difference in neutron dose. Cerrobend has previously been shown to have little minimal to no neutron effects, meaning the LVAD block should not have caused much change in the measurements.[30] Finally, acrylic beam spoiler has a high hydrogen component, explaining the 12.5% decrease in neutron dose when the beam spoiler was present.

Monte Carlo methods would be capable of generating improved photon and neutron dose estimates to the patient and LVAD, along with the controller. However, there are multiple challenges in doing so, most notably, the limitation of available Monte Carlo packages readily applicable to extended distance treatments such as TBI and a lack of 3D imaging of the specific patient in the treatment positions. Future work with Monte Carlo simulations for this context would be helpful.

Multiple case studies have reported on patients with LVADs receiving external beam radiation.[6–15] All these studies looked at directed radiation, with none involving a patient receiving TBI or LVAD controller dose. Directly comparing techniques and dose estimates is challenging. These studies looked at multiple generations of devices as new models are commonly being released.[22,26] In addition, many of the case reports only reported the prescription dose without any dose estimates to the LVAD. Of the ones reporting a dose, the dose calculation method is highly variable, with various external beam software, TLDs, and Mosfets were all used. Comparing doses between different algorithm types has well-known challenges and cross comparing between algorithms and various dosimeters is even more challenging.[31]

Data around other implanted cardiac devices, such as defibrillators and pacemakers, has shown a large degree of variability in dose sensitivity in these devices.[32] This is likely the case with LVADs, as well.

Most of the studies on LVAD radiation sensitivity have been limited to treatments using low-energy photons (>10 MV). Treatments produce neutrons above when photon energies exceed 10 MV, which is associated with malfunctions of contemporary implantable cardiac devices.[4] It is reasonable to assume a similar correlation with LVADs. Gossman et al found that LVADs ($n=2$) did not have any changes in pump operation during radiation with 18 MV doses of 64–75 Gy.[14] However, this study lacked any follow-up on the functionality of the LVADs irradiated despite long-term damage from radiation being a large concern with CIEDs. More studies are required to fully determine the effect of photon and neutron radiation to LVADs.

Overall, we can be optimistic for this patient's future, although the cardiovascular disease in stem cell transplant survivors remains a concern.[33]

There is a lack of consistency in TBI techniques across different institutions.[34,35] There is a wide variety

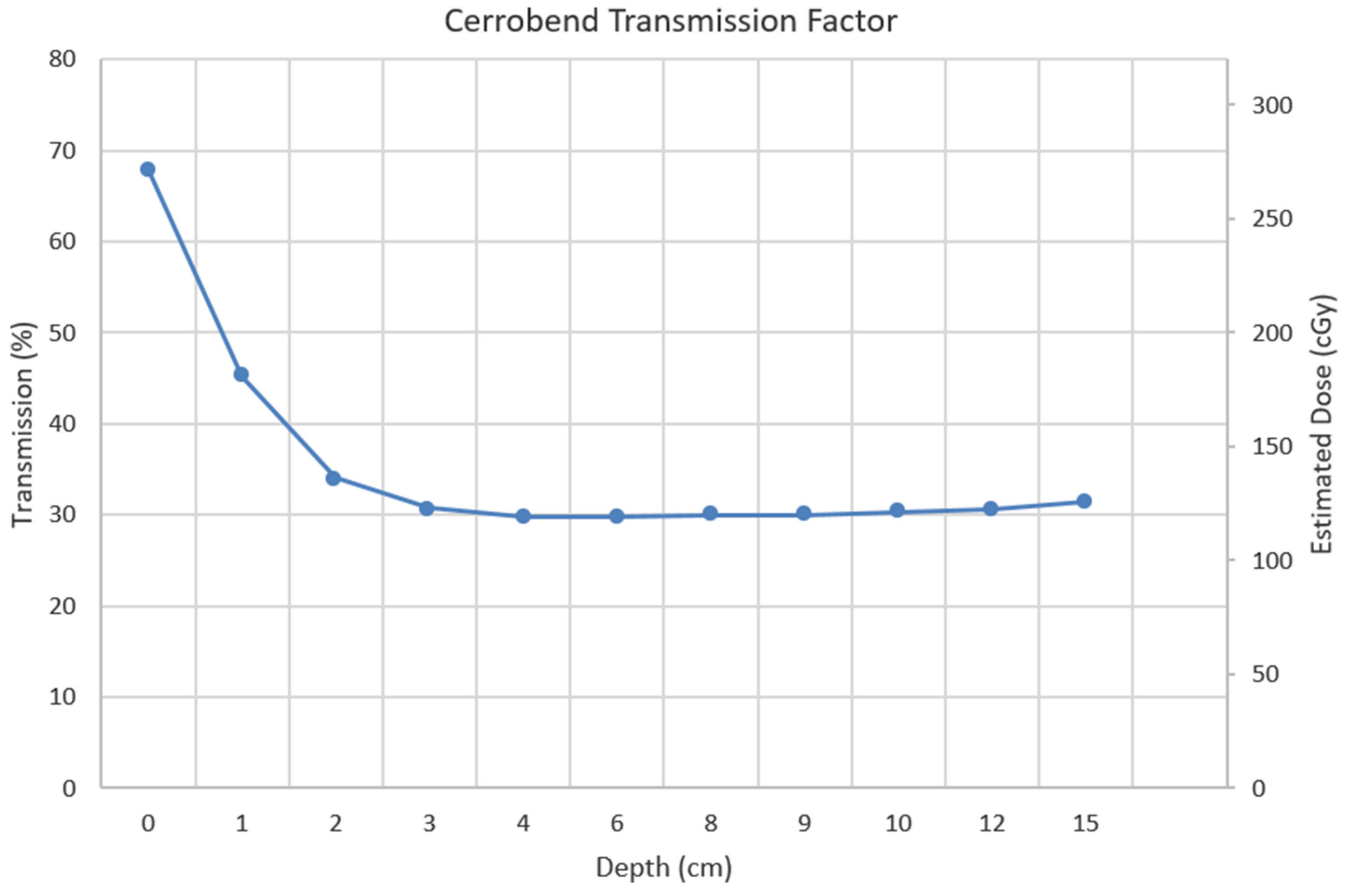

FIGURE 4 The relative dose and estimated dose behind the LVAD block. Surface dose was measured by OSLD and all other points from ion chamber measurements. Estimated dose is based on 400 cGy prescription to patient.

TABLE 2 Neutron dose measurements along the central axis using the TBI setup. All four combinations of including and excluding the LVAD black and acrylic beam spoiler present in the beam were measured.

Neutron dose (μrem/MU)	Without spoiler	With spoiler
Without LVAD block	44.4	38.6
With LVAD block	44.7	38.9

in treatment techniques, beam energy, patient positioning, and treatment distance, among other things. Other institutions attempting to treat a patient with an LVAD using TBI will encounter some differences in the details of the treatment, but the general concepts and approach reported in this case study will offer useful guidance and information that can be generalized to many different techniques. One technique, volumetric modulated arc therapy (VMAT), has been gaining wider use for TBI treatment. While VMAT TBI presents its own challenges, it allows for greater flexibility in tissue sparing and higher accuracy of the dose calculations. This technique would be better suited for the treatment of patients with LVADs, or any other implanted devices, which would benefit for reduced radiation. While our institution would have preferred to treat with this method, the modality was not clinically available at our institution at the time of treatment.

5 | CONCLUSION

This case documents the total body irradiation administered to a patient with a HeartMate 3 LVAD and concomitant cancer. Despite direct radiation to the patient's LVAD motor and scatter radiation to the controller, no inappropriate device function was found during device interrogations performed throughout treatment or within 15 months following treatment. The current literature on the effects of radiation on LVADs is limited. As an increasing number of cardiac device-dependent patients will need cancer treatment, it is imperative to understand the best treatment approaches that can be safely offered to this unique population. Further research to address the safety of radiation therapy in patients with LVADs devices is needed.

AUTHOR CONTRIBUTIONS

Matthew Webster: Conceptualization; data curation; formal analysis; investigation; methodology; project administration; supervision; validation; visualization; writing – original draft; writing – review and editing. **Olga M. Dona Lemus:** Conceptualization; methodology; writing – review and editing. **Dandan Zheng:** Conceptualization; investigation; methodology; supervision; writing – review and editing. **Joshua N. Wancura:** Conceptualization; data curation; investigation; visualization; writing – review and editing. **Sean Tanny:** Conceptualization; methodology; writing – review and editing. **Gukan Sakthivel:** Data curation; investigation; writing – original draft; writing – review and editing. **Louis Constine:** Conceptualization; investigation; resources; supervision; writing – review and editing.

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CONFLICT OF INTEREST STATEMENT

The authors report no conflict of interest.

DATA AVAILABILITY STATEMENT

Data can be obtained from the corresponding author upon request.

CONSENT

Written informed consent was obtained from the patient to publish this report in accordance with the journal's patient consent policy.

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