Technical Note

Impact of lung block shape on cardiac dose for total body irradiation

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ABSTRACT

Evaluating cardiac dose during total body irradiation (TBI) is of increasing interest. A three-dimensional beam model for TBI was commissioned and lung shielding was simulated in a treatment planning system with the cardiac silhouette partially blocked and unblocked. When blocked, the median heart dose decreased by 6% (IQR = 6%) and the median cardiac V12Gy decreased by 27% (IQR = 17%). The median left anterior descending artery dose decreased 20% (IQR = 12%) for blocked cases. Because using partial heart shielding may result in considerable changes in dose to cardiac structures, TBI protocols should explicitly consider lung block design parameters and their potential effects.

1. Introduction

Total body radiation (TBI) is an integral component of hematopoietic stem cell transplants (SCT), used increasingly around the world for treatment of acute myeloid leukemia, acute lymphocytic leukemia, myelodysplastic syndromes and other less common conditions [1]. The role of TBI includes immune suppression, eradication of disease, and ablating the bone marrow for donor stem cells.

While external beam radiation has evolved to high levels of technical complexity, the technical aspects of most TBI techniques remain relatively simplistic in many clinics [1]. TBI is typically delivered at an extended source-to-surface distance (SSD) with minimally modified wide-angle beams to produce an approximately uniform dose distribution. When lung toxicity was determined to be a limiting factor, shielding were introduced to limit the lung doses [2,3]. Treatment set-ups vary widely, with patients prone, standing or in lateral decubitus. Technical parameters are highly variable between institutions, including beam orientations, compensation, and shielding techniques. Software inconsistencies include use (or lack) of three-dimensional dose distribution calculations. Variable clinical parameters include lack of guidance regarding cardiac shielding techniques [4]. To fully optimize a patients treatment, one should consider these factors in aggregate.

While SCT with TBI can increase long-term survivorship of patients with leukemia or other conditions, this treatment can also result in multiple toxicities, including pneumonitis, infection, and graft-versus-host disease. The risk of treatment-related death following these procedures is estimated to range from 10 to 30% [5]. Among these toxicities, cardiovascular disease (CVD) is several-fold higher than expected in TBI patients [6,7]. With lower survival rates in the past, late cardiovascular events received relatively little attention; however, with increasing numbers of longer-term survivors, late cardiovascular toxicities may be of interest in the management of TBI treatments [8]. The cause of late CVD is still not fully understood, but even low doses of TBI lead to altered lipid and glucose metabolisms - conditions that could precipitate coronary heart disease [9,10]. It is understood that mean cardiac doses far below those of TBI can lead to late cardiac morbidity, highlighting the necessity to understand how TBI methodologies may impact late survivorship [11].

Previous investigators have explored the potential for three-dimensional TBI treatment planning and delivery [12–15]. However, cardiac shielding, with respect to TBI treatment planning, has received little attention to date, and variations in shielding design persist. A recent technical summary guideline did not address cardiac dose specifically, but illustrated lung blocking that would shield a large portion of the left ventricle [1]. In contrast, other current texts document the absence of cardiac shielding as a part of shielding design (Fig. 1a) [16,17] or even complete heart blocking [18]. These variations in approach can potentially lead to different doses and/or outcomes related to cardiac health and should be clarified to better inform potential patient outcomes. To bridge this gap, our goal of this work was to

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identify the impact of the inclusion of partial cardiac shielding on heart and lung dose using 3D treatment planning for TBI in order to inform whether more context is needed in TBI protocol descriptions.

2. Material and methods

To assess the 3-dimensional dose distribution in tissues of interest, an 18 MV beam was commissioned in RayStation (RaySearch Laboratories; Stockholm, Sweden) for the standing TBI setup at an extended SSD. This model was validated for accuracy with clinical tissue-phantom ratio measurements, off-axis ratio measurements, and treatment monitor units following our current clinical treatment protocol, which was based on 2D hand calculation [7]. For this arrangement, the patient was treated as if standing on a platform at an extended SSD of 475 cm from source to patient midline and treated with AP and PA beams. Additionally a 1.2 cm Lucite beam spoiler was placed 40 cm away from patient midline to ensure optimal surface dose.

Additional compensation is often required in TBI treatments in order to improve dose uniformity across the patient's full body. Structures serving as compensation (e.g. water-equivalent bolus) were generated alongside patient scans to simulate the patient-specific lead compensators used in current practice to produce a uniform thickness, and thus created the uniform dose in the patient. These compensator structures appropriately accounted for differences in patient thickness and electron scatter conditions.

Eleven patients representing a diverse range of lung and heart volumes were selected for this IRB-approved study. Lung volumes ranged from approximately 1900 cm^3 to 6000 cm^3 and heart volumes ranged
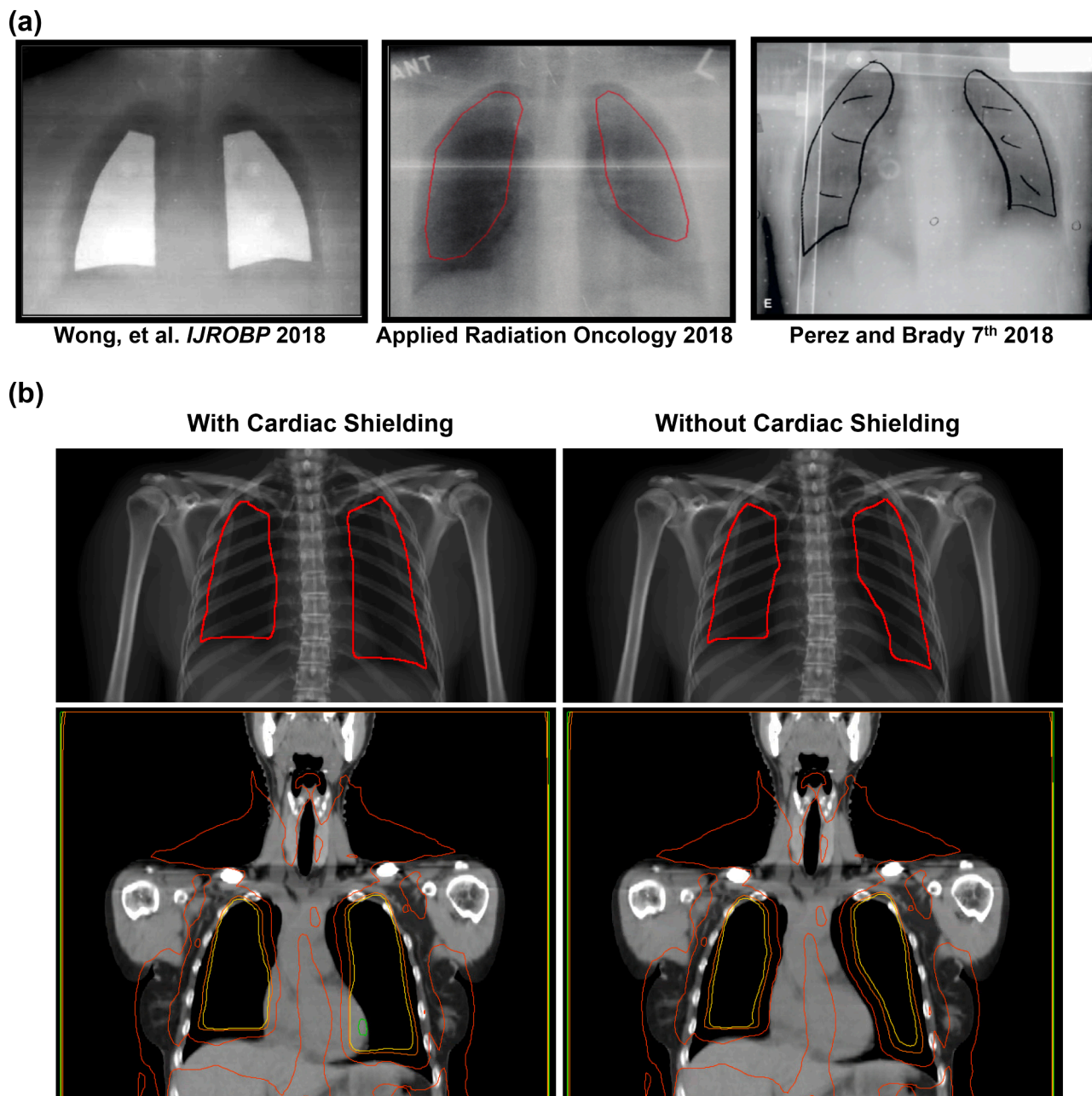
Fig. 1. Blocks with cardiac shielding (left) and without cardiac shielding (right): (a) Published examples of variable lung shielding strategies; (b) Lung block shapes and resultant dose distributions for a simulated TBI patient, utilizing cardiac shielding (left column) and 1 cm cardiac margin (right column). Red = 12 Gy, orange = 10 Gy, yellow = 9.5 Gy, green = 8.5 Gy. Published examples were reprinted with permission. (For interpretation of the references to colour in this figure legend, the reader is referred to the web version of this article.)

from 330 to 800 cm^3. Relative volumes between heart and lung volumes ranged from 10% to 35%. These eleven patients were scanned in the supine position and planned to receive a myeloablative TBI dose prescription of 2 Gy per fraction for 6 fractions, delivering 12 Gy total to the umbilicus, with 3 of the 6 fractions utilizing lung blocks. Patients were planned to be treated standing in AP/PA orientations. Two HVL lung blocks were automatically generated using contours of the lungs, heart, clavicle, spine, and diaphragm for margin definition. These margins were assigned to create uniform blocks: 1.0 cm margins for the inferior and lateral thoracic borders, 1.0 cm inferior to the clavicle, and 2.25 cm margin lateral to the vertebral bodies (Fig. 1b). Together, these factors typically resulted in shielding the left lateral aspect of the heart. For the unblocked cases, a uniform 1.0 cm margin around the heart was removed from the lung block shapes for the AP and PA fields.

To evaluate dose to the heart and left anterior descending artery (LAD), contours were generated following the cardiac atlas from Feng and colleagues [19]. To account for potential cardiac motion due to patient respiration, the LAD contour was expanded based on studies

from MR angiography [20,21]: 10 mm in the superior-inferior direction, 2 mm right-left, and 5 mm anterior-posterior. This expanded contour representing the realistic range of LAD motion, was then used for generating LAD dose statistics.

Dose changes were evaluated on the aggregate dose from the combined treatment utilizing lung blocking on half of the fractions. Evaluations considered changes in mean lung and heart dose, V12Gy for the heart, as well as mean LAD dose. These measures were determined to be of interest, for mean heart dose has been validated among breast and Hodgkin lymphoma survivors as a predictor for risk of RT-associated heart disease [22,23]. Mean LAD dose has likewise been previously correlated with clinical outcomes [24,25].

3. Results

Blocking the cardiac silhouette resulted in a median decrease of 6% (IQR = 6%) in average heart dose. In contrast, approximately one third of the heart volume was spared from receiving the full prescription dose
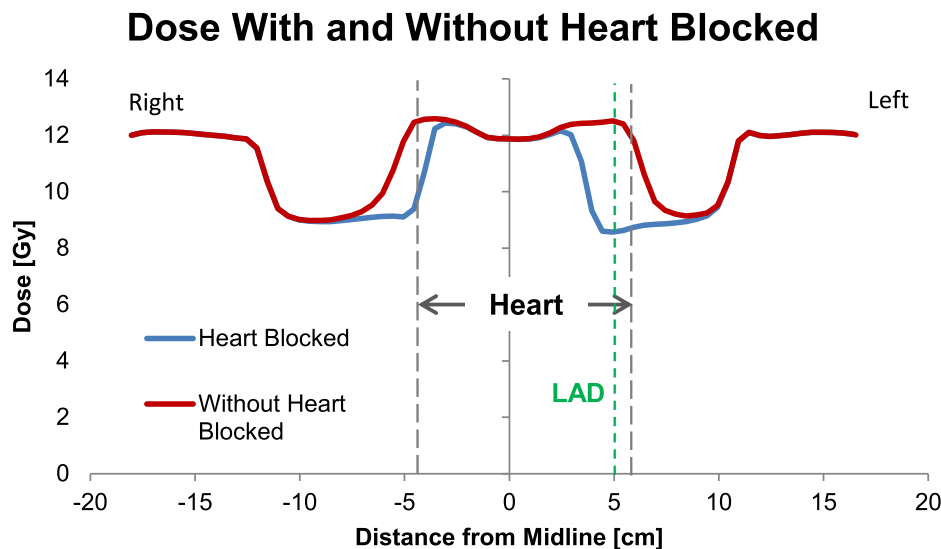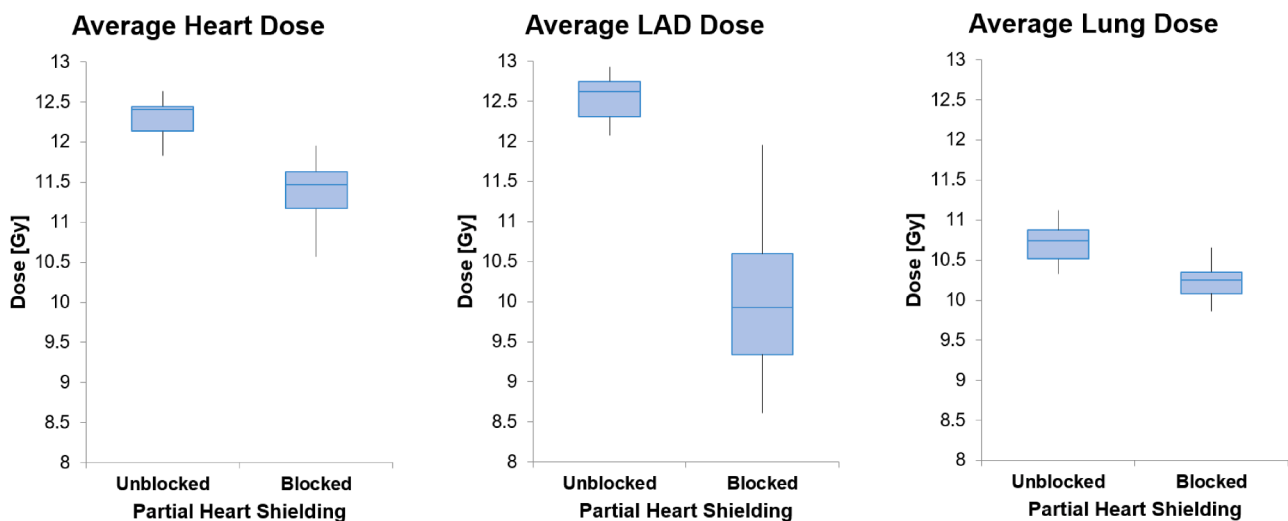

Fig. 2. Changes in dose as a result of cardiac blocking: (a) left–right dose profiles from one simulated TBI patient demonstrating the effect of lung block shape on cardiac dose; (b) change in mean heart (left), left anterior descending (LAD) artery (center), and lung (right) dose between blocked and unblocked cases.

(V12Gy), with median values decreasing from 83% (IQR = 28%) to 43% (IQR = 36%) for the patients in this study. In addition, the average left anterior descending coronary artery (LAD) dose was reduced by up to 31% (20% median reduction, IQR = 12%) by a lung block that covers the left side of the heart (Fig. 2). In contrast, changes in mean lung dose were more modest, with median values decreasing only 4% (IQR = 1%).

4. Discussion

In this work we have shown here that a simple difference in block-drawing technique results in appreciable cardiac doses changes, especially in the LAD vicinity. We demonstrated that the choice to include a partial heart shielding may appreciably reduce dose to the LAD by 20%, and decrease volume of heart receiving high doses by over one third. This was possible without drastically affecting the lung dose (here mean dose was decreased by only 4%).

While we were able to demonstrate a marked reduction in dose to the LAD, this is not the only risk factor for TBI. In fact, dose to the lungs, liver, and kidneys have been shown to be limiting factors in treatment and markedly affect patient outcomes following SCT with TBI [26–28], whereas cardiac dose is still in need of further investigation. Other investigators have reported preliminary studies regarding calculated dose changes in heart blocking strategies [18]. However, their work employed all-or-none heart-blocking. Blocking the entire heart may be unacceptable clinically, due to extensive shielding of central lymphatic tissue, thus we opted to test only partial heart shielding. Given that the heart and circulating cells are among the volume to treat for disease, the inclusion of a partial heart block may present a tradeoff of risk of relapse while potentially improving cardiac toxicities. However, to date this has not yet been explored.

Even relatively low average cardiac doses received from gastric radiation for peptic ulcer disease have been shown to increase the occurrence of late coronary vascular disease (CVD). Carr and colleagues showed a 50% increase in late CVD from inadvertent heart doses of 2–6 Gy – doses far lower than are used in standard myeloablative TBI regimens, using a fractionation scheme of 1.5 Gy for 6–14 daily fractions [29]. Similarly, mean cardiac doses of as little as 1.5 Gy from tangential breast radiation have been shown to result in an increased risk of late CVD [23]. Cardiac dose from a fractionated TBI treatment may fall within similar or higher doses and could potentially benefit from partial shielding.

There are a number of limitations when extrapolating the results shown here to clinical practice. Firstly, our calculations were performed on only eleven patients, which could have produced a selection bias or uncertainty in the results of this work. We opted to include patients with a range of lung and heart volumes to reduce this bias. Additionally, TBI treatments are typically delivered in the standing position, whereas our patient scans were supine. It is currently unfeasible to collect CT scans in the standing position, as scanners are still only in the developmental phase [30]. Positional differences between the supine and standing position could affect the expected doses. While this change among standing and supine positions cannot currently be quantified, works in MR-angiography demonstrated that heart and LAD positional differences due to respiratory motion are primarily dominated by motion in the superior-inferior direction [19,20]. With limited right-left motion, the left aspect of the heart may remain behind the lung block depending on margins used in block delineation, but this would require further investigation. In clinical implementation, additional limitations in accurate cardiac dose can result from the uncertainties in block positioning, although this may also be mitigated by assessments using kV imaging.

Next, contouring the LAD is subject to some inaccuracy given the difficulty of visualization using CT. In contouring the LAD, we followed the previously validated methodology of Feng, et al., which is widely accepted and limits the uncertainty associated with the identification of the LAD [19]. To account for additional positional uncertainties, we incorporated an additional margin on the LAD to encompass the realistic extent of heart motion from respiration. Additionally, we also chose to evaluate the mean LAD and heart dose as opposed to other potential endpoints, because mean dose has been most consistently used by previous investigators to correlate clinical outcomes with cardiac and LAD dose [18,29,31]. In particular, doses to the LAD may be of clinical significance in SCT long-term survivors, as dose to the LAD has been associated with risk of late cardiac morbidities [31]. Conversely, it is possible that partial heart shielding could increase the relapse rate with TBI-based regimens, an issue for which there is no published information yet.

We have shown in this work that the widely divergent methods of blocking (or not blocking) the heart can lead to modest variations in average lung and cardiac dose and greater changes in LAD dose. Because variations in TBI protocols exist, considering an explicit description of lung block design (i.e., the inclusion or exclusion of cardiac shielding) is a necessary step to better understanding potential cardiac toxicities from TBI regimens.

Informed Consent and Patient Details

The authors affirm that the referenced human-subjects research project involving retrospective review of anonymized patient data has been approved by the University of Washington Institutional Review Board (IRB).

Declaration of Competing Interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

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