NIH Public Access
Author Manuscript
Int J Radiat Oncol Biol Phys. Author manuscript; available in PMC 2012 March 15.

Published in final edited form as:
Int J Radiat Oncol Biol Phys. 2011 March 15; 79(4): 1248–1255. doi:10.1016/j.ijrobp.2010.05.036.

Renal Shielding and Dosimetry for Patients with Severe Systemic Sclerosis Receiving Immunoablation with Total Body Irradiation on the SCOT (Scleroderma: Cyclophosphamide or Transplantation) Trial

Oana I. Cracinescu, Ph.D.[1], **Beverly A. Steffey, M.S.**[1], **Chris R. Kelsey, M.D.**[1], **Nicole A. Larrier, M.D.**[1], **Cathy J. Paarz-Largay, PA-C, M.S.**[2], **Robert G. Prosnitz, M.D.**[3], **Nelson Chao, M.D., MBA**[2], **John Chute, M.D.**[2], **Cristina Gasparetto, M.D.**[2], **Mitchell Horwitz, M.D.**[2], **Gwynn Long, M.D.**[2], **David Rizzieri, M.D.**[2], and **Keith M. Sullivan, M.D.**[2]

[1]Department of Radiation Oncology, Duke University Medical Center, Durham, NC, USA

[2]Division of Cellular Therapy, Duke University Medical Center, Durham, NC, USA

[3]Department of Radiation Oncology, University of Pennsylvania, Philadelphia, PA, USA

Abstract

Purpose—To describe renal shielding techniques and dosimetry in delivering total body irradiation (TBI) to patients with severe systemic sclerosis (SSc) enrolled on a hematopoietic stem cell transplant protocol.

Methods and Materials—The SCOT protocol employs a lymphoablative preparative regime including 800cGy TBI delivered in two 200 cGy fractions twice a day before CD34+ selected autologous hematopoietic stem cell transplantation. Lung and kidney dose is limited to 200 cGy to protect organs damaged by SSc. Kidney block proximity to the spinal cord was investigated and guidelines were developed for acceptable lumbar area TBI dosing. Information on kidney size and the organ shifts from supine to standing positions were recorded using diagnostic ultrasound (US). Minimum distance between the kidney blocks (dkB) and the lumbar spine region dose were recorded and *in vivo* dosimetry was performed at several locations to determine doses of irradiation delivered.

Results—Eleven patients were treated at our center with an AP/PA TBI technique. A 10–20% dose inhomogeneity in the lumbar spine region was achieved with a minimum kidney block separation of 4–5 cm. The average lumbar spine dose was 179.6 ± 18.1 cGy, with an average dkB of 5.0 ± 1.0 cm. Kidney block shield design was accomplished using a combination of US and non-contrast CT (computerized tomography) or CT imaging alone. The renal US revealed a wide range of kidney displacement from upright to supine positions. Overall, the average *in vivo* dose for the kidney prescription point was 193.4 ± 5.1 cGy.

© 2010 Elsevier Inc. All rights reserved

Corresponding author: Oana Craciunescu, PhD, Box 3295 Duke University Medical Center, Durham, NC, 27710, oana.craciunescu@duke.edu, Tel: (919) 660-2192, Fax: (919) 681-7183.

Publisher's Disclaimer: This is a PDF file of an unedited manuscript that has been accepted for publication. As a service to our customers we are providing this early version of the manuscript. The manuscript will undergo copyediting, typesetting, and review of the resulting proof before it is published in its final citable form. Please note that during the production process errors may be discovered which could affect the content, and all legal disclaimers that apply to the journal pertain.

Conflict of interest: All authors report no conflict of interest.

NIH-PA Author Manuscript
NIH-PA Author Manuscript
NIH-PA Author Manuscript

NIH-PA Author Manuscript

NIH-PA Author Manuscript

NIH-PA Author Manuscript

Conclusions—The dose to the kidneys can be attenuated while maintaining a 10–20% dose inhomogeneity in the lumbar spine area. The kidneys were localized more accurately using both US and CT imaging. With this technique, renal function has been preserved and the study continues to enroll.

Keywords

total body irradiation; renal shielding; hematopoietic stem cell transplant; autoimmune disease; scleroderma; systemic sclerosis

INTRODUCTION

Scleroderma with internal organ involvement, also known as systemic sclerosis (SSc), is an autoimmune disease with considerable morbidity and mortality. Five year survival with conventional care is less than 50% (1,2). Disease modifying agents, successful in controlling symptoms in other autoimmune diseases are not effective in severe SSc(3).

Based upon seminal animal experiments, lymphoablative conditioning with total body irradiation followed by allogeneic or autologous hematopoietic stem cell transplantation (HCT) was shown to prevent progression or reverse organ damage from inherited (genetic) or acquired (antigen-induced) autoimmune diseases (4,5). Resetting of immunity and restoration of immune regulation and tolerance have been demonstrated and clinical trials with sufficient follow-up have shown long-term efficacy and safety (3,6,7).

It has been reported that high-dose, involved-field irradiation given during cancer treatment can accelerate dermal scleroderma (8). However, this is not the case with immune resetting following immunoablative conditioning and HCT. Clinical trials from both Europe and the USA demonstrate a significant reduction in dermal fibrosis after lymphoablation and autologous HCT (7,9). In a pilot study of treatment of patients with severe SSc with internal organ involvement, transplant conditioning with 800 cGy TBI, 120 mg/kg cyclophosphamide (CY) and 90 mg/kg equine antithymocyte globulin (ATGAM) followed by infusion of lymphocyte-depleted (CD34+selected) autologous peripheral blood stem cells demonstrated dramatic improvement/resolution of dermal sclerosis and stabilization/ improvement of scleroderma pulmonary dysfunction. (7,10) While the lymphoablative TBI conditioning was well tolerated by most subjects, treatment-related interstitial pneumonias were observed among the initial 8 patients treated without lung shielding. No interstitial pneumonias were observed in the next 26 patients after TBI was delivered with shielding to 200 cGy lung transmission (7).

Like the lung, the kidney is a radiosensitive organ often damaged by SSc (11). The TBI threshold dose associated with radiation nephrotoxicity in patients with neoplastic disease is approximately 1200 cGy. (12–14) The contribution of high-dose chemotherapy, TBI dose and dose rate on renal toxicity has been reported revealing a dose response for renal damage after TBI. (15) While 800 cGy TBI is substantially lower than levels associated with radiation nephropathy reported in the literature, the involvement of the renal vasculature with SSc may make the kidneys more susceptible to radiotoxicity. (16)

Our institution is a member of a multi-center, randomized study comparing immunoablation with 800 cGy TBI, 120 mg/kg CY, 90 mg/kg ATGAM and CD34+ selected autologous HCT versus immunosuppression with 12 monthly intravenous cycles of 750 mg/m2 CY for the treatment of severe SSc. This randomized study is known as the Scleroderma: Cyclophosphamide or Transplantation (SCOT) trial which enrolls individuals with poor prognosis SSc with internal organ involvement (www.sclerodermatrial.org). This includes

NIH-PA Author Manuscript

NIH-PA Author Manuscript

NIH-PA Author Manuscript

subjects with diffuse cutaneous SSc and scleroderma lung disease (forced vital capacity, FVC, or diffusion capacity, DLCO, between 45% and 70% predicted normal) or a history of scleroderma renal crisis. In the HCT arm of the SCOT trial, TBI is delivered using photons produced by linear accelerators in four 200 cGy fractions given twice daily for 2 days, at a dose rate of 7–15 cGy/minute with a minimum of 5 hours between fractions. Skin dose (determined at a depth of 2–3 mm) must be at least 90% of the prescribed dose. Both lungs and kidneys are shielded during TBI to 200 cGy transmission.

Shielding of the kidneys has the potential to reduce the TBI dose to the adjacent lumbar spine and para-aortic lymph nodes. In this manuscript, we describe the methodology developed to shield the kidneys in SSc patients and the dosimetric results obtained using these methods. A series of questions had to be addressed in the design of the kidney blocks: 1) how can the kidneys be localized without IV contrast administration, as contrast is contraindicated in this group of patients with impaired baseline kidney function?; 2) how close can the blocks be placed while still allowing for adequate dose to the bone marrow in the lumbar spine?; 3) how much is the lumbar spine under-dosed if the block separation is below this threshold; and 4) how does the size, shape, and location of the kidneys change when patients are transferred from a supine to a standing position? In this manuscript, we address these questions and report on the initial dosimetic results achieved in patients on the transplant arm of the SCOT protocol treated at Duke University Medical Center.

METHODS AND MATERIALS

Patients

Individuals were enrolled at Duke University Medical Center after giving informed consent for screening and study treatment. Consents were approved by the Institutional Review Board at the center. The first 11 patients transplanted on the SCOT trial at Duke are reported with data analyzed as of 8/31/09.

TBI Technique

To deliver the prescribed doses of irradiation (800 cGy) and allow for precise shielding of lungs and kidneys (to 200 cGy), patients were treated with an AP/PA technique using a 6MV beam and a ½ inch beam spoiler. Brass compensators were assembled to allow for homogeneous doses of ± 10% in the head, neck, supraclavicular area and lower leg. Subjects were positioned on an in-house fabricated TBI stand modified to allow both lung and kidney block placement (Figure 1a). The monitor units necessary to deliver the prescribed dose were determined based on a mid-plane calculation for parallel opposed fields that we have verified thoroughly during the TBI commissioning process on an anthropomorphic phantom (17).

Lung blocks were drawn using anterior and posterior films obtained with a conventional simulator, with the patients in a standing position to replicate the torso position during treatment. The thickness of the lung blocks was determined on an individual patient basis. Blocks were delineated following the guidelines outlined in the protocol: the lateral edges 1.0–1.5 cm from the inner border of the ribs, the inferior edges 1.0–1.5 cm from the dome of the apex of the diaphragm, 1.0–1.5 cm below the clavicles and the medial border, and 2.0–2.5 cm from the lateral edges of the thoracic vertebral bodies, with contouring to incorporate the hilar regions in the field. Accurate placement of the lung blocks was verified with port films. To aid in the verification, three landmarks were tattooed on the patients' anterior and posterior skin surface midline through the body: the first point was 50 cm inferior from the top of the head, near the xiphoid process (BB1), the second was 15 cm superior from BB1, near the sternal notch (BB2), and the third was 15 cm inferior to BB1, near the umbilicus

NIH-PA Author Manuscript

NIH-PA Author Manuscript

NIH-PA Author Manuscript

(BB3). Radio-opaque wire was placed over these points for simulation, CT imaging and treatment (Figure 1b).

Design of the kidney blocks was based on computerized tomography (CT)-simulation (for block shape) and on ultrasound (US) imaging (for block position). Due to the proximity of the kidneys to the vertebral bodies, and the thickness of the kidney blocks required to allow partial transmission of just 25% of the prescribed dose, the region between the kidney blocks (approximately L1–L3 in most patients) could be underdosed. Film dosimetry was performed to establish the level of under-dosage as a function of the distance between the kidney blocks. Film dosimetry using Kodak EDR2 film (Eastman Kodak Company, Rochester, NY) was performed on an anthropomorphic phantom positioned on the TBI stand in treatment position, and variable distances between the kidney blocks (dkb) were used: between 3 cm (corresponding to kidney blocks overlapping the cord), 5 cm (typical width of the vertebral body + 1 cm), and 8 cm (to show that the kidney block separation plays a role in the under-dosage).

To define adequate margins for the kidney blocks that would account for kidney displacement with respiration and with change upon supine to standing positions, two techniques were considered for kidney block definition: 1) combined US and non-contrast CT, and 2) non-contrast CT alone. When blocks were created from CT data alone, the published literature was consulted for kidney displacement due to respiration and positional change and this information was incorporated in the kidney block margins. (18)

The shape of the kidneys, hence the overall block shape and size, was determined from CT images. Imaging by US was used to localize the kidneys with the patient in the various treatment positions. A supine CT scan was acquired and kidneys were contoured on axial CT slices. Beam's eye views of the kidney projected on skin were then generated. The contours and the BB locations were transferred to a transparency template. Kidneys were then imaged by US performed with the patient first prone, then standing. The superior and inferior extent of each kidney was marked on the patient's posterior skin surface in each position. The length of the kidneys from the prone US was recorded and compared to the kidney length obtained by the CT image. By positioning the transparency template on the patient posterior skin surface and aligning the localization BBs, changes from CT to US locations were recorded. In the treatment planning system (Eclipse, Varian Medical Corp., Palo Alto, CA), kidney blocks were defined per protocol recommendations and adjusted using the US-generated shifts. The inferior portion of the block was trimmed to avoid shielding the superior iliac crest. In all cases, even if trimming of the blocks were necessary, the kidneys remained fully shielded.

Prescription and Reference Points

The prescription point was defined as the location along the longitudinal axis of the patient at midline, at the level of the umbilicus. The doses at prescription point and selected anatomical points were measured using OneDose® dosimeters (Sicel, Morrisvile, NC). Other selected anatomical points were defined as follows:

- *Head*: This reference point was defined along the longitudinal axis of the skull at the level of the supraorbital ridge.
- *Neck:* This reference point was defined along the subject's longitudinal axis at approximately mid-neck (C3/C4 vertebral levels).
- *Shoulder*: This reference point was defined as just inferior to the lateral 1/3 of the clavicle. This point was in the plane midway between the anterior and posterior subject surfaces.

NIH-PA Author Manuscript

NIH-PA Author Manuscript

NIH-PA Author Manuscript

- *Mid-mediastinum*: This reference point was defined along the subject's longitudinal axis midway between the sternoclavicular joints and the xiphisternal junction.
- *Lumbar Spine*: This reference point was defined along the subject's longitudinal axis, midway between the kidney blocks where the blocks were separated by the smallest distance. This reading helped quantify any under dosage in the lumbar spine area due to the distance between the kidney blocks (dkB). The expected dose was allowed to be 10–20% lower than prescription for a distance between the kidney blocks of at least 4–5 cm (see Results Section).
- *Hip:* This reference point was defined along the subject's longitudinal axis in the center of the pelvis at a level that is 1 cm superior to the pubic symphysis.
- *Knee:* This reference point was defined along the midline in the midplane of the knee at the level of the middle of the patella.
- *Ankle*: This reference point was defined along the midline at the midplane of the ankle at the level of the lateral malleolus.
- *Right Lung:* This reference point was defined in the center of the right lung block.
- *Right Kidney:* This reference point was defined in the center of the right kidney block.

RESULTS

Kidney Block Separation

Phantom-based film dosimetry revealed that an under-dosage of as much as 25% is possible if the distance between the kidney blocks were less then 4 cm. This under-dosage did not exceed 10–20 % if the distance between the kidney blocks at the treatment plane was 4–5 cm or greater. Based on the above results, two methods of localizing the kidneys and design of the kidney blocks were developed:

1) CT-based Kidney Localization—If US imaging is not available, custom lead or cerrobend blocking is designed to the shape of the kidney as imaged on the supine CT. Blocking exceeds its perimeter radially by asymmetric margins to account for the inferior displacement of the kidney when the patient moves from a supine to a seated position, (19) and for respiratory movement of the kidneys. (18) The blocking was 0.5 cm superior to the kidney, 1.5cm laterally, 0 cm medially, and 4 cm inferiorly. A medial margin of 0 cm was used for the reasons given above.

2) Combined US-guided and CT-based Kidney Localization—Block design and placement can be achieved using a combination of CT and US. Blocks are drawn which shield the kidneys with a 1.5–3.0 cm margin in the superior, inferior, and lateral directions. Identical blocks are used for both the anterior and posterior fields. In order to reduce the problem of underdosing the portion of the target volume (lumbar spine marrow and paraaortic lymph nodes) which lies between the kidneys, blocks had no medial margin (ie, the medial edge of the block should coincide with the medial edge of the kidney). Block margins of 1.5–3.0 cm were required to account for setup error and for the movement of the kidneys with respiration

The eleven SCOT transplant patients treated at Duke all had combined US and CT localization. The procedure for determining the kidney shifts from US is depicted in Figure 2: a) AP DRR with kidney contours; b) Marks on posterior skin surface that reflect the kidney shifts, as measured by US, from supine position (blue marks) to standing position

NIH-PA Author Manuscript

NIH-PA Author Manuscript

NIH-PA Author Manuscript

(red marks). Please note that the blue and red marks on the skin don't reflect a lateral displacement; c) AP DRR with kidney blocks drawn per current protocol guidelines when US is available. In this case, 1.5 cm superior, inferior and lateral margin, no medial margin; and d) AP DRR with kidney blocks shifted per US findings. The values for the CT- vs. US-measured lengths of the left kidneys are shown in Table 1.

Kidney displacements per US from supine to standing position with the CT kidney position as a reference are shown in Figure 3 for: a) left kidney and b) right kidney. The solid lines in Figure 3 represent the CT-based inferior and superior aspect of an average kidney, with an average length of 11 cm (see Table 1). Variability is noticed in kidney travel for the 11 patients. Kidneys compressed, shifted inferiorly, and even shifted superiorly (see right kidney, patient Pt5). For 3 of the 11 patients (Pt1, Pt4, Pt11), the kidney blocks were not shifted. For another three subjects, either the right (Pt3), or the left (Pt7, Pt10) kidney blocks had to be shifted, and for the remaining five patients (Pt2, Pt5, Pt6, Pt8, Pt9), both kidney blocks had to be shifted. The shifts ranged from 1 to 4 cm inferiorly. In addition, there was one superior shift of 3.5 cm on the right kidney block of patient Pt5.

Figure 4 depicts CT-based kidney contours showing use of standardized kidney blocks. The red dotted contours represent an envelope of the 11 kidney contours for right and left kidneys, respectively. The blue dotted contours represent hypothetical kidney blocks defined per current protocol, when US-aided CT block delineations were employed.

Prescription and Reference Points

Figure 5 presents dose averages for eleven patients measured at selected anatomic points. The error bars represent the standard deviation: umbilicus 193 ± 5.0 cGy, head 185.7 ± 4.2, mid-mediastinum 196.6 ± 10.6 cGy, hip 206 ± 11.8 cGy. The average lumbar spine dose was 179.6 ± 18.1 cGy, with an average dkB of 5.0 ± 1.0. Figure 6 shows the dose to the lumbar spine area binned as a function of the distance between the kidney blocks (dkB). With dkB > 4 cm, a 10–20 % inhomogeneity in the lumbar spine area is achievable, as the average lumbar spine dose for 10 of 11 patients with dkB > 4 cm was 184 ± 9.9 cGy. For the one patient with a dbK of 3.5 cm, the lumbar spine dose was 133 cGy, a 33.5% underdosage. Figure 6 also plots the average dose recorded under the lung and kidney blocks. For lungs, the average recorded single fraction (of four doses) was 54.7 ± 7.7 cGy, and for kidney was 50.8 ± 7.1 cGy. The average total renal dose measured for the prescription point was 193.4 ± 5.1 cGy.

DISCUSSION

While there are some comprehensive reports that address the optimum kidney dose or shielding for TBI. (12,20–22), they primarily address shielding the kidney to doses of 10–12 Gy. This study describes the technique, challenges and dosimetry of renal shielding during TBI for patients treated for SSc which requires stringent dosimetry control levels (2Gy) imposed by the SCOT clinical trial. The shielding technique employed included establishing margins for the kidney blocks and establishing methods to visualize and quantify the kidney travel due to change in position from respiration and from supine to standing/sitting positions. It also determined the potential for underdosage in the lumbar area due to small anatomic distance in some individuals between the kidney blocks.

The initial draft of this protocol recommended: “Kidney blocks will be designed to be larger than the contour of the renal parenchyma so as to account for differences in kidney position attributable to the patient positioning at the time of imaging (supine) versus the time of treatment (upright). Custom lead or cerrobend blocking will be designed to the shape of the kidney, but will exceed its perimeter radially by 3 cm in the superior, medial, and lateral

NIH-PA Author Manuscript

NIH-PA Author Manuscript

NIH-PA Author Manuscript

dimensions, and 5 cm in the inferior dimension (to account for inferior displacement with the upright position." If kidney blocks had always been designed per these recommendations, a potentially large area of the lumbar spine and para-aortic lymph nodes would have been blocked.

Phantom-based film dosimetry showed that an under-dosage as much as 25% can occur if the distance between kidney blocks is < 4 cm. This under-dosage is not expected to exceed 10–20 % if the distance between the kidney blocks at the treatment plane is 4–5 cm or greater. In the rare patient in whom the medial aspect of the kidneys overlaps the lumbar spine, we concluded that shielding of the kidneys should take precedence over delivering the full radiation dose midway in the lumbar spine area. To check the underdosage, the protocol requires an *in vivo* dosimetry reading in the lumbar spine area, at the level of least kidney block separation. Measurements on eleven patients in this report confirmed the results of the phantom study. For 10 of 11 patients for whom the distance between the kidney blocks (dkB) was greater then 4 cm, the lumbar spine dose was 184 ± 9.8 cGy (i.e, within 8% from prescription). However, an underdosage of 33.5 % was measured for one individual with a small distance between the kidney blocks (3.5 cm). This was a case for which medical shielding of the kidney took precedence over delivering the prescribed dose.

We found that good dose uniformity was achieved for the eleven subjects. The dose uniformity, as measured by the dose to the reference points described in the *in vivo* dosimetry section, was kept in the range of ± 10% of the prescription dose. For some patients, the dosimetry under the lung blocks was challenging. Depending on the anatomy (small lateral separation in the upper torso area), the lung blocks drawn per protocol were relatively narrow and scatter from the large fields typical for TBI procedures contributed more dose to the measurement point under these blocks. In the event that the measured dose under the lung block is greater than 20% of the prescribed dose due to lung block size and scatter conditions, the blocks should be redrawn to shield more lung. In this group of patients, no lung blocks modifications were performed on any of the eleven patients treated to date.

Because the CT scan was performed with the patient supine and individuals received TBI in a seated or standing position, an additional imaging procedure was helpful to determine the displacement of the kidneys which occurs with positional change. Typically such a task can be accomplished with intravenous contrast, but not without potential nephrotoxicity (19,23). Valuable information was gained by performing renal US with the intent to quantify the amount of kidney travel. As shown in Figure 3, high variability was noticed in kidney travel. Kidneys compressed, traveled inferiorly, and even shifted superiorly when going from prone to the standing position. For patient Pt5, both the CT and the US were performed twice at a few days interval to confirm the superior shift of 3.5 cm of the right kidney from supine to standing. With no US, the superior aspect of the kidneys would not have been shielded appropriately. For eight of the eleven patients we shifted the kidney blocks defined by CT to match the position of the kidney. For accurate renal shielding, US imaging is recommended to determine the position of the kidneys in treatment positions.

Although US seems a reasonable alternative to IV contrast in this group of patients for kidney localization, the precision, accuracy and repeatability of renal ultrasound imaging is limited and very dependent on inter- and intra- observer variation. The development of our US kidney localization protocol included pilot testing of our procedures in several volunteer patients (non-SCOT patients who had undergone treatment planning abdominal CT scanning in our department) and in several healthy volunteers (employees in our department). Through pilot testing we discovered that 1) it is imperative to use the SAME highly trained US technologist to be able to reproduce the measurements and to limit the inter-technician

NIH-PA Author Manuscript

NIH-PA Author Manuscript

NIH-PA Author Manuscript

variability in recording the length of the kidneys; and 2) A member of the TBI team should be present during the US exam to assure reproducibility of patient positioning and of the procedure in general. Even with these efforts, there were still some discrepancies between CT and US due in part to the medical condition of these SSc patients. At the time of the US the patients had just had a port placed and it was very uncomfortable for them to assume the prone position required to perform the US. Another factor was their skin condition secondary to their disease that limited their ability to assume the position requested by the US technologist.

The benefit of kidney shielding in the SCOT trial became apparent with a recent analysis of renal dysfunction in patients with SSc participating in several HCT studies. (16) This review included 34 subjects enrolled on the pilot study of autologous transplantation (7), 55 patients randomized to date nation-wide on the SCOT trial (28 HCT and 27 monthly CY) (3), and 2 other patients who underwent allogeneic transplantation. (24) Of these 91 patients with severe SSc, 11 (12%) developed significant renal dysfunction. With renal shielding, only 2 transplant recipients on the SCOT trial developed transient renal abnormalities and both survive with normal renal function.

CONCLUSIONS

Optimal renal shielding is accomplished using a combination of CT and US imaging allowing for more precise kidney localization for patients with severe SSc receiving TBI. Using US allows one to determine shifts which occur when patients change position from supine to upright. We found that kidney travel varies widely among individuals. With adequate kidney localization and margins, kidney blocks can be properly fabricated and positioned to deliver the intended doses of lymphoablative TBI. Although patients in the SCOT trial received 800 cGy of TBI with a maximal kidney exposure of 200 cGy, the methods we describe herein should be applicable to patients receiving TBI for a broad range of diseases, doses, and needs for shielding the renal parenchyma.

Acknowledgments

This work was supported in part by award AI-005419 from the National Institute of Allergy and Infectious Diseases, NIH.

REFERENCES

1. Altman RD, Medsger TA Jr. Bloch DA, et al. Predictors of survival in systemic sclerosis (scleroderma). Arthritis Rheum 1991;34:403–413. [PubMed: 1901491]
2. Bulpitt KJ, Clements PJ, Lachenbruch PA, et al. Early undifferentiated connective tissue disease: III. Outcome and prognostic indicators in early scleroderma (systemic sclerosis). Ann Intern Med 1993;118:602–609. [PubMed: 8452326]
3. Sullivan KM, Muraro P, Tyndall A. Hematopoietic cell transplantation for autoimmune disease: Updates from Europe and the United States. Biol Blood Marrow Transplant. in press.
4. Ikehara S, Good RA, Nakamura T, et al. Rationale for bone marrow transplantation in the treatment of autoimmune diseases. Proc Natl Acad Sci U S A 1985;82:2483–2487. [PubMed: 3887403]
5. van Bekkum DW, Bohre EP, Houben PF, et al. Regression of adjuvant-induced arthritis in rats following bone marrow transplantation. Proc Natl Acad Sci U S A 1989;86:10090–10094. [PubMed: 2690067]
6. Muraro PA, Douek DC, Packer A, et al. Thymic output generates a new and diverse TCR repertoire after autologous stem cell transplantation in multiple sclerosis patients. J Exp Med 2005;201:805–816. [PubMed: 15738052]

NIH-PA Author Manuscript

NIH-PA Author Manuscript

NIH-PA Author Manuscript

7. Nash RA, McSweeney PA, Crofford LJ, et al. High-dose immunosuppressive therapy and autologous hematopoietic cell transplantation for severe systemic sclerosis: long-term follow-up of the US multicenter pilot study. Blood 2007;110:1388–1396. [PubMed: 17452515]
8. Abu-Shakra M, Lee P. Exaggerated fibrosis in patients with systemic sclerosis (scleroderma) following radiation therapy. J Rheumatol 1993;20:1601–1603. [PubMed: 8164225]
9. Farge D, Marolleau JP, Zohar S, et al. Autologous bone marrow transplantation in the treatment of refractory systemic sclerosis: early results from a French multicentre phase I–II study. Br J Haematol 2002;119:726–739. [PubMed: 12437652]
10. McSweeney PA, Nash RA, Sullivan KM, et al. High-dose immunosuppressive therapy for severe systemic sclerosis: initial outcomes. Blood 2002;100:1602–1610. [PubMed: 12176878]
11. Steen VD, Syzd A, Johnson JP, et al. Kidney disease other than renal crisis in patients with diffuse scleroderma. J Rheumatol 2005;32:649–655. [PubMed: 15801020]
12. Lawton CA, Cohen EP, Murray KJ, et al. Long-term results of selective renal shielding in patients undergoing total body irradiation in preparation for bone marrow transplantation. Bone Marrow Transplant 1997;20:1069–1074. [PubMed: 9466280]
13. Cohen EP, Robbins ME. Radiation nephropathy. Semin Nephrol 2003;23:486–499. [PubMed: 13680538]
14. Miralbell R, Sancho G, Bieri S, et al. Renal insufficiency in patients with hematologic malignancies undergoing total body irradiation and bone marrow transplantation: a prospective assessment. Int J Radiat Oncol Biol Phys 2004;58:809–816. [PubMed: 14967438]
15. Cheng JC, Schultheiss TE, Wong JY. Impact of drug therapy, radiation dose, and dose rate on renal toxicity following bone marrow transplantation. Int J Radiat Oncol Biol Phys 2008;71:1436–1443. [PubMed: 18355974]
16. Hosing C N, R.; McSwenney, P.; Mineishi, S.; Siebold, J.; Griffith, L.; Shulman, H.; Goldmuntz, E.; Mayes, M.; Parikh, C.; Crofford, L.; Furst, D.; Steen, V.; Sullivan, K. Acute Kidney Injury In Patients With Systemic Sclerosis Participating In Hempatopoietic Cell Transplantation Trials In The United States: Cases Series And Review Of The Literature. 2010. Submitted
17. Craciunescu, O.; Steffey, B.; Whiddon, C.; Halperin, E. Rethinking Total Body Irradiation (TBI) at Duke University Medical Center (DUMC). In: Physics, M., editor. 2004 AAPM Annual Meeting; Pittsburgh, PA: Medical Physics; 2004. p. 1916
18. Ahmad NR, Huq MS, Corn BW. Respiration-induced motion of the kidneys in whole abdominal radiotherapy: implications for treatment planning and late toxicity. Radiother Oncol 1997;42:87–90. [PubMed: 9132831]
19. Reiff JE, Werner-Wasik M, Valicenti RK, et al. Changes in the size and location of kidneys from the supine to standing positions and the implications for block placement during total body irradiation. Int J Radiat Oncol Biol Phys 1999;45:447–449. [PubMed: 10487569]
20. Malicki J, Skrobala A, Kosicka G, et al. The efficacy and reliability of lung protection during total body irradiation of patients with disseminated malignancies. Neoplasma 2005;52:325–329. [PubMed: 16059650]
21. Greig JR, Miller RW, Okunieff P. An approach to dose measurement for total body irradiation. Int J Radiat Oncol Biol Phys 1996;36:463–468. [PubMed: 8892472]
22. Lawton CA, Barber-Derus SW, Murray KJ, et al. Influence of renal shielding on the incidence of late renal dysfunction associated with T-lymphocyte deplete bone marrow transplantation in adult patients. Int J Radiat Oncol Biol Phys 1992;23:681–686. [PubMed: 1612975]
23. Rao QA, Newhouse JH. Risk of nephropathy after intravenous administration of contrast material: a critical literature analysis. Radiology 2006;239:392–397. [PubMed: 16543592]
24. Nash RA, McSweeney PA, Nelson JL, et al. Allogeneic marrow transplantation in patients with severe systemic sclerosis: resolution of dermal fibrosis. Arthritis Rheum 2006;54:1982–1986. [PubMed: 16732546]

NIH-PA Author Manuscript

NIH-PA Author Manuscript

NIH-PA Author Manuscript

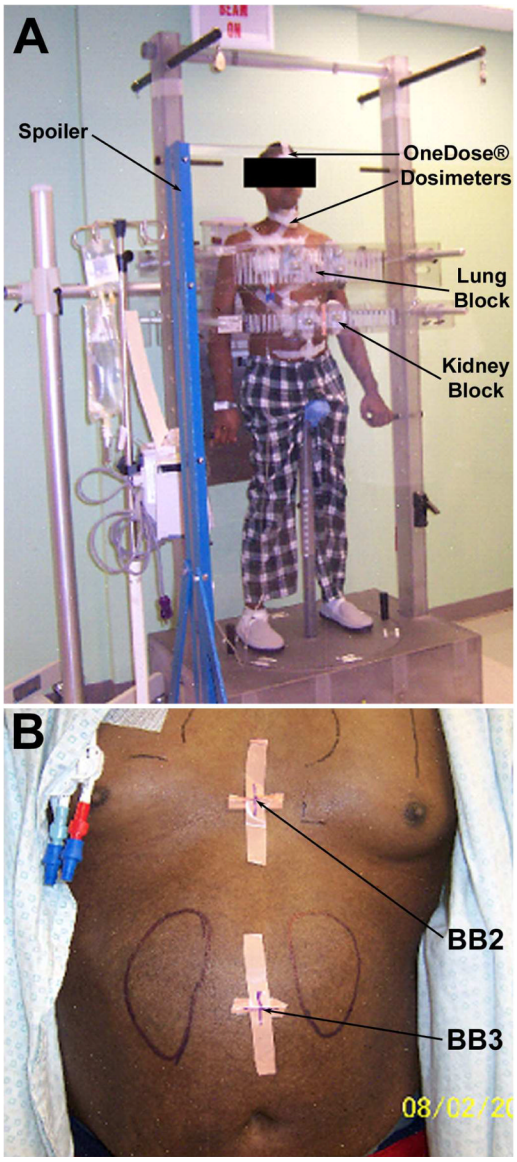

Figure 1.

a) Patient in treatment position on the TBI stand with lung and kidney blocks in place. Spoiler is also visible, as well as the positioning of the in vivo dosimeters; b) Detail of patient's torso and abdomen with skin marks for the lung and kidney block placement and the location of the anterior surface positioning BBs.

NIH-PA Author Manuscript

NIH-PA Author Manuscript

NIH-PA Author Manuscript

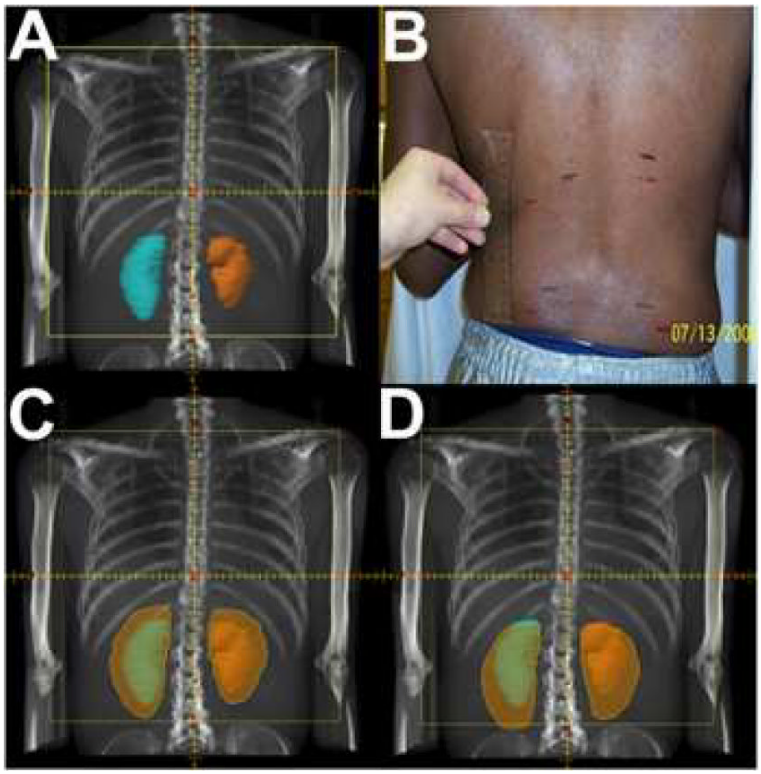

Figure 2.

a) AP DRR with kidney contours; b) Marks on posterior skin surface that reflect the kidney shifts, as measured by US, from supine position (blue marks) to standing position (red marks); c) AP DRR with kidney blocks drawn per current protocol guidelines when ultrasound (US) is available. In this case, 1.5 cm superior, inferior and lateral margin, no medial margin; d) AP DRR with kidney blocks shifted per US findings.

NIH-PA Author Manuscript

NIH-PA Author Manuscript

NIH-PA Author Manuscript

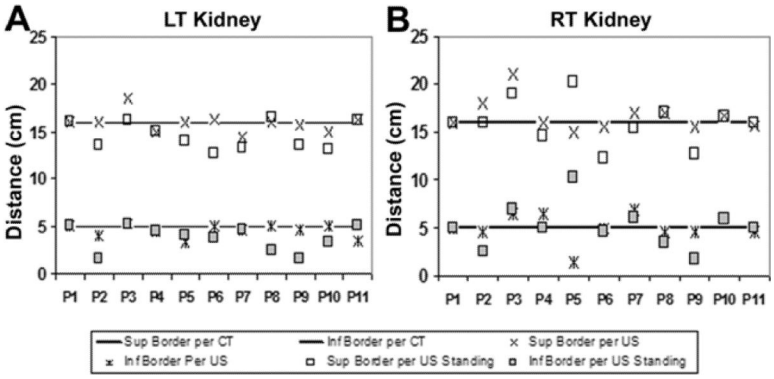

Figure 3.

Kidney displacement from supine to standing position assuming the computerized tomography (CT) kidney position as reference for the a) left (LT) kidney and b) right (RT) kidney. High variability is noticed in the kidney travel for the 11 patients treated so far. Kidneys compressed, shifted inferiorly, and even shifted superiorly (see RT kidney, patient Pt5).

NIH-PA Author Manuscript

NIH-PA Author Manuscript

NIH-PA Author Manuscript

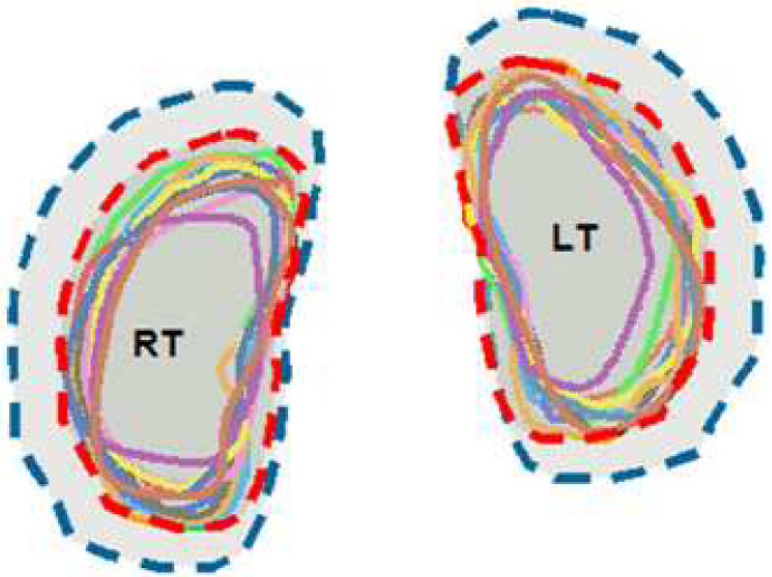

Figure 4.
Computerized tomography (CT)-based kidney contours showing the possibility to use standardized kidney blocks. The red dotted contours represent an envelope of all the kidney contours for right (RT) and left (LT) kidneys, respectively. The blue dotted contours represent hypothetical kidney blocks defined per current protocol.

NIH-PA Author Manuscript

NIH-PA Author Manuscript

NIH-PA Author Manuscript

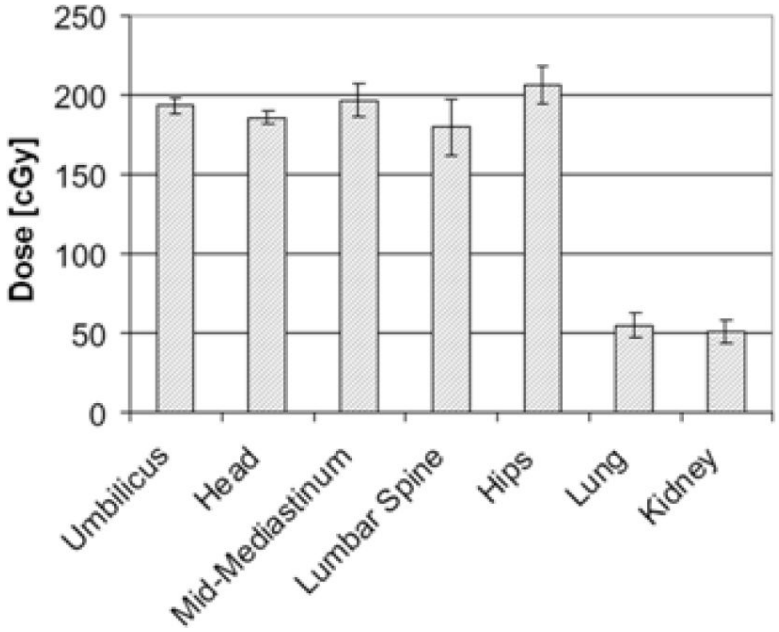

Figure 5.
Single dose average for 11 patients measured at selected anatomical points. The error bars represent the standard deviation.

NIH-PA Author Manuscript

NIH-PA Author Manuscript

NIH-PA Author Manuscript

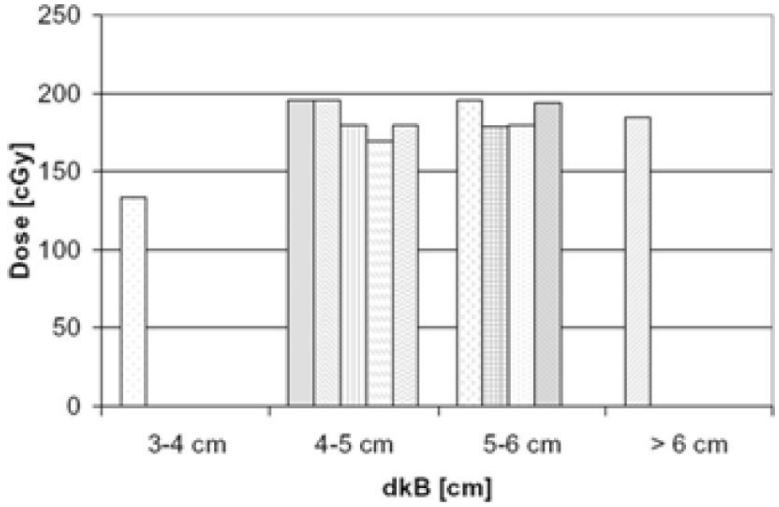

Figure 6.

Total dose to the lumbar spine area for 11 subjects binned as a function of the distance between the kidney blocks (dkB). With dkB > 4 cm, a 10–20 % inhomogeneity in the lumbar spine area is achievable.

NIH-PA Author Manuscript NIH-PA Author Manuscript NIH-PA Author Manuscript

Table 1

Length of the left (LT) kidney as measured by supine computerized tomography (CT) and prone ultrasound (US) imaging

Patient	P1	P2	P3	P4	P5	P6	P7	P8	P9	P10	P11	Average	STDEV
Lt_CT [cm]	11.5	12.4	11.4	10.4	12.9	11.1	10	9.4	9.9	9.4	12.5	10.99	1.26
Lt_US [cm]	10.9	12.5	11	12.3	11.5	11.4	10.3	9.97	9.4	9.4	12.1	10.98	1.11
% Difference	−5.2	0.8	−3.5	18.3	−10.9	2.7	3.0	6.1	−5.1	0.0	−3.2	0.27	7.61
Diff [cm]	0.6	−0.1	0.4	−1.9	1.4	−0.3	−0.3	−0.57	0.5	0	0.4	0.01	0.84