

Bone Strength Assessment Based on CT Images Using a Network Spring Model for Radiation Therapy Patients

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INTRODUCTION

In radiation therapy, especially using intensity modulated radiation therapy (IMRT), a high dose of ionizing radiation is delivered to the patient and, therefore, the bone health is a major concern for young patients. What is more, many tumors, like soft tissue sarcomas, are located in close proximity to bone. High energy radiation unavoidably exerts negative impacts not only on bone physiological properties, but also on its mechanical and structural properties. As a result, bone fracture risk for these patients is increased significantly. Thus, it is necessary to develop a quantitative noninvasive screening technique to identify these high risk patients.

BACKGROUND

Recently, IMRT has been increasingly used as an adjuvant treatment in conjunction with surgical resection for soft tissue sarcoma. Clinical studies have shown that wide excision followed by irradiation has resulted in excellent local control. Because most tumors extend to bones, particularly long bones, it is, therefore, necessary to perform excision of periosteum to obtain a clear margin. However, periosteal stripping destroys the nutrient vessels to bone and, thus, compromises the vasculature of the outer cortex. In addition, although IMRT is superior to conventional radiation techniques

in critical organ sparing, for certain tumor sites such as soft tissue sarcoma, it still delivers a significantly high dose to bones. This affects bones negatively in many aspects. Hematopoietic cells of bone marrow are extremely sensitive to radiation. Clinical data have indicated that radiation dose at the level of ~ 1 Gy can produce bone marrow suppression. Lethal or sublethal damage to stem cells caused by radiation therapy prevents them from developing into differentiated myeloid and lymphocytic cells. Furthermore, osteoblasts and mesenchymal stem cells are also radiosensitive. Irradiation can reduce metabolic bone formative activity. It has been reported that as low as 8 Gy can inhibit the formation of heterotopic ossification.

The most common type of radiation treatment related to bone fracture is a stress fracture. The fracture risk rate may be as high as 24% in sarcoma patients who have undergone periosteal stripping and received chemotherapy. Thus, it is clinically relevant and significant to have a viable screening tool to identify those patients with high risk for IMRT treatment induced fracture. Since most sarcoma patients receive a follow-up CT scan upon completion of IMRT treatments to assess the treatment response, it would be very meaningful and cost-effective to develop a technique to assess bone fracture risk based on CT scans. Currently, bone densitometry is the most widely accepted method to detect bone fragility and to assess bone fracture risk. The established technique for measuring bone mineral

density (BMD) is dual-energy X-ray absorptiometry (DXA). However, studies have shown that BMD is not the only determinant for bone fracture and other factors also contribute to bone fracture risk in other ways. *In vitro* experiments have revealed that bone strength depends not only on bone mass, but also on several mechanical and structural properties of bone, such as Young's modulus, bone microstructure, and geometric characteristics. These factors are not directly linked to BMD and, therefore, are not accounted for by dual-energy X-ray absorptiometry. In this article, we present a mathematical model for quantitatively assessing bone strength. The model, termed the spring-network model, takes these mechanical and structural factors into account and could provide a potential screening tool for predicting IMRT treatment related bone fracture risk.

METHODOLOGY

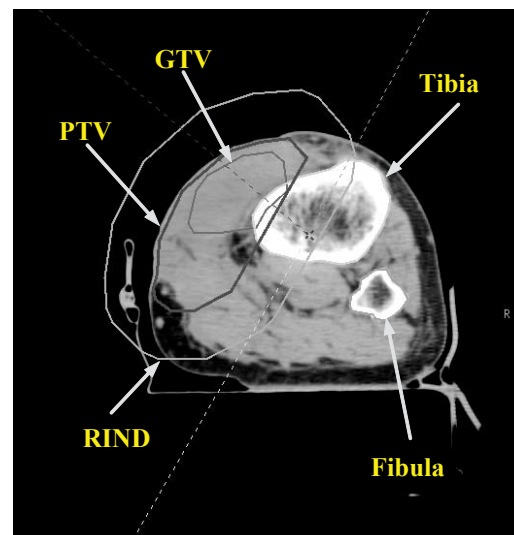
IMRT

Since 2000, IMRT has emerged as the most important radiation therapy modality for soft tissue sarcoma treatment. Like conventional techniques, IMRT also employs the use of ionizing radiation to control and destroy malignant cells. The process of IMRT treatment planning consists of patient simulation, CT scan, target volume delineation, plan optimization, multileaf collimator (MLC) leaf sequence generation, and final dose calculation (Song, 2004; Xing, Wu, Yang, Boyer, 2004). The patient is first simulated on a simulator to determine the iso-center position and the possible treatment beam angles. In theory, the iso-center should be placed at the geometric center of the target. The goals are to fully use the central portion of the beam that poses most desirable beam properties and to minimize the probability of violating the MLC hardware constraints. Once the simulation is completed, the patient is CT scanned in the same position as in the simulation in a customized thermoplastic mold to minimize patient movement during the imaging process. At our cancer center, CT images of 2.5 mm slice thickness are acquired over the entire treatment region for treatment planning purpose. The planning target volume (PTV) is delineated on the CT images by the radiation oncologist. The PTV is created by adding a certain amount of margin around the gross tumor volume (GTV) to account for microscopic extension of the disease and

treatment setup uncertainty. To achieve a better target dose coverage, a new structure named PTV_X is created by extending PTV superiorly and inferiorly one slice. In addition, a tuning structure, RIND, is also generated by expanding PTV_X by 2 cm axially to fine tune the dose distribution and to remove radiation hot spots from normal tissues. The treatment planner delineates the involved bones because they are the organ at risk in this setting and need to be spared.

Based on our clinical experience, a four or five-beam plan is necessary to create a concave dose distribution around the long bones. In selecting beam angles, all the beams enter the target from one side of the leg to spare a longitudinal strip of soft tissue. In addition, efforts are made to ensure that no beams enter or exit through the uninvolved leg. Furthermore, all beams should not pass through or be close to genital organs for patients with a tumor in the upper thigh and pelvic region. The collimator of each beam should be rotated to conform to the contour of the PTV for the best beam shaping. Figure 1 shows the volume definitions for a representative soft tissue sarcoma IMRT plan. The IMRT plan is computed using an in-house treatment planning system. Given a set of dose constraints, each IMRT plan is optimized based on a quadratic objective function. Once optimal beam intensity profiles or maps are obtained, MLC leaf sequences are generated using the

Figure 1. Structure definitions used in IMRT inverse treatment planning optimization. In this particular case, the tumor was in the right leg



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