Application of CT-based Structural Rigidity Analysis to Fracture Risk Assessment for Patients with Skeletal Metastasis

I. Entezari, V; Nazarian, A; Snyder, BD; Hipp, JA; Calderon, N; Damron, TA; Terek, RM; Cheng, EY; Aboulafia, AJ; Anderson, ME; Gebhardt, MC

+ Beth Israel Deaconess Medical Center, Harvard Medical School, Boston, MA
+ Baylor College of Medicine, Houston, TX
+ Upstate Medical University, Syracuse, NY
+ Rhode Island Hospital, Providence, RI
+ University of Minnesota Medical Center, Minneapolis, MN
+ Sinai Hospital, Baltimore, MD

Brian.Snyder@childrens.harvard.edu

INTRODUCTION

The skeleton is the third most common site of metastatic cancer and a third to half of all cancers metastasize to bone. While much has been learned about the mechanisms of skeletal metastasis, little headway has been made to establish guidelines to estimate fracture risk associated with skeletal metastasis. Clinicians make subjective assessments regarding fracture risk based on clinical and radiographic guidelines now recognized to be inaccurate. The prevention of fractures due to skeletal metastases depends on objective criteria for evaluating changes in bone structure that reflect the interaction of the tumor with the host bone. The risk that a bone will fracture through a metastasis depends on the reduction in the load capacity of the bone induced by the cancer and the loads applied to the bone. The load capacity of the bone depends on its structural properties, which are determined by the geometry, location and biological activity of the tumor and the geometry and material properties of the host bone. Therefore, any image based method that assesses fracture risk must be able to measure changes in the properties of both the bone tissue and bone geometry. The geometry at any cross-section through the bone is quantified by its cross-sectional area (A), moment of inertia (I) and polar moment of inertia (J). Rigidity, the product of the bone tissue modulus and bone cross-sectional geometry is the structural property that portrays the mechanical behavior of the bone and its resistance to deformation when subjected to axial forces, bending and/or twisting moments. In particular, it is the weakest cross-section through a bone that dictates the load bearing capacity of the entire bone.

The CT-based Structural Rigidity Analysis (CTRA) is developed and validated in a series of ex-vivo and in-vivo experiments to monitor the fracture risk associated with osteolytic lesions by measuring the minimal cross-sectional rigidity of affected bones. A multi-center, prospective, in-vivo study sponsored by Musculoskeletal Tumor Society is being conducted to compare CT-based, structural rigidity analysis (CTRA) to current clinical and radiographic methods for predicting pathologic fractures. The aim of this study was to evaluate whether medical and/or surgical interventions for individual patients based on standard clinical and radiographic fracture risk assessments was changed by introducing CTRA results to physicians.

METHODS

Institutional Review Board approvals were obtained from all participating institutions: Upstate Medical University, Rhode Island Hospital, University of Minnesota Medical Center, Sinai Hospital and Beth Israel Deaconess Center. Planar radiographs and transaxial CT scans of the involved bones were obtained on all patients. A hydroxyapatite phantom was imaged with each bone to convert the X-ray attenuation for each pixel to an equivalent bone density. The load capacity of the bone is determined by the modulus of elasticity E and shear modulus G, for each pixel was calculated from the equivalent bone density using empirically derived constitutive relationships for cancellous and cortical bone. Axial rigidity (EA) provides a measure of the bone’s resistance to uniaxial loads; bending rigidity (EI) provides a measure of the bone’s resistance to bending moments; torsional rigidity (GJ) provides a measure of the bone’s resistance to torsional moments. For each trans-axial image, EA, EI and GJ were calculated by summing the modulus-weighted area of each pixel within the bone contour by the position of the pixel relative to the centroid of the bone cross-section. The cross-section through the affected bone that has the largest reduction in rigidity is the weakest and assumed to govern failure of the entire bone.

Treatment plans based initially on clinical guidelines and then again after CTRA were compared to identify cases where the treatment plan was changed as a result of CTRA.

RESULTS

69 patients (male/female=0.86, Age =60.3 ± 14.4) with metastasis to appendicular skeleton were enrolled into the study. Lung, breast, multiple myeloma, kidney and prostate were major sources of metastasis. There were total of 81 lesions of the femur (n=72), humerus (n=7), acetabulum (n=1) and clavicle (n=1) which 62% were lytic, 28% were mixed (23) and the rest was blastic in nature. The median total Mirel's score for the lesions was 9 (range:7-12). Considering the full range of treatments options, CTRA would have changed the initial treatment plan in 26% (n=21) of the times. Based on the Mirel's criteria alone (Score e 9), 68% of lesions (n=55) were at high risk for fracture. According to physicians' initial judgment, 44% of these lesions (n=36) needed surgical fixation, while CTRA alone recommended surgery in 40% (n=33) of lesions.

DISCUSSION

For bones with metastatic cancer, we hypothesize that the cross-section through the bone with the minimum rigidity predicts its fracture risk better than current clinical and radiographic guidelines, and that this metric provides a guideline for selecting surgical versus medical treatment and for monitoring a patient’s response to treatment. The goal of this study was to identify when the CT-based rigidity analysis would be the most useful clinically. The results suggest that more than 25% of the clinical treatment recommendations would potentially be altered by use of CTRA. Treatment plans were similar in cases where there was either marked bony destruction or minimal bone involvement. However in 6 of 16 cases the treating physician did not change the treatment plan in spite of the CTRA based recommendation. We expect physician’s to become more confident in CTRA as they gain experience with the technology during the course of this prospective, multi-center study.

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