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Peripheral Quantitative CT (pQCT) Using a Dedicated Extremity Cone-Beam CT Scanner

A. A. Muhit^a, S. Arora^a, M. Ogawa^a, Y. Ding^a, W. Zbijewski^a, J. W. Stayman^a, G. Thawait^b, N. Packard^c, R. Senn^c, D. Yang^c, J. Yorkston^c, C.O. Bingham III^e, K. Means^d, J. A. Carrino^b, and J. H. Siewerdsen^{a,b}

^aDepartment of Biomedical Engineering, Johns Hopkins University, Baltimore MD

^bRussell H. Morgan Department of Radiology, Johns Hopkins University, Baltimore MD

^cCarestream Health Inc., Rochester NY

^dCurtis National Hand Center, Union Memorial Hospital, Baltimore MD

^eDivisions of Rheumatology, Allergy and Clinical Immunology, Department of Medicine, Johns Hopkins University, Baltimore MD

Abstract

Purpose—We describe the initial assessment of the peripheral quantitative CT (pQCT) imaging capabilities of a cone-beam CT (CBCT) scanner dedicated to musculoskeletal extremity imaging. The aim is to accurately measure and quantify bone and joint morphology using information automatically acquired with each CBCT scan, thereby reducing the need for a separate pQCT exam.

Methods—A prototype CBCT scanner providing isotropic, sub-millimeter spatial resolution and soft-tissue contrast resolution comparable or superior to standard multi-detector CT (MDCT) has been developed for extremity imaging, including the capability for weight-bearing exams and multi-mode (radiography, fluoroscopy, and volumetric) imaging. Assessment of pQCT performance included measurement of bone mineral density (BMD), morphometric parameters of subchondral bone architecture, and joint space analysis. Measurements employed phantoms, cadavers, and patients from an ongoing pilot study imaged with the CBCT prototype (at various acquisition, calibration, and reconstruction techniques) in comparison to MDCT (using pQCT protocols for analysis of BMD) and micro-CT (for analysis of subchondral morphometry).

Results—The CBCT extremity scanner yielded BMD measurement within ± 2 –3% error in both phantom studies and cadaver extremity specimens. Subchondral bone architecture (bone volume fraction, trabecular thickness, degree of anisotropy, and structure model index) exhibited good correlation with gold standard micro-CT (error $\sim 5\%$), surpassing the conventional limitations of spatial resolution in clinical MDCT scanners. Joint space analysis demonstrated the potential for sensitive 3D joint space mapping beyond that of qualitative radiographic scores in application to non-weight-bearing versus weight-bearing lower extremities and assessment of phalangeal joint space integrity in the upper extremities.

Conclusion—The CBCT extremity scanner demonstrated promising initial results in accurate pQCT analysis from images acquired with each CBCT scan. Future studies will include improved

x-ray scatter correction and image reconstruction techniques to further improve accuracy and to correlate pQCT metrics with known pathology.

Keywords

peripheral quantitative computed tomography (pQCT); cone-beam CT (CBCT); osteoporosis; osteoarthritis; rheumatoid arthritis; bone mineral density; bone morphometry; joint morphology; joint space analysis

1. INTRODUCTION

Diagnosis and treatment of a spectrum of musculoskeletal diseases stand to benefit from high-quality, accurate imaging and morphological assessment as provided by peripheral quantitative CT (pQCT). For example, osteoporosis presents a growing health burden involving reduction in bone density leading to fragility fractures. Similarly, and particularly in an aging and obese population, osteoarthritis (OA) is an increasingly common degenerative joint disease caused by biomechanical stressors and an attendant dysregulated response characterized by cartilage loss, with concomitant new bone growth, subchondral bony cysts, and other morphologic changes. Rheumatoid arthritis (RA) and other forms of inflammatory arthritis are autoimmune diseases characterized by hypertrophic synovium, cartilage loss, bone erosion, and tendon damage. Such pathologies across a spectrum of bone and joint disorders exhibit signatures in intra-articular morphology, bone density, and bone morphometry [1, 2], and the ability to more accurately assess these structures quantitatively could provide a means of earlier detection and improved assessment of treatment response.

Bone mineral density (BMD) is commonly measured for characterization of osteoporosis using dual-energy x-ray absorptiometry (DEXA) or quantitative CT (QCT). Other image-based measures present additional, potentially more sensitive assessments of pathology, including bone volume fraction (BV/TV), trabecular thickness (Tb.Th), structure model index (SMI), degree of anisotropy (DA), and high-resolution characterization of the joint space morphology. Such metrics have been conventionally challenged because of the limited spatial resolution of clinical (whole-body) CT scanners and have therefore been less frequently utilized. However, these potential biomarkers offer important insight into different bone and joint-related disorders, disease progression and response. Our group has recently developed a cone-beam CT (CBCT) system specifically for musculoskeletal imaging (Fig. 1) [3] which provides superior spatial resolution in comparison to MDCT, opening the possibility for pQCT on such dedicated systems. Compared to extremity micro-CT (for example, XTremeTM CT, ScanCo, Switzerland) such CBCT scanners provide a large field of view (~22 cm) and spatial resolution and soft-tissue contrast resolution comparable or superior to MDCT. The system also allows imaging of weight-bearing lower extremities as well as multi-mode planar (radiography), kinematic (fluoroscopy), and 3D volumetric (CBCT) imaging on the same platform.

The prototype is currently undergoing technical and clinical assessment in pilot studies in patients with OA and RA. Initial technical assessment [3] of the CBCT scanner demonstrated sub-mm (~0.5 mm) isotropic spatial resolution, providing superior visualization of trabecular and cortical bone details compared to MDCT at low dose (~10

mGy; ~0.1 mSv to the distal extremities). Initial patient studies suggest that soft-tissue contrast resolution is satisfactory for visualization of ligaments, tendons, and cartilage at a level comparable to state-of-the-art MDCT, though soft-tissue contrast resolution remains an area of ongoing improvement in artifact correction techniques and novel image reconstruction methods. The compact design of the system allows a $22 \times 22 \times 22$ cm³ field of view (FOV) for scanning the hand, wrist, elbow, knee, foot, and ankle. The objective of this paper is to investigate the ability to derive pQCT analysis directly from CBCT images acquired with each scan, potentially eliminating the need for a separate DEXA or pQCT examination. Such quantitative imaging capability could offer an advance to diagnosis, staging, and treatment response assessment in osteoporosis, osteoarthritis, rheumatoid arthritis, and trauma.

2. ASSESSMENT OF BONE MINERAL DENSITY (BMD)

Measurement of bone mineral density (BMD) is important in the detection and staging of osteoporosis as well as assessment of fracture risk. To obtain BMD information automatically from each CBCT scan, we integrated a QCT calibration phantom directly in the scanner enclosure (Figure 2), providing automatic Hounsfield Unit (HU) calibration with every scan. The known HU values and calcium content of the phantoms allow automatic HU calibration and BMD measurement with each scan in a manner that accounts for variations arising from the size of the subject as well as spatial variation along the axial direction. The calibration phantom included six rods oriented longitudinally in a ring about the inner bore of the scanner (Figure 2), each presenting a known HU and calcium density. In addition to the correction provided by the calibration phantom, the results below incorporated a simple x-ray scatter correction (viz., subtraction of a constant scatter fluence estimate in projection data), with future work to include more sophisticated scatter correction methods. The accuracy in BMD measurements was assessed in a 16 cm diameter polyethylene cylinder incorporating inserts representing a range of calcium density (Figure 2). As shown in Figure 3, the CBCT system provided BMD measurements typically within 3% of the true values (i.e. 75, 150 mg/mL CaHA), matching the accuracy of MDCT within ~2%.

These initial results are promising, and further improvements in scatter correction and calibration methods which is a challenge in CBCT are anticipated to provide further improvement in BMD accuracy. Methods under development include a fast Monte Carlo scatter correction technique and an iterative beam-hardening correction.

3. SUBCHONDRAL BONE STRUCTURE (MORPHOMETRY)

Changes in intra-osseous architecture represent an important component of the pathobiology of a spectrum of bone and joint disorders, including osteoporosis and osteoarthritis [1, 2]. Subchondral bone morphology metrics, such as bone volume fraction (BV/TV), trabecular thickness (Tb.Th), and trabecular spacing (Tb.Sp), characterize the quality of trabecular architecture. Similarly, the degree of anisotropy (DA) is a measure of isotropic nature/orientation of trabeculae within a volume (DA: 0 = isotropic, 1 = anisotropic), and the structure model index (SMI) describes the plate-like, rod-like, or sphere-like geometry of

trabeculae (SMI: 0 = plate-like, 3 = rod-like, 4 = sphere). These metrics were defined as follows:

$$BV/TV = \frac{\text{bone vol}}{\text{total vol}} \quad (1)$$

$$Tb.Th = \frac{\sum d_n}{N} \quad (2)$$

where d is the diameter of the largest sphere that can be fitted within a trabecular structure at a point, and N is the total number of points. The SMI was given by:

$$SMI = 6 \times \left(\frac{S' \times V}{S^2} \right) \quad (3)$$

where S' is the change in surface area after voxel dilation, S is the original surface area, and V is the volume size. Finally, the DA was given by:

$$DA = 1 - \left(\frac{sx}{lx} \right) \quad (4)$$

where sx and lx refer to the short axis and long axis of an ellipsoid fit to the trabecular structures. Evaluation of such pQCT morphological metrics in CBCT images of a cadaveric knee and hand are shown in Figures 4–6 in comparison to micro-CT (taken as gold-standard) and clinical MDCT. The results demonstrate an improvement in accuracy for each metric assessed from CBCT in comparison to MDCT, with accuracy approaching that of micro-CT within ~5%.

4. ASSESSMENT OF JOINT SPACE

Joint space width is a surrogate measure for diagnosis and monitoring of different forms of arthritis, including OA and RA [5]. Typically, Sharp-Larsen scores derived from radiographs are used to measure RA progression in hands and wrists, although such assessment is known to exhibit high inter-reader variability, inability to differentiate overlapping structures, and insensitivity to subtle joint space changes. Similarly, OARSI grading is used for OA, which may exhibit similar variability. Volumetric assessment of cartilage (closely linked with OA) is possible from MRI, although segmentation can be a challenge. In high-resolution CBCT, the opportunity arises for exquisite quantification of 3D joint space in the form of a joint space map as a substitute for underlying cartilage quantification. To overcome inaccuracy and degeneracy associated with conventional measures (e.g., closest point methods or distance along a given axis), we have developed a method to characterize joint space that provides a non-degenerate correspondence across the intra-articular space. The technique employs a physics-based model in which bone surfaces are treated as surfaces of a ‘capacitor,’ and the associated ‘field lines’ present a unique characterization of the intra-articular space. The distance between proximal and distal surfaces is uniquely computed as the distance along field lines using the Laplacian

$\Delta^2 V = \frac{\partial V}{\partial x^2} + \frac{\partial V}{\partial y^2} + \frac{\partial V}{\partial z^2} = 0$ (where V is the potential and x , y , and z are Cartesian coordinates), yielding a unique, robust, and quantitative assessment of the joint space, since field lines are always orthogonal to the surface, as shown in Figure 7. Application to CBCT images of the knee (sitting and standing) and hand (various patients and pathologies) are shown in Figures 8 and 9.

5. DISCUSSION & CONCLUSIONS

Initial investigation of the potential for pQCT using a dedicated CBCT scanner for musculoskeletal extremity imaging shows promising results. The system demonstrates accuracy in BMD within ~5% of a clinical standard QCT system based on MDCT. Intra-osseous bone structure morphometry shows an improvement over MDCT and good correlation with gold standard micro CT. Agreement in most morphometric indices were found to be within 5%, with the exception of DA, which may require further improvement in spatial resolution. Joint space maps calculated using high-resolution CBCT were able to measure and visualize subtle changes in joint space morphology between weight-bearing and non-weight bearing scans that are not possible using conventional whole-body MDCT. Moreover, the preliminary results demonstrated the ability to identify slight anatomical differences in pathologic fractures with reduced and disrupted joint space morphology. Further improvement in the accuracy of pQCT metrics derived from CBCT is currently underway via improved x-ray scatter correction techniques, beam-hardening corrections, system calibration, and novel reconstruction methods, including statistical iterative reconstruction. The ability to perform automatic pQCT analysis in the extremities with each CBCT scan could offer a valuable addition to diagnostic performance and assessment of treatment response in a spectrum of bone and joint diseases, enabling early detection, treatment planning and longitudinal monitoring as well as reduction in cost, workflow, and radiation dose.

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Figure 1.

A dedicated CBCT scanner for extremity imaging. The compact design of the system allows a $22 \times 22 \times 22 \text{ cm}^3$ FOV with the side entry (via sliding door) facilitating patient setup and weight-bearing imaging (b). The system is undergoing pilot and feasibility testing in a spectrum of musculoskeletal disorders, including osteoporosis, osteoarthritis, rheumatoid arthritis, and trauma.

Figure 2.

Calibration system (a) integrated with the scanner door or gantry for bone mineral density estimation. This integrated approach provides accurate BMD calibration by taking into account scatter fluence due to variation in the type of extremity and patient body habitus as well as changes in the axial direction. A polyethylene phantom (b) with known BMD inserts was used for initial testing of BMD accuracy.

Figure 3.

BMD measurements using the CBCT scanner in comparison to MDCT [6]. The BMD boxplots show quartiles, range, etc. for two inserts: (a) 75 mg/mL (osteoporotic) and (b) 150 mg/mL (normal) equivalent BMD computed across 20 axial slices. Good agreement is evident in comparison to the the true values. (d) Mean BMD calculated on a cadaver distal radius specimen (c) shows close agreement with a clinical QCT system (MindwaysTM QCT system on a Siemens SomatomTM Definition CT scanner). Variation in BMD across different slices within the radius ROI is evident from the CBCT boxplot, whereas the clinical QCT system only provided the mean BMD.

Figure 4.

Assessment of trabecular morphometry from a cadaveric radius using high resolution CBCT. Trabecular details are visualized in (a) a cadaver specimen in the region of the distal radius and ulna. Trabecular thickness (b) and spacing (c) maps from a $6 \times 6 \text{ mm}^2$ volume of interest demonstrate the ability to precisely measure trabecular thickness and spacing using the CBCT scanner.

Figure 5.

Assessment of trabecular morphometry from a cadaveric distal radius. Various morphometry parameters (BV/TV, Mean Tb.Th, SMI, and DA) are plotted as a function of reconstruction voxel size in CBCT (1×1 binning, 0.13 mm pixels). Results from high resolution MDCT images (voxel size = 0.26 mm) are also plotted for purposes of comparison. Analysis of each parameter guided selection of nominal pQCT reconstruction methods offering performance comparable to or exceeding that of MDCT.

Figure 6.

Morphometry analysis in a cadaveric distal radius specimen. The specimen was scanned ex vivo (i.e., dissected from surrounding tissue) using (a) micro-CT (taken as gold-standard, with results shown for voxels size $a_{\text{vox}} = 0.1$ mm) as well as in situ (i.e., prior to dissection) using (c) CBCT ($a_{\text{vox}} = 0.1$ mm) and (b) MDCT ($a_{\text{vox}} = 0.36$ mm). Comparative analysis shows that most structure parameters (ie. (d) Bone Volume Ratio, (e) Mean Trabecular Thickness, (f) Structure Model Index) calculated using CBCT are in good agreement with micro-CT to within a few percent. For the same parameters, MDCT shows relatively large errors associated with limited spatial resolution. Degree of Anisotropy (g) has a relatively large error in both CBCT and MDCT, possibly owing to lower spatial resolution than micro-CT and subject to future investigation.

Figure 7.

Joint space width calculation using an electrostatic 'capacitor' model in which field lines describe a unique, non-degenerate map of the intra-articular space.

Figure 8.

(a) Difference in joint space and surrounding structure of musculature and ligaments observed in non-weight-bearing (i.e., sitting) and weight-bearing (i.e. standing) images of the knee. CBCT images demonstrate the laxity of the patellar tendon and motion of the patella & femur in the sitting versus standing knee. High-resolution CBCT combined with quantitative analysis of the joint space shows subtle differences in the medial compartment between (b) sitting and (c) standing knees of a patient from the ongoing pilot study.

Figure 9.

Joint space map calculation applied to a patient hand. A normal metacarpal-phalangeal (MCP) joint (a) is highlighted in comparison to a fractured proximal inter-phalangeal (PIP) joint (c). The respective 3D joint space maps show a smooth variation in joint space $\sim 0.5 - 2$ mm for the MCP (b) in comparison to a reduced and spatially irregular map (d) likely associated with architectural disruption (trauma) in the PIP.

Joint space maps calculated in the hand from an ongoing pilot study in OA, RA and trauma patients. The top and middle rows show joint space maps computed for a single trauma/fracture patient for each MCP (top row) and PIP (middle row). Note the disruption in PIP5 associated with trauma. The bottom row demonstrates inter-patient differences in joint space, with narrowing of the MCP 1 in Patients #4 and #5 potentially associated with pathology.