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Original Article

Vertebral Bone Mineral Density Measured by Quantitative Computed Tomography With and Without a Calibration Phantom: A Comparison Between 2 Different Software Solutions

Josephine Therkildsen,[1] Jesper Thygesen,[2] Simon Winther,[3] My Svensson,[4] Ellen-Margrethe Hauge,[5] Morten Böttcher,[1] Per Ivarsen,[6] and Hanne Skou Jørgensen[6,]*

[1]Department of Internal Medicine, Hospital Unit West, Herning, Denmark; [2]Department of Clinical Engineering, Aarhus University Hospital, Aarhus, Denmark; [3]Department of Cardiology, Aarhus University Hospital, Aarhus, Denmark; [4]Department of Nephrology, Division of Medicine, Akershus University Hospital, Oslo, Norway; [5]Department of Rheumatology, Aarhus University Hospital, and Department of Clinical Medicine, Aarhus University, Denmark; and [6]Department of Nephrology, Aarhus University Hospital, Aarhus, Denmark

Abstract

Quantitative computed tomography (CT) can be used to quantify bone mineral density (BMD) in the spine from clinical CT scans. We aimed to determine agreement and precision of BMD measurements by 2 different methods: phantom-less internal tissue calibration and asynchronous phantom-based calibration in a cohort of patients with chronic kidney disease (CKD). Patients with CKD were recruited for CT angiography of the chest, abdomen, and pelvis. BMD was analyzed by 2 different software solutions using different calibration techniques; phantom-based by QCT Pro (Mindways Inc.) and phantom-less by Extended Brilliance Workspace (Philips Healthcare). Intraoperator reanalysis was performed on 53 patients (36%) for both methods. An interoperator reanalysis on 30 patients (20%) using the phantom-based method and 29 patients (19%) using the phantom-less method was made. XY- and Bland-Altman plots were used to evaluate method agreement. Phantom-based measured BMD was systematically higher than phantom-less measured BMD. Despite a small absolute difference of 3.3 mg/cm^3 (CI: -0.2–6.9 mg/cm^3) and a relative difference of 5.1% (CI: 2.2%–8.1%), interindividual differences were large, as seen by a wide prediction interval (PI: -47–40 mg/cm^3). The Bland-Altman plot showed no systematic bias, apart from 5 outliers. Intraoperator variability was high for the phantom-less method (5.8%) compared to the phantom-based (0.8%) and the interoperator variability was also high for the phantom-less method (5.8%) compared to the phantom-based (1.8%). Despite high correlation between methods, the between-method difference on an individual level showed great variability. Our results suggest agreement between these 2 methods is insufficient to allow them to be used interchangeably in patients with CKD.

Key Words: Bone density; chronic renal insufficiency; computed tomography; osteoporosis.

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*Address correspondence to: Hanne Skou Jørgensen, MD, PhD, Department of Nephrology, Aarhus University Hospital, Aarhus, Denmark. E-mail: hsjorgensen@clin.au.dk

Introduction

Quantitative computed tomography (QCT) is an accepted method for assessing bone mineral density (BMD) to detect osteoporosis and monitor BMD changes over time *(1)*. BMD can be measured using routine whole-body computed tomography (CT) scans, which is a widely used diagnostic modality *(1)*.

Any CT scanner-produced image can be used for BMD analyses as long as a suitable calibration technique is utilized *(2)*. Two calibration methods exist: phantom-based and phantom-less calibration. Phantom-based calibration uses reference values from a scanned phantom, which contains regions of known concentrations of calcium hydroxyapatite. The phantom can be scanned simultaneously with the patient (synchronous) or separately as a series of phantom scans (asynchronous), which the software will then use to generate calibration data. In contrast, internal calibration uses reference values from conversion factors calculated based on the patient's own tissues. The literature on phantom-less internal calibration software is limited, and the 2015 ISCD official position statement is that: "There is insufficient evidence to judge the feasibility of internal calibration" *(3)*.

There are many different commercially available software solutions for BMD analysis, but there is a lack of knowledge as to the interchangeability of these methods. Mueller et al found that precision of the phantom-less method was inferior to the phantom-based, but still concluded that the phantom-less method is robust in measuring BMD *(4)*.

This study aimed to determine agreement and precision between BMD measurements by the phantom-less internal tissue calibration method by Extended Brilliance Workspace (Philips Healthcare, Cleveland, OH) and the asynchronous phantom-based calibration by QCT Pro (Mindways Software Inc., Austin, TX) in a group of patients with chronic kidney disease (CKD).

Materials and Methods

Patients

Patients with CKD, referred for cardiovascular assessment before kidney transplantation, were included from 9 hospitals. Criteria of inclusion and exclusion have been described in a prior publication *(5)*. Written informed consent was obtained from all patients. The study followed the principles of the declaration of Helsinki and approval was given by the Central Denmark Regional Committee on Health Research Ethics and the Danish Data Protection Agency. The study was registered at clinicaltrials.gov (NCT01344434).

Images Acquisition

The scan protocol for the CT angiography has been described in detail in a previous paper *(6)*. In brief, CT scans were performed using a dual-source scanner (SOMATOM definition Flash; Siemens Healthcare, Erlangen, Germany) with contrast-enhancement. A contrast dose of 95 mL ioversol (Optiray 350 mg/mL; Mallinckrodt, Hennef, Germany) was given intravenously. A mean delay time of 30 ± 5 s was present between contrast administration and the imaging procedure. CT scans were high-pitch flash scans with a gantry rotation of 0.28 s and a pitch of 3.4. The detector collimation was $2 \times 64 \times 0.6$ mm, and images were reconstructed to 3-mm thickness. A standard soft tissue kernel was used throughout (syngo.via; Siemens Healthcare, Erlangen, Germany).

Bone Density Analyses and Fracture

Mean BMD value in units of milligram per cubic centimeter (mg/cm^3), as well as BMD for each separate vertebra was derived from both software solutions. Fractured vertebrae were excluded from BMD analyses. Deformed vertebrae were identified on 2-dimensional sagittal reconstruction images *(7)* by 1 investigator (HSJ), and reviewed by a radiologist and signed a final fracture grade *(8)* based on the classification described by Genant et al *(9)*.

Phantom-Based BMD

The phantom-based BMD measurements were performed using the software solution QCT Pro (Mindways Software Inc., Austin, TX) and the quality assurance calibration phantom Mindways Solid (Mindways Software Inc.; Fig. 1). BMD measurements were performed on 3 consecutive vertebrae from T12 to L4 by a single investigator (HSJ) blinded to study data. L1 to L3 were preferred, although T12 and/or L4 were allowed in cases of observed deformity, pathology, or fractures of L1, L2, or L3. An elliptical volume of interest (VOI) was automatically placed in the anterior part of the vertebral body (Fig. 2A) and manually adjusted when necessary. We aimed at placing the largest possible VOI, avoiding the posterior venous plexus and any focal pathology, such as bone islands and calcified herniated disks.

Phantom-Less BMD

The phantom-less measurements were performed using the Extended Brilliance Workspace (Philips Healthcare, Cleveland, OH). BMD analysis was performed by a single investigator (JT) blinded to study data and to the phantom-based results. The analyses were anatomically matched to the phantom-based measurements. Elliptical VOIs were manually placed in the anterior part of the mid-vertebral body (Fig. 2B) by a procedure identical to the one detailed for the phantom-based measurement. VOIs of muscle and fat were placed in approximately the same position on each image, in the posterior subcutaneous fat on the right side and the paraspinal muscle group on the left side, throughout. VOI size and shape for muscle and fat were adjusted for optimal fit. The main goal was to achieve a normal distribution on the Hounsfield unit (HU) histogram