Performance Evaluation of Bone Mineral Densitometry Techniques by a Novel Phantom

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ABSTRACT

Purpose: Accurate performance assessment of bone mineral density (BMD) methods is crucial due to the fact that a high level of exact estimation of bone situation is needed for correct diagnosis. Variation of parameters like sensitivity and error ratio highly affects the densitometry results that may induce some level of uncertainty in diagnosis. So, designing an algorithm for correction is necessary to assure examiners about measurement results.

Methods: In this study several phantoms consisting of soft tissue- and bone-equivalent materials were devised to accurately test bone densitometry systems. To the best of our knowledge there is no unique phantom to be able to use for evaluation of both Dual Energy X-ray Absorptiometry (DEXA) and Quantitative Computed Tomography (QCT) in a wide range of density. The main motivation of this study was to design a reliable and easy to use phantom. A QCT quality control, quality assurance, and Plexiglas cylindrical phantoms as a spine phantom were designed and constructed to assess different bone densities. Four inserts in spine phantom with precisely wide range of K_2HPO_4 solutions were used for simulation of bone tissues and to determine the BMD systems characteristics. The designed phantoms were also used for performance assessment of BMD systems. We used a sinogram-based analytical CT simulator to model the complete chain of CT data acquisition for QCT method as well.

Results: In this research it is demonstrated that by decreasing of bone mineral densities an increasing trend in error ratio of measured densities and declining trend in methods sensitivities were observed in the both DEXA and QCT methods, that may cause some level of uncertainty in low densities. It has been shown that between the ranges of 20 and 100 mg/cc K_2HPO_4 concentrations, the error ratio in both DEXA and QCT techniques is more than 20%. Sensitivity values in incremental mineral contents ranges between 20-60 mg/cm^3 and 260-300 mg/cm^3 reveal an upward trend between 0.93 and 1.45 for QCT and from 0.59 to 1.44 for DEXA, respectively.

Conclusion: A novel phantom was designed with capability of easily supporting wide range of densities and using in both DEXA and QCT techniques to measure and compare the sensitivity and error of systems. Our phantom showed excellent capability for accurate determination of BMD, particularly in low density bones. In this study it is demonstrated that the sensitivity and error ratio is affected by bone density that may cause uncertain results especially in low densities.

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1. Introduction

Bone mineral density (BMD) studies can be used to identify individuals with osteoporosis and monitor response to osteoporosis treatment, with the goal of reducing the risk of fracture. Osteoporosis is a disease characterized by low bone mass and deterioration of bone tissue[1, 2]. BMD is a primary indication for pharmacologic therapy in patients with osteoporosis and/or other metabolic bone diseases[3]. BMD is commonly evaluated with DEXA, QCT, Ultrasound methods and radiographic absorptiometry techniques, in which DEXA and QCT have attracted more attentions[4] and are more common in the clinic.

DEXA are currently considered as gold standard for making a diagnosis of osteoporosis and predicting fracture risk. This technique can accurately measure the areal BMD (in mg/cm^2), however, it cannot measure the cortical and trabecular bones separately[5].

QCT is unique as it provides true three-dimensional image and reports BMD as true volumetric BMD (in mg/cm^3) measurements. The advantage of QCT is the ability to evaluate bone geometry and provide separate trabecular and cortical bone evaluations. It can assess BMD in mg/cm3 (compared with DXA, which measures areal BMD in mg/cm2)[6].

Healthcare and professional organizations expressed their concern about the lack of standardization, assessment of accuracy and precision, variation of sensitivity and error by variation of bone density in bone mineral measurement techniques like QCT and DEXA, whereas there are generally recognized as important and unresolved issues[7]. Sensitivity, or local sensitivity, can be defined as the ratio of the change in the result to an incremental change in input variable or the slope of transformation function. An alternate definition of the sensitivity is called gain which transforms the input value to output value[8].

As quality control is absolutely necessary in bone assessment techniques, especially in treatment followups, a phantom that could be able to determine variety of specifications regarding to measurement system would be crucial. As a result, several attempts were made to accurately assess the bone mineral densitometry techniques and many standard phantoms were designed for this purpose: European Spine Phantom (ESP) is designed as a geometrically defined and semianthropomorphic phantom [9]. It contains a spine insert consisting of three vertebrae of increasing bone mineral densities and thicknesses of cortical structures. Hologic anthropomorphic spine phantom consists of four vertebras with similar densities [10]. Bio-Imaging Technology Inc. phantom (called Bona Fide).[11], Lunar aluminum spine phantom[12], Norland hydroxyapatite spine phantom[10] and some other phantoms that design for quality assurance of bone densitometer. Because of the bone mineral content of all phantoms remained constant, all phantoms have limited capability to measure the sensitivity and error in a wide range of densities, for instance, in lower densities which related to severe osteoporosis. Moreover, being capable in the assessment of both DEXA and QCT using a single phantom is of importance due to its simplicity and comparability.

In order to accurately estimate the error and sensitivity in both DEXA and QCT techniques in a wide range of densities, it needs to scan a vast amount of densities in the full range of probable bone density. In addition, the related phantom should be able to be used in both mentioned techniques.

Variation of parameters like local sensitivity and accuracy highly affects the results of bone densitometry examinations. This may be of more importance when the amount of induced error is not constant and varies for different densities. So, designing a set of phantoms to assess the local sensitivity and accuracy of BMD methods in the wide range of densities can be helpful.

In this study a series of exclusive and in-house phantom with capability of easily supporting wide range of densities and using in both QCT and DEXA techniques was designed. Our novel set of phantoms made it possible to evaluate both the QCT and DEXA methods in a large range of densities.

2. Materiels and Methods

2.1. Scanners

QCT was performed using a 64-slice GE LightSpeed VCT scanner (GE Healthcare Technologies, Waukesha, WI) with volumetric data acquisition capability using the following acquisition protocol: 120 kVp, 300 mAs, and 5 mm slice thickness. DEXA was measured with GE Lunar DPX (GE Healthcare Technologies, Madison, WI, USA) scanner using AP spine standard technique as, 76 keV, 3 mA, 0.6×1.2 mm pixel size, 1.68 mm beam size.

2.2. Designing of Dedicated in-House Phantoms

2.2.1. QCT Calibration Phantom

Calibration phantom in a QCT procedure is experimentally used to obtain calibration curve in which the Hounsfield Units (HU) are converted to corresponding BMD values. The phantom was made up of a plastic base material, polyethylene; containing 5 cylindrical holes with 190 ± 0.5 mm diameter Figure 1(d). Each hole is filled with the reference solutions. Four cavities are filled with 0, 50, 100 and 200 mg/cm^3 solutions of K_2HPO_4 in distilled water, as known reference bone substitutes, and the fifth is a fat equivalent that is filled with 60% ethanol [13].

2.2.2. Quality Assurance (QA) Phantom

QCT set of phantoms generally includes QA phantom. It is of high requirement due to the fact that in the clinical QCT procedure performing daily Quality Assurance, in which QA phantom is used, is mandatory. QA phantom helps to assure about the correctness of QCT procedure results. For this study, aQA phantom was designed and constructed to assess performance of CT scanner and QCT procedure. It is made up of polyethylene with four cavities which is filled with the same solutions which were used in QCT calibration phantom except the ethanol. The QA phantom is designed such that it could be settled on the QCT calibration phantom Figure 1(c).
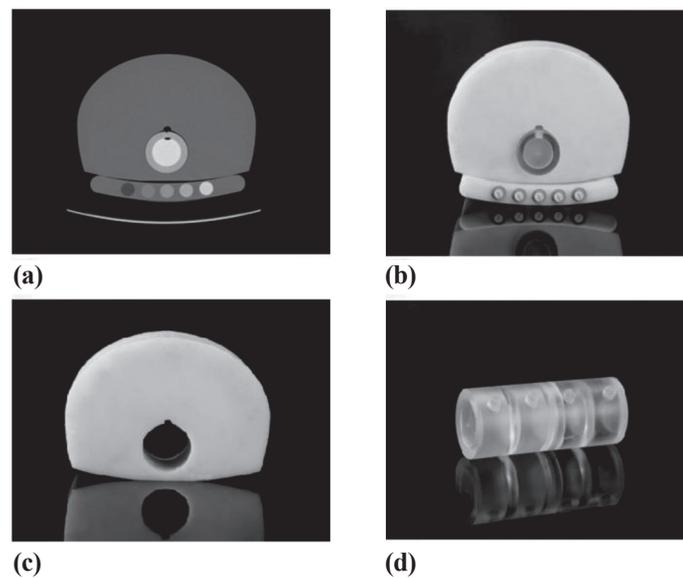
2.2.3. Spine and Torso Phantom

To avoid controversy with respect to the definition of different tissue-substitute materials, it was decided to limit the phantom constituents to soft tissue, fat and bone-equivalent materials. A Plexiglas cylindrical phantom was designed and constructed to mimic variety of human spine bones in terms of shape and BMD. This phantom contained four cascaded cylinders with individual filling caps. By this, filling and emptying the cavities with K_2HPO_4 solutions would be fast and reliable. The polyethylene materials used to fabricate the torso Phantom provide optimal tissue simulation of contour of human body. A dedicated hole in the low-middle part of torso phantom was made with the same diameter as spine phantom. In the imaging procedure, the spine phantom must be plugged into the torso phantom (Figure 2).

Regarding spine phantom filling materials, we consider the World Health Organization (WHO) and Mindways (Mindways Software, Inc) classification of mineral densities. Some thresholds of BMD determine the osteoporosis situation: for example density below 50 mg/cc is categorized as definite osteoporosis and over 140 mg/cc is categorized as normal. As a result, wide range of solutions from 20 to 300 mg/cc with step of 20 mg/cm^3 was prepared.

(a)

(b)

(c)

(d)
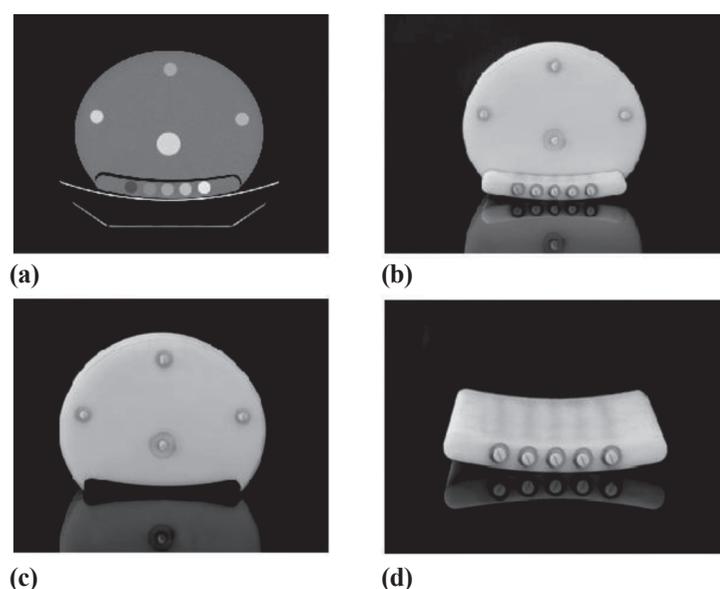
Figure 1. Calibration and QA Phantom, **(a)** CT image of Calibration and QA Phantoms; **(b)** Photograph of Calibration and QA Phantoms; **(c)** Photograph of QA Phantom, and **(d)** Photograph of QCT Calibration Phantom.

(a)

(b)

(c)

(d)

Figure 2. Spine and torso Phantom. **(a)** Axial CT image of a torso and spine phantom, which set over calibration phantom. **(b)** Photographoftorso phantom, spine phantom, and calibration phantom plugged to each other. **(c)** Photograph of torso phantom, and **(d)** Photograph of spine phantom.

For weighing of K_2HPO_4 powder, an accurate balance, Sartorius Model TE124S with built-in motorized calibration weight, ensures the highest weighing accuracy. Graduated cylinder was used to accurately measure the volume of distilled water used for solutions making. To minimize concentration error, solutions were made in large volumes and divided into small amounts.

2.3. QCT Software

Analysis of values in QCT technique was performed by using in-house designed software with a graphical user interface (GUI) which is running under C# coding language with a capability of: receiving and viewing DICOM image, ROI placing, average and standard deviation calculation for pixel values inside ROIs, ROI indexing to feed to QCT calibration curve calculator, and report generation. According to the information provided and options selected by the user, the software loads the CT images in DICOM format which can be viewed in any desired mode (surface or skeleton) with the possibility of changing the colour scale and contrast. Several measurements and viewing features such as drawing region of interest (ROIs) have been considered. To provide sufficient precision for the CT number measurement, a circular region of interest (ROI) of approximately 50% of region under question area was used.

The software was equipped with graphic user interface. To validate the output of the designed software, values from ImageJ software (National Institute of Health, US) and a series of analytical calculations were used.

To estimate the mineral density of spine, a calibration based analytic QCT algorithm was implemented. In QCT method the calibration curve converts the HU values to mineral contents in mg/cm^3. For this, the calibration phantom is scanned simultaneously with patient/phantom and HU values of known densities are extracted from an image of calibration phantom. To obtain the calibration curve, a least square curve fitting algorithm is used to obtain the correlation between known mineral densities and corresponding HU values for each slice. Normally, a linear conversion equation is obtained as below,

$$BMD = a \times HU + b \tag{1}$$

Where a and b are constants as slope and intercept of conversion equation, respectively. Then, by using (1) any HU in the bone regions of patient/phantom images can be converted to mineral density values.

2.4. Analytic Simulation

Due to the limitation of having access to various models of CT systems, we tried to repeat the experiments by simulation but with different specifications for CT in order to obtain a general assessment of QCT method.

For this, a sinogram-based analytic CT simulator, implemented in our lab, was also used for QCT method assessment. This simulator was previously explained [14, 15] and examined in the several works[16]. This CT analytic model includes the capability of X-ray spectrum generation according to the values of kVp, mAs, inherent and added filter, and slice thickness. The above-mentioned parameters have been set to be consistent with a typical clinical CT system.

For image reconstruction, MATLAB (Math Works, Inc., Natick, MA) functions of fan beam filtered-back-projection was used to reconstruct the calculated line integrals as a 512 × 512 image size. The QCT calibration phantom, spine phantom, and torso phantom were modeled inside CT simulator with the same geometries and materials as experimental ones.

2.5. Assessment Strategy

The following equation (2) was used to calculate the error ratios in the measure BMD by using QCT and DEXA method,

$$Error\ Ratio = \frac{Measured\ Density\text{-}Real\ Density}{Real\ Density} \quad (2)$$

A simplified first order local sensitivity analysis was used. To this end, an incremental range of mineral densities as input and variation of measured values as output was used to calculate local sensitivity of the system. Eleven sub-ranges were considered within input ranges which have equal width of 40 mg/cm³ except one region which has 60 mg/cm³ width. The slope of the line representing output variation vs. input variation was calculated in each range denoting local sensitivity.

All measurements were performed based on placing ROIs on the desired locations in the images and using the average values of pixels inside the ROIs.

3. Results

The designed phantoms were used for performance assessment of QCT and DEXA methods. Measured vs. true values in both techniques were examined to assure the validity of methods in a wide range of bone mineral densities.

Table 1. Correlation coefficient derived from calibration phantom for QCT method

Density(mg/cm³)	Slope	Intercept
20	0.79	29.57
40	0.81	26.78
60	0.82	27.59
80	0.81	27.40
100	0.80	29.47
120	0.80	28.08
140	0.79	30.81
160	0.80	28.10
180	0.80	29.54
200	0.80	28.10
240	0.76	34.03
260	0.81	28.27
300	0.80	29.64

Table 1 gives the slopes and intercepts of conversion equation (1) when different spine mineral densities were existent. These data were extracted by averaging of ROI values of at least three images for each solution density. The table shows inconsiderable change on calibration curve due to the variation of spine mineral density. Our results show that despite the influence of changing mineral density has partial effect on data was obtained by QCT and error ratio.

Figure 3. shows the measured densities by using QCT techniques vs. true values in a wide range of BMDs. The fitted line on the measured values is also reported in Figure 3.

y = 1.01x + 21.03

R² = 0.9911
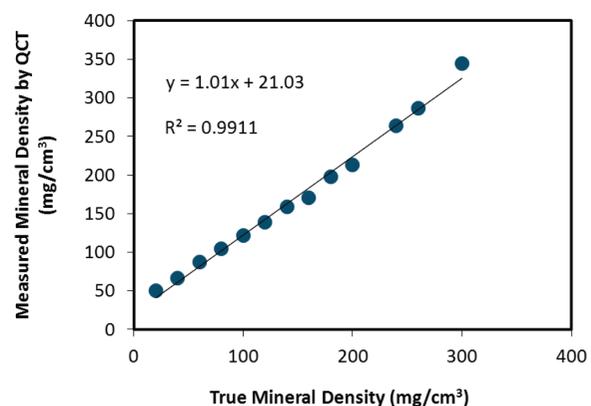
Figure 3. Measured vs. true mineral densities using QCT technique.

Figure 4 shows the error ratio in the QCT technique. Large error ratio values for small densities were seen in the QCT method.
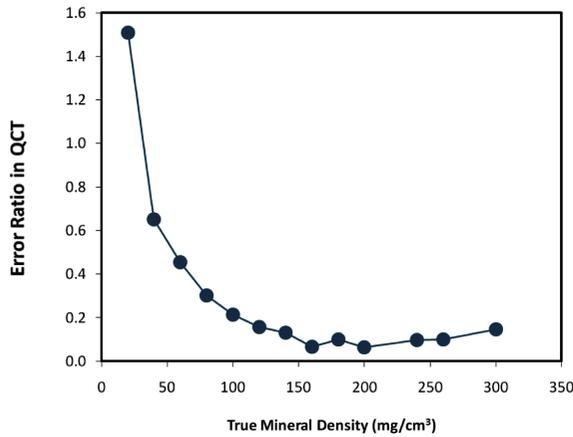

Figure 4. Variation of error ratio vs. true mineral density in QCT technique

For DEXA, true areal BMDs (in mg/cm^2) are calculated by dividing the mineral content of solution in each spine phantom cavity to its corresponding projected area. Figure 5 depicts the measured density by using DEXA method vs. true areal density values. The fitted line on the measured values is also reported in Figure 5.
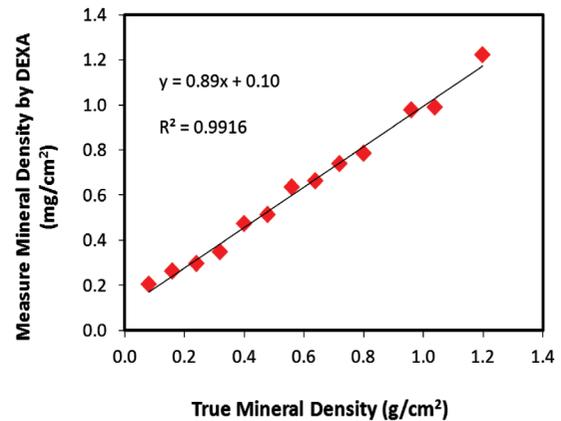
Regarding the error ratio in measure BMD in wide scale of mineral content in DEXA and QCT, are shown in Figure 4 and 6, respectively.

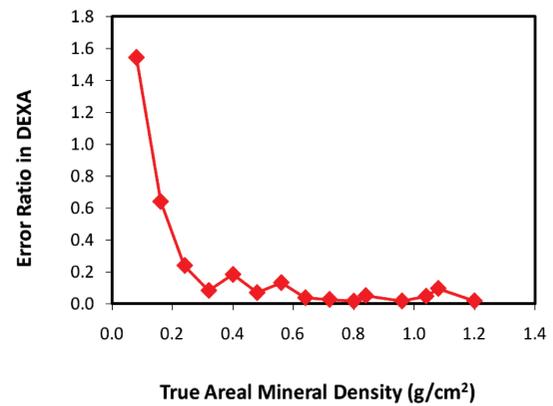It is demonstrated that by decreasing bone mineral densities an increasing trend in error ratio of measured densities is happened that may cause some level of uncertainty in low densities. The error ratio of QCT varies from 151 to 21 and 154 to 18 in DEXA methods for 20 to 100 mg/cc K_2HPO_4 concentrations. Overall, large error ratio values for small densities were seen in the QCT method as well as DEXA.
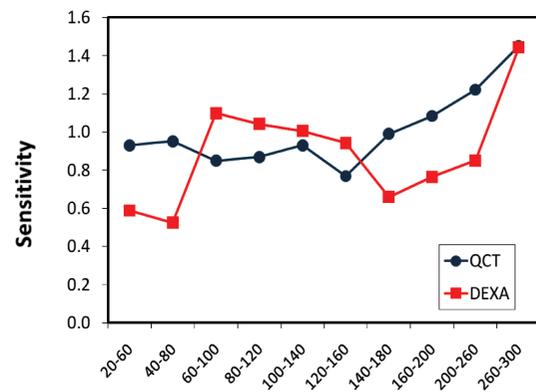
Sensitivity variation in the DEXA and QCT methods are shown in Figure 7. Sensitivity values in incremental mineral contents ranges for 20-60 mg/cm^3 to 260-300 mg/cm^3 shows an increasing trend for both QCT and DEXA methods.

Figure 5. Measured vs. true areal mineral density in DEXA system

Figure 6. Variation of error ratio vs. true mineral density in DEXA technique.

Figure 7. Variation of sensitivity vs. true mineral density QCT and DEXA

QCT technique was also evaluated by CT simulator. Simulated data of the CT Simulator in QCT method are shown as Figure 8. The CT scanner was simulated with acquisition protocol: 120kVp, 200 mAs for different densities. The simulated data shows a large error in
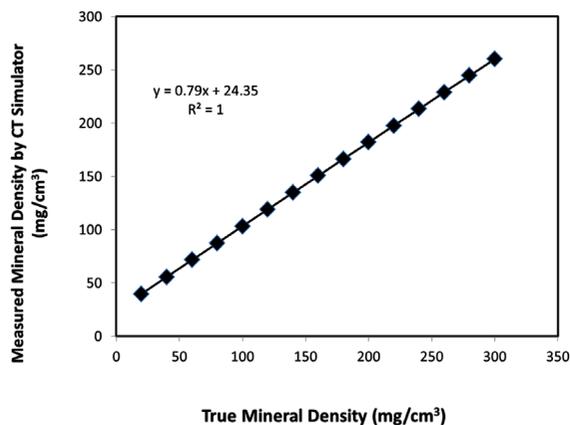
Figure 8. Measured vs. true mineral density calculated by CT Simulator using QCT technique
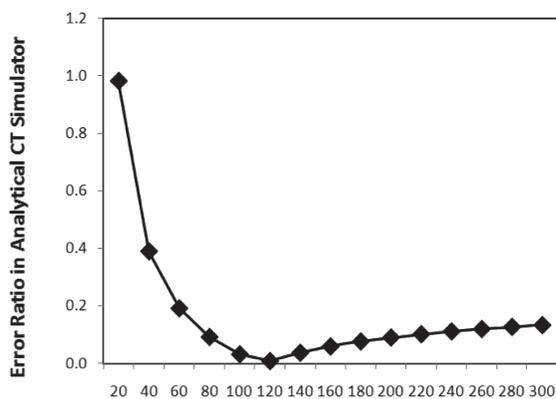
Figure 9. Variation of error ratio vs. true mineral density in Analytical CT Simulator

4. Discussion

The need for exact estimation of bone mineral density to diagnose its diseases and treatment follow-up, require an accurate assessment of measurement technique behavior. Some crucial properties like sensitivity and error ratio, which undoubtedly affect the densitometry results, have to be completely determined. As it is shown in our results, sensitivity and error ratio vary by mineral density of spine results in an uncertainty in measurement procedure. Although a linear regression between measured and true density can be observed (Figure 4, Figure 6, and Figure 9), but as far as the authors are concerned, it is not enough to assure the examiner about the results. As we demonstrated, by examining the wide range of densities, especially low densities, which became feasible by designed dual-purpose phantom in this study, an undesirable variation in error due to changing bone mineral density was observed in both techniques. Moreover, we observed that despite of being an influence of spine mineral density value on cali-

bration curve, this influence was inconsiderable on the data obtained by QCT method and the error ratios.

The most noticeable factor affected by mineral density was error ratio. Our results showed that by decreasing, a dramatic increase can be observed in error ratio in both DEXA and QCT methods (Figure 4, Figure 6, and Figure 9). The values of error ratio in low mineral densities in DEXA and QCT methods reveal about 50% over estimation in mineral content measurement. In QCT technique, HU measurement methods in the bone ROI, and HU values of known densities extraction, detect error. Also, machine related artifacts such as beam hardening, detected scatter and system drift can introduce errors. In addition, variations in soft tissue composition within the X-ray beam, drifts in scanner calibration, and beam hardening affecting the accuracy of DEXA measurements. These innate inaccuracies make relative error brighter remarkably in low densities. It should be noted that, by decreasing bone mineral densities, the mineral density to less than 50 mg/cm^3, an increasing trend in error ratio of measured densities is happened. The error ratio of QCT varies from 151 to 21 for 20 to 100 mg/cc K_2HPO_4 concentrations. Large error ratio values for small densities were seen. The figure shows some fluctuated over the range of densities but overall a downward trend is seen. However, going toward higher densities leads to increasing the error ratio values which can be due to beam hardening effect which is happened in the presence of high density/atomic number materials.

Sensitivity values in incremental mineral contents ranges for 20-60 mg/cm^3 to 260-300 mg/cm^3 reveal an increasing trend from 0.93 to 1.45 for QCT and 0.59 to 1.44 for DEXA, respectively (Figure 7). This variation can be due to the system inaccuracy especially in very low and very high mineral densities. As can be seen in CT Simulator, there is a linear regression between the measured and true densities (Figure 8).

The average values of sensitivity in DEXA and QCT were respectively 0.89 and 1.00. It can be concluded that the tendency of sensitivity in QCT is more likely to be unit compared to DEXA. Regarding the measure of sensitivity dispersing, a larger coefficient of variation in DEXA was observed. It means that the rate of fluctuation of sensitivity in DEXA is higher than in QCT. The major finding of this study was that the coefficient of variation in sensitivity of DEXA was 0.31 while it was 0.2 in QCT. As a result, we have found that BMD estimated by QCT are more reliable than DEXA in case of large variation of bone mineral content in the body.

It is worth to mention that, obtaining many correction coefficients to stabilize the sensitivity in each range of

density may improve the accuracy of bone densitometry techniques. For this, a wide range of known densities have to be scanned to calculate calibration curve in order to correct the error ratio and sensitivity.

5. Conclusion

A special spine phantom, a calibration phantom for QCT bone mineral density determination, a quality assurance phantom, an analytic CT simulator, and the bone mineral density analysis software were designed and produced to evaluate the sensitivity and error ratio variation in bone densitometry measurements. The spine phantom offers a range of densities (20-300 mg/cm^3), to verify instrument function over the clinically relevant range, not just at a single, healthy BMD. Linearity of BMD over the clinically range is critical for full instruments evaluation. The Spine phantom uses K$_2$HPO$_4$ solutions insert for the direct assessment of bone density accuracy. In this study it is demonstrated that the sensitivity and error ratio is affected by bone density that may cause uncertain results especially in low densities. Furthermore, it is shown that by using a spine phantom which can be easily filled or emptied from different solutions of K$_2$HPO$_4$, a correction algorithm may obtain to stabilize the sensitivity over the wide range of density. BMD was measured by DEXA and QCT methods. We designed a novel phantom with capability of easily supporting wide range of densities and using in both DEXA and QCT techniques. Performing bone densitometry measurement in large scale of densities by this phantom make it more reliable to measure and compare the sensitivity and error of systems especially in low densities, and using the general QCT calibration phantom to obtain the basis material attenuation coefficients. Our phantom showed excellent capability for accurate determination of BMD, particularly in low density bones.

Acknowledgment

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