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Research Article

Design and Validation of Synchronous QCT Calibration Phantom: Practical Methodology

Malakeh Malekzadeh, MSc[a], Shahrokh Abbasi-Rad, MSc[bc], Mohamad Shahgholi, PhD[d], Parisa Naghdi, MSc[b], Marzieh Sadat Hoseini, MSc[b], Niloofar Ayoobi Yazdi, MD[e], Mohammad Bagher Shiran, PhD[a] and Hamidreza Saligheh Rad, PhD[bc]*

[a] *Medical Physics Department, School of Medicine, Iran University of Medical Sciences, Tehran, Iran*
[b] *Quantitative Medical Imaging Systems Group, Research Center for Molecular and Cellular Imaging, Tehran University of Medical Sciences, Tehran, Iran*
[c] *Medical Physics and Biomedical Engineering Department, Tehran University of Medical Sciences, Tehran, Iran*
[d] *Young Researchers and Elite Club, Najafabad Branch, Islamic Azad University, Najafabad, Iran*
[e] *Advanced Diagnostic and Interventional Radiology (ADIR) Research Center, Tehran University of Medical Sciences, Tehran, Iran*

ABSTRACT

Introduction: Quantitative computed tomography (QCT) can supplement dual x-ray absorptiometry by enabling geometric and compartmental bone assessments. Whole-body spiral CT scanners are widely available and require a short scanning time of seconds, in contrast to peripheral QCT scanners, which require several minutes of scanning time. This study designed and evaluated the accuracy and precision of a homemade QCT calibration phantom using a whole-body spiral CT scanner.

Materials and Methods: The QCT calibration phantom consisted of K_2HPO_4 solutions as reference. The reference material with various concentrations of 0, 50, 100, 200, 400, 1000, and 1200 mg/cc of K_2HPO_4 in water were used. For designing the phantom, we used the ABAQUS software.

Results: The phantoms were used for performance assessment of QCT method through measurement of accuracy and precision errors, which were generally less than 5.1% for different concentrations. The correlation between CT numbers and concentration were close to one ($R^2 = 0.99$).

Discussion: Because whole-body spiral CT scanners allow central bone densitometry, evaluating the accuracy and precision for the easy to use calibration phantom may improve the QCT bone densitometry test.

Conclusion: This study provides practical directions for applying a homemade calibration phantom for bone mineral density quantification in QCT technique.

RÉSUMÉ

Introduction : La tomodensitométrie quantitative (QCT) peut servir de complément à la DXA en facilitant les évaluations géométriques et des compartiments des os. Les tomodensitomètres hélicoïdaux pour corps entier sont largement accessibles et sont rapides comparativement à la QCT périphérique qui, elle, peut nécessiter plusieurs minutes. Dans le cadre de cette étude, nous avons évalué la justesse et la fidélité d'un fantôme de QCT préparé à la main pour des tomodensitomètres hélicoïdaux pour corps entier dans le contexte des évaluations quantitatives.

Matériaux et méthodes : Le fantôme pour l'étalonnage de la QCT comprenait une matière plastique et une solution de K2HPO4 qui servaient de base et de référence respectivement. Des matériaux de référence dont les concentrations de K_2HPO_4 étaient de 0, 50, 100, 200, 400, 1000 et 1200 mg/cm^3 en solution aqueuse ont été utilisés. Pour créer le fantôme, nous avons eu recours au logiciel ABAQUS.

Résultats : Nous avons utilisé les fantômes créés pour évaluer le rendement de la méthode de QCT en mesurant les erreurs de justesse et de fidélité, qui étaient, de façon générale, inférieures à 5,1% pour diverses concentrations. La corrélation entre les données de tomodensitométrie et les concentrations se rapprochaient d'un ($R^2 = 0{,}99$).

Discussion : Puisque les tomodensitomètres hélicoïdaux pour corps entier permettent de déterminer la densitométrie osseuse centrale, le fait d'évaluer la justesse et la fidélité du fantôme d'étalonnage facile pourrait améliorer le test de densitométrie osseuse effectué au moyen de la QCT.

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* Corresponding author. Hamidreza Saligheh Rad, Department of Medical Physics and Biomedical Engineering, School of Medicine, Tehran University of Medical Sciences, P.O. Box: 14155-6447, Tehran, Iran.

E-mail address: h-salighehrad@tums.ac.ir (H.S. Rad).

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Conclusion : Cette étude a permis d'établir la stabilité du fantôme d'étalonnage K_2HPO_4 au cours d'une période limitée de trois mois. De plus, la grande plage dynamique des concentrations pourrait servir à quantifier la faible et la forte densité des os avec un pourcentage d'erreur relative acceptable.

Keywords: Quantitative computed tomography; bone mineral density; calibration phantom; ABAQUS software

Introduction

Bone mineral density (BMD) is a pillar for influencing bone strength and a key predictor of fracture risk in patients with different metabolic bone diseases, such as osteoporosis. Research shows that about 50% of women and 20% of men experience an osteoporotic fracture during their lives. Quantitative computed tomography (QCT) can supplement dual x-ray absorptiometry, a gold standard method defined by WHO, by performing both morphological and 3D mineral bone assessments [1,2].

Since being implemented in late 1970s, the CT (computed tomography) scanner has rapidly developed, and seen higher rates of clinical use [3]. CT imaging has made progress in different aspects ranging from the detector to the recent varied x-ray energy system and state-of-the-art dose reduction reconstruction algorithms. Whole-body spiral CT scanners are widely available and require only seconds per scan. CT imaging provides a new lens for understanding BMD. Owing to their capability of separating trabecular and cortical volume BMD (vBMD) of spine, they make the measurement of trabecular changes possible, especially as a follow-up technique for therapeutic applications.

Typical calibration phantoms containing either rods with different concentrations of hydroxyapatite (HA), or liquid dipotassium phosphate (K_2HPO_4) provide equivalent densities in units of HA mg/cm^3 or K_2HPO_4 mg/cm^3 [4]. Calibrated vBMD or quantitative equivalent CT density (ρQCT) is calculated by measuring the CT number at specific phantom's calibrated standards. The calibration phantom was originally designed by Cann et al (Mindway, South San Francisco, CA). Other standard phantoms are also used, developed by Image Analysis (Columbia, KY) and Siemens Medical System (Erlangen, Germany). Those phantoms consist of a solid resin matrix as water equivalent and rods filled by a calcium material (K_2HPO_4 or calcium hydroxyapatite [CaHA]) [5].

Cann and Genant showed that, because of short-term scanner drift and existing differences among scanners, using a calibration phantom simultaneously with the object is necessary [6]. For accurate estimation of the bone density in QCT techniques, a wide range of densities were studied in the full range of probable BMDs such as trabecular (150 mg/cm^3) and extremity cortical (about 1200 mg/cm^3) [7].

Quantification of vBMD needs a phantom mimicking characteristics of bone in CT scanner, meaning a phantom with linear attenuation coefficient (μ) equal to that of the bone is needed. In this study, we evaluated the accuracy and precision of a handmade QCT phantom for whole-body spiral CT scanners for quantitative assessments.

Methods and Materials

Phantom Designing

The phantom consists of a plastic base (polyethylene) with 5 cylinders (diameter of each ∼19 mm) of reference K_2HPO_4 (liquid). The polyethylene as a base is not a reference material for quantification and is used only for the protection and maintenance of the cylinders. Also, the bottom of the phantom conformed to the flat CT scanner table. The polyethylene has the mechanical properties as follows: physical density, Young's modulus, and yield-stress equal to 958 Kg/m^3, 900 MPa, and 23 MPa, respectively, showing the degree of flexibility of the matter. Moreover, to calculate the von Mises tension contour plan, a permissible weight (90 Kg), was performed as following steps in the block diagram shown in Figure 1 and described in the following:

Modelling

In the first step, the phantom was modelled in the ABAQUS software (Abaqus 6.14, Dassault Systems Simulia Corp, RI) based on its true mechanical properties, such as Poisson ratio and elastic modulus. Dimensions of the phantom were indicated according to the dimensions measured on the QCT Mindways phantom.

Loading

The model aims to simulate von Mises stress on the phantom corresponding with a 90-kg standard back-laying body weight load. To represent the adequate strength of the phantom material (polyethylene), an isotropic constitutive law has been implemented into the commercial finite element (FE) code ABAQUS/Standard, which has been suitably developed to fit the phantom properties and the related loadings. As the model has the symmetric criteria on the geometric shape and loading area, using a symmetric model in FE analysis has been an accepted approach for long time. Therefore, as our phantom model has one symmetric plane, only one-half of the object was enough to be modelled and simulated. The loading was applied with the assumption that a 90 kg person puts half of his weight on the phantom when he is laying. Because

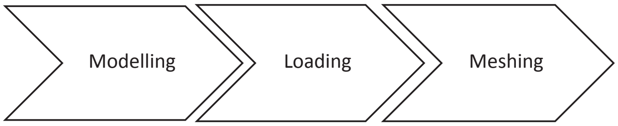

Figure 1. Block diagram of mechanical testing steps.

half of the phantom was simulated, half of the load was symmetrically performed on it.

Meshing

In the next step, the model was meshed by tetrahedral elements for tension analysis and safety factor calculation.

K_2HPO_4 Solution

A liquid phantom was been used in our research to generate conversion equations to map Hounsfield units (HU) to BMD in which hydrogen dipotassium phosphate (K_2HPO_4) (7758-11-4 - (Merck)) was used. The reference material (K_2HPO_4 solution) has the effective atomic number same as HA (15.58 vs. 15.86 for HA at 80 keV) with various concentrations of 0, 50, 100, 200, 400, 1000, and 1200 mg/cc of K_2HPO_4 in water as standards to cover a wide range of bone density values. The solution samples were prepared in sterile situation in terms of having a known concentration of the solute in deionized water solvent (18 μΩ). For the calibration phantom, the concentrations were selected based on commercial QCT Mindways spine calibration phantom (0, 50, 100, and 200 mg/cm^3) as low concentration (LC). Close to 90% of all patient examinations have trabecular bone densities in the range of 50 to 200 mg/cm^3 [8]. For high concentration (HC) range, the solutions 400, 1000, and 1200 mg/cm^3 were made. The solubility of K_2HPO_4 is about 1600 mg/cc [9].

The mean HU for each cylinder were determined against the known K_2HPO_4 concentrations as a calibration equation (Equation1):

$$\text{CT number} = a * K_2HPO_4\ \text{Concentration} + b, \qquad (1)$$

where a and b are the slope and intercept associating with CT number to K_2HPO_4 concentration, respectively.

Phantom Validation

Image Acquisition

Image acquisitions were carried out on 16-row Siemens Emotion CT scanner in Imam Khomeini Hospital (Tehran), with exposure settings as follows; tube voltage 110, tube current about 65, pitch 0.92, pixel size 0.65 mm, 343×343 mm^2 field of view and exposure time 0.6s, slice thickness 2 mm, and B41s kernel in an abdomen routine exam.

Images were analysed with an open-source Java image processing software (Image J). A circular region of interest was placed at the center of each reference level (approximately 50% of the circular area) in the calibration phantom in each image for avoiding edge effects.

Accuracy

For verifying accuracy of the phantom, the intermediate concentrations were made individually, three times, and were filled into three separate centrifuged tubes. This strategy reduced the human errors associated with the preparation of the target densities. For the calibration phantom with accepted reference values 0, 50, 100, 200 mg/cm^3 and alcohol, the intermediate concentrations of 30, 75, and 150 mg/cm^3 were chosen as hypothetical patients' BMD. Based on the American College of Radiology guidelines for QCT, osteoporosis and osteopenia have their upper thresholds at 80 and 120 mg/cm^3, respectively [10]. For the HC phantom (400, 1000, and 1200 mg/cm^3), the concentration of 700 and 1100 mg/cm^3 were chosen as intermediate densities and these were scanned with HC phantom simultaneously. It should be noted that these tests were repeated 3 times.

A percentage of relative error is defined as the closeness of values between the average measurements of quantity

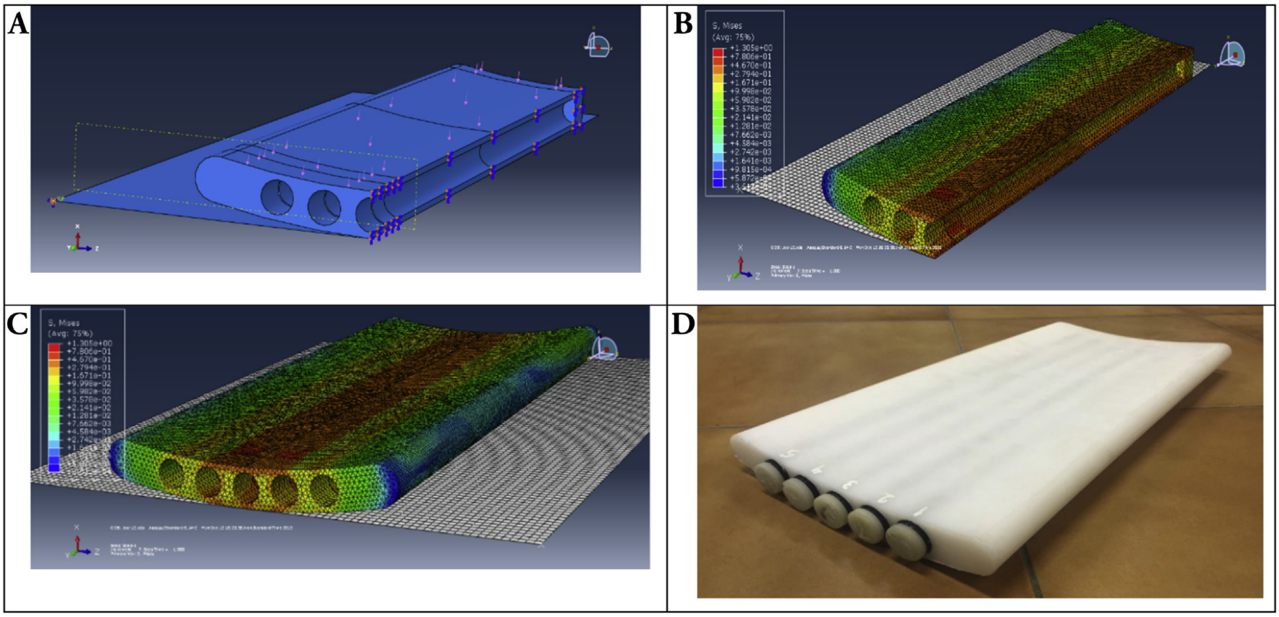

Figure 2. The (A) loading and (B and C) meshing onto the phantom in half of the phantom structure with von Mises stress analysis performed in the ABAQUS software (D) The photographic of the synchronous QCT calibration phantom.

Table 1
The Average and Relative Errors for Different Concentrations (Hypothetical Patients) 30, 75, 150, 700, and 1100 mg/cm^3 Over 3 Months

Concentration (μ) mg/cm^3	Low Concentration (LC)			High Concentration (HC)	
	30	75	150	700	1100
Average ($\bar{A}$) mg/cm^3	28.98	71.22	149.60	735.51	1080.25
Relative Error (%)	3.50	5.04	0.26	5.07	1.79

obtained from series of test results ($\bar{A}$) and the accepted reference values (μ) divided on μ in this study (Equation 2).

$$\%\text{Relative Error} = \left(\left(\bar{A} - \mu\right)/\mu\right) * 100 \tag{2}$$

Linear regression analysis between the reference values and BMD were performed.

Precision

Precision was determined by acquiring five sets of calibration data over 3 months, where the calibration phantoms under identical ambient and imaging conditions were scanned and stored away from direct light and heat at all other times. The mean and coefficient of variation (CV%) for HU measurements were calculated for each concentration.

Results

Figure 2 shows the loading and meshing onto the half of the phantom in which the von Mises stress analysis performed in the ABAQUS software. It is noticeable that the maximum von Mises stress is estimated 1.3 Mpa on the critical point in the midline of the phantom.

Along with this designed phantom, measured versus the true values were examined to assure the validity of the methods. Table 1 displays the highest percentage of the relative error for LC and HC phantoms among five and three tests, respectively.

Based on linear relationship between CT number and the standards concentration (Equation 1), the R^2 for both phantoms in different measurements are close to 1. Moreover, the y-intercepts (b) are lower in LC phantom than HC (Table 2).

Precision was determined by measuring the coefficient of variation (CV%) for HUs in each concentrations over the 3 months. The results in Table 3 show that the highest CV% is 4% for 50 mg/cm^3 standard and the lowest is 0.2% for 1200 mg/cm^3 standard.

Table 2
The Slopes and Intercepts Arise From the Calibration Equation (Equation 1) for LC and HC Phantoms

QCT Phantom	Test	Slope	Intercept	r^2
Low Concentration (LC)	1	1.505	4.30	0.999
	2	1.426	5.80	0.998
	3	1.662	0.52	0.999
	4	1.574	−1.83	0.999
	5	1.570	−0.52	0.999
High Concentration (HC)	1	0.977	162.99	0.986
	2	1.020	111.37	0.987
	3	1.015	118.50	0.988

Table 3
The Stability of CT Numbers (HUs) for Each Concentration Were Determined via Measuring the Mean (M), Standard Deviation (SD) and Coefficient of Variation (CV)

Standards (mg/cc)	50	100	200	400	1000	1200
M (HU)	77.37	160.50	315.58	509.03	1184.57	1298.51
SD (HU)	3.13	4.88	8.06	3.71	3.29	2.63
CV%	4.0	3.0	2.5	0.7	0.3	0.2

Moreover, in this study, only sensitivity of the low ranges of concentration were investigated (10–100 and 100–200 mg/cm^3) (Figure 3) ($R^2 \geq 0.96$).

Discussion

To date, quantitative extraction of structural features using 3D bone scans could open the door to introducing a practical method for accurate diagnosis of bone-related diseases. There are several different BMD quantification strategies using a CT scanner, with different calibration phantoms (solid and liquid) or only CT number base [2,11–13]. Hence, owing to the role of the calibration phantom, which translates the computed tomography Hounsfield units to the bone units (mg/cm^3) in this study, one should pay attention to practical methodology for making an in-house QCT calibration phantom.

In this study, based on ABAQUS software, the most critical stress area is revealed by FE simulation on the midline of the curve area in the phantom and based on the ratio of polyethylene yield-stress (23 Mpa) to numerical estimation of maximum von Mises stress at the most critical point (1.3 Mpa), a 17.7 safety factor were calculated, which is apparently acceptable.

The liquid calibration phantom (K_2HPO_4) can be used to assess equivalent bone density with acceptable accuracy. The results showed that percentage of relative error was up to 5.1% (Table 1). This study revealed the stability of K_2HPO_4 calibration phantoms over a limited duration of 3 months, with less than 4% variation from the initial to the end time point for 50 mg/cm^3 and 0.2% for the highest concentration (1200 mg/cm^3) (Table 3). Therefore, these liquid phantoms were shown not to be leakage and bubble for at least 3 months and should get refilled after 3 months as recommended in the other study [7]. The relatively long life of the K_2HPO_4 calibration phantom makes this QCT calibration phantom a reasonable method for BMD quantification. However, sensitivity and long-time reproducibility, especially for high-concentration calibration phantoms, must be investigated. The K_2HPO_4 liquid calibration phantom has some advantages: a cost-effective measurement system, easy to make, and convenient means to provide various concentrations including high values. One of the main disadvantages of a liquid phantom is the bubble generation in the K_2HPO_4 solution, which was reduced by using an ultrasonic bath to

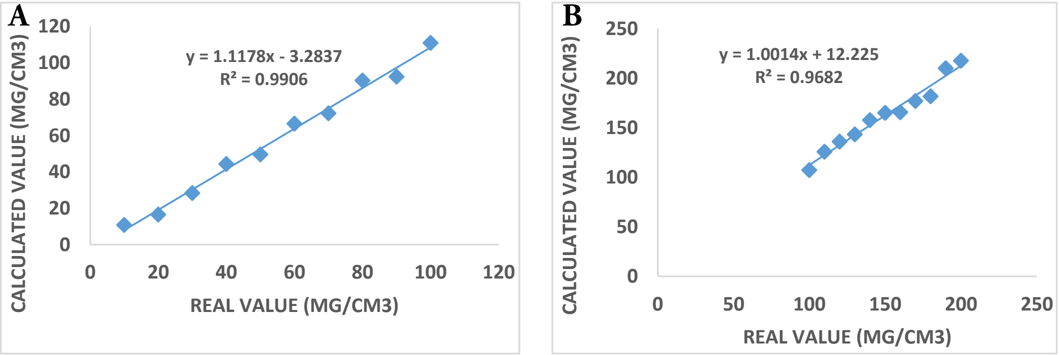

Figure 3. The sensitivity tests for two ranges of K_2HPO_4 concentration (A) (10–100 mg/cm^3) (B) (100–200 mg/cm^3).

vibrate the trapped microbubbles and make them surface during the process of solution-making and capping in this study. It should be noted that, giving extra time before the capping was another strategy for avoiding the generation of bubbles.

In this study, the linear relationship between the concentration and CT number was seen for low and high concentrations, as well as Smith et al, who confirmed that linear relationship achieved between predicted cortical BMD values via extrapolation from LC solid standards and high-density phantom under standard exposure (120 kVp and 220 effective mAs) [14]. These relationships depend on the scanner settings and protocol, as well as anatomical site and phantom type (liquid/solid). In this work, the slopes for the equations were about 0.9–1.6 for the phantoms, which were comparable with other study [12]. In the LC phantom, because of low standard concentration, 0 mg/cm^3, y-intercept (b) was small (<4.3 HU). While in the HC phantom with higher concentration of K_2HPO_4, 400 mg/cc, there was a relatively high intercept (>100 HU).

Regarding the measure of sensitivity, the relationship between calculated values and true standards are strong (R = 0.9).Then in low ranges, the sensitivity is reliable in terms of measuring low BMD (Figure 3).

The using of QCT bone mineral measurement has been controversial. One of these controversies is related to the radiation dose. Recently, by the advent of new generation of scanners (eg, dual-layer detector and iterative-based reconstruction scanner), the radiation dose challenges could be solved [15].

The results of this study provide the practical directions for applying homemade calibration phantom for BMD quantification in QCT technique. However, there exist some limitations. First, the results were obtained by only a specific system (16-row Siemens Emotion CT scanner), which might not correlate with other brands directly. Therefore, the scanner-dependency of the results should be considered in future studies. Second, the range of concentrations could be extended to wider range of densities. Third, technical parametric tests such as slice thickness, pixel size, distance from isocenter, etc. could be considered to reduce the source of error. Finally, QCT under iterative reconstruction, especially for the HC standards in calibration phantoms, needs to be investigated in future studies.

Conclusion

This study revealed the stability of a K_2HPO_4 calibration phantom over a limited duration of 3 months. In addition, the wide dynamic ranges of concentrations could be used for low- and high-density bone quantification with an acceptable percentage of relative error.

Footnotes

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Competing interests: All authors have completed the ICMJE uniform disclosure form at www.icmje.org/coi_disclosure.pdf and declare: no financial relationships with any organizations that might have an interest in the submitted work in the previous three years; no other relationships or activities that could appear to have influenced the submitted work.

Ethics approval: Not required.

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