J Neurol Disord
Volume 10:5, 2022

Journal of Neurological Disorders

Research Article

Open Access

Feasibility of Assessing Bone Mineral Density Based on Hydroxyapatite-(Iodine) Image Analysis in Contrast-Enhanced Dual-Energy Spectral CT Imaging

Mingyue Zhao[1], Yijun Liu[1*], Lei Liu[2], Zijing Zhang[1], Jianying Li[3] and Wei Wei[1]

[1]Department of Radiology, The First Affiliated Hospital of Dalian Medical University, PR China
[2]Department of Urology, The First Affiliated Hospital of Dalian Medical University, PR China
[3]Department of GE Healthcare, Computed Tomography Research Center, PR China

Abstract

Objective: To explore the feasibility of using hydroxyapatite (HAP) measurement based on the material decomposition in dual-energy spectral CT imaging to evaluate bone mineral density (BMD).

Methods: 247 patients (aged 16 to 97 years, 156 males and 91 females) who underwent both unenhanced and contrast-enhanced (arterial, venous and delayed) phase abdominal dual-energy spectral CT were retrospectively collected. Patients were divided into four groups according to their ages: group A (<30 years, n=40), group B (30-49 years, n=90), group C (50-69 years, n=73) and group D (≥70 years, n=44). HAP densities of trabecular bone of the third lumbar vertebrae in four phases were measured on the HAP material decomposition images using HAP-Iodine as the basis material pair and recorded. HAP as function of age was established and measurements in four phases were statistically compared using that in unenhanced phase as the reference standard.

Results: No statistical difference was found in HAP value among different imaging phases (P>0.05). The HAP value was positively correlated with age in group A (r=0.393, P<0.05) and negatively correlated with age in groups B, C and D (r=-0.298, -0.361, -0.361, P<0.05), and overall high negative correlation with age for patients ≥30years (r=-0.775, P<0.05).

Conclusion: The HAP measurement is not affected by contrast agent and stable in different imaging phases in dual-energy spectral CT, enabling a phase-independent HAP measurement. HAP has correlation with age which may be used to reflect the change of vertebral BMD, providing a reference for evaluating BMD according to the linear regression equation.

Keywords: Bone mineral density • Dual-energy spectral CT imaging • Material decomposition technique • Hydroxyapatite • Iodine

Abbreviations

(HAP) Hydroxyapatite; (BMD) Bone Mineral Density; (DXA) Dual Energy X-ray Absorptiometry; (QCT) Quantitative CT

Introduction

Bone mineral density (BMD) is an important index of bone strength, which can reflect the physiological or pathological alterations of bone mass. The decrease of BMD is directly related to several bone diseases [1], and BMD also changes with age. Osteoporosis has become an important public health issue [2]. The measurement of BMD has an important clinical significance for the prevention, diagnosis and treatment of bone diseases [3]. Therefore, improving the methods for the measurement of BMD will have a profound clinical value.

At present, the methods of measuring BMD include dual energy X-ray absorptiometry (DXA), quantitative CT (QCT), quantitative ultrasound, MRI, and dual-energy CT [4]. Among them, DXA and quantitative CT are the widely employed techniques [5,6]. However, DXA cannot accurately distinguish the cortical bone and trabecular bone, and thus what is measured in DXA is the total density, which is easily affected by surrounding structures [7,8]. For QCT, the complicated operation and the high radiation dose limited its application. In recent years, dual-energy CT has been widely accepted in clinical applications. It has been proposed that the BMD of vertebrae may be measured in body dual-energy imaging, such as abdominal CT, which does not increase the radiation burden.

One of the methods to realize dual-energy CT uses the rapid dual tube voltage (kVp) switching technology (dual-energy spectral CT) [9]. According to the material decomposition theory in dual-energy spectral CT, the object imaged by the high and low tube voltages can be expressed as the density images of two basic materials [10]. Each individual voxel in the material decomposition images reflects the corresponding material density information, which provides more specific and accurate measurement of material density. Theoretically, the selection of basis material pairs is not limited. Any two natural substances can be selected, and they would be specific identifiable markers for tissues when they are the main components of tissues [11]. Multiple clinical studies have mentioned the application of dual-energy CT basis material pairs [12,13], especially in the field of measuring BMD. It is a highly sensitive BMD measurement method, which can reflect the changes of bone mineral content in the early stage. Van Hamersvelt et al. [14] inferred that dual-energy CT allowed accurate BMD quantification in vitro by using two validated anthropomorphic phantoms with material-specific known concentrations and found a strong correlation between BMD measured by dual-energy CT and DXA. Zhou et al. [15] analyzed the densities of four basis material pairs [DCa (Water), DHAP

---

[*]**Address for Correspondence:** *Yijun Liu, Department of Radiology, The First Affiliated Hospital of Dalian Medical University, PR China, Email:yijunliu1965@126.com*

Copyright: *©2022 Liu Yijun et al. This is an open-access article distributed under the terms of the creative commons attribution license which permits unrestricted use, distribution and reproduction in any medium, provided the original author and source are credited.*

Received: 02-May-2022, Manuscript No. jnd-22-63925; **Editor assigned:** 04-May-2022, PreQC No. P-63925 (PQ); **Reviewed:** 18-May-2022; QC No. Q-63925; **Revised:** 23-May-2022, Manuscript No. R-63925; **Published:** 30-May-2022, **DOI:** 10.4172/2329-6895.10.5.494

(Water), DCa (Fat) and DHAP (Fat)], with significant correlations found between BMD values measured by dual-energy CT and QCT. To date, few studies have investigated the use of dual-energy spectral CT.

Traditionally, the accurate measurement of BMD in CT requires the use of unenhanced scans to avoid the impact of iodine contrast. However, there are a lot of contrast-enhanced-only dual-energy spectral CT scans in clinical applications, and the requirement for unenhanced scans would mean additional radiation dose to patients for BMD measurement [16]. Our hypothesis was that when using an appropriate basis material pair in dual-energy spectral CT, such as HAP and iodine pair, the impact of iodine contrast on the measurement accuracy of HAP density could be greatly reduced or removed in contrast-enhanced phases. Therefore, the purpose of the present study was to investigate the stability of HAP measurement value using HAP and iodine as the basis material pair in both the unenhanced and contrast-enhanced phases and also evaluate the feasibility of using HAP density to reflect the correlation between age and BMD, which may provide a reference for clinical diagnosis under the condition of reducing radiation dose and examination cost of patients.

Methods

Patient selection

This retrospective study was approved by our institutional review board, and the requirement for informed consent was waived. Data from subjects who underwent both the unenhanced and contrast-enhanced abdominal dual-energy spectral CT examinations for diagnosing abdominal diseases from December 2019 to July 2020 were collected (n=270). The exclusion criteria included iodine contrast agent adverse reaction; spinal tumor; spinal tumor-like lesions or infection; lumbar fracture; spinal surgery (implants, hardware, or other foreign material); severe degenerative changes; deformity; and other diseases that affect bone mineral density (such as hematologic disorder, rheumatic diseases, endocrine diseases, long-term use of hormones, etc.). Finally, 156 males and 91 females were enrolled following the guidelines of standard diagnostic reports and images (ages ranged from 16 to 97 years, mean age: 50 ± 19 years). Patients were divided into four groups according to their ages: group A (<30 years, n=40), group B (30-49 years, n=90), group C (50-69 years, n=73) and group D (≥ 70 years, n=44).

Examination methods

All patients were scanned on a 256-slice CT scanner (Revolution CT, GE Healthcare, USA) using the dual-energy spectral CT imaging mode. The scans included both the unenhanced and contrast-enhanced (arterial, venous and delayed) abdominal scans, and the scan range was from the superior border of the diaphragm to the inferior border of the pubic symphysis. The scanning parameters were as follows: fast tube voltage switching between 80 and 140 kV, pitch 0.992, gantry rotation time 0.6 s, SFOV 50 cm. The standardized iodine contrast agent injection scheme was adopted (iodine intake was calculated based on the patient's body weight: 500 mgI/kg, injection rate=(contrast agent dosage+physiological saline dosage) ml/25 s, and iohexol (350 mgI/ml) or ioversol (320 mgI/ml) was applied. Contrast agent was injected via the median elbow vein using a dual-tube power injector (Ulrich, German). The material decomposition images using HAP and iodine as the basis material pair were reconstruction at the slice thickness of 1.25mm.

Image analysis

The HAP and iodine-based images of four phases were transferred to an AW 4.7 workstation (GE Healthcare, USA). The HAP (Iodine) density was measured on the HAP-based material decomposition images by a radiologist with three years of experience in musculoskeletal imaging. Region of interest (ROI) was placed in the middle layer of the third lumbar vertebral body (L3) with a distance of more than 5mm from the vertebral edge to avoid vertebral vein plexus and bone island [17] (Figure 1). Three consecutive slice levels were measured, and ROIs were remained the same at about 100 mm^2. The average value of the three measurements was taken and the unit of density of HAP (Iodine) was expressed in 2 mg/cm^3.

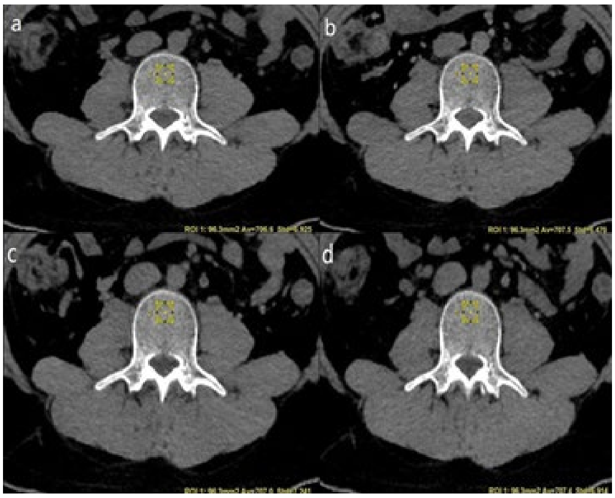

Figure 1. The HAP-based material decomposition images in dual-energy spectral CT using HAP and iodine as the basis material pair. The examples of ROIs were set on the third lumbar vertebral trabecular bone. (a), (b), (c), (d) are corresponding images in four phases (unenhanced, arterial, venous, and delayed phases). The iodine contrast was largely removed in the enhanced images.

Statistical analysis

All statistical analyses were performed using SPSS 24.0 (SPSS Inc. Chicago, IL). The HAP (Iodine) value in the unenhanced phase was used as the reference standard to evaluate the accuracy of HAP measurements. The repeated measures analysis of variance with bonferroni correction was used to compare the differences among the density measurements in four phases; Pearson correlation analysis was performed between HAP (Iodine) value and age in different age groups; by using the linear regression analysis, a fitting curve model and linear regression equation between HAP (Iodine) value and age could be established. Values were listed as mean with standard deviation (SD), unless stated otherwise. P<0.05 was considered to indicate statistical significance.

Results

No statistical difference was found in HAP (Iodine) value among different imaging phases [F (2.708, 666.275) =1.454, P>0.05]. The deviation of HAP (Iodine) value between enhanced phases and unenhanced scan was close to 0 (Figure 2).

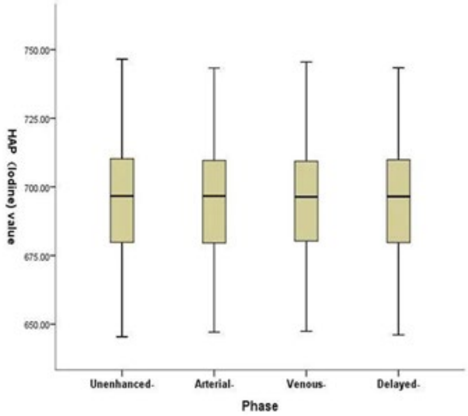

Figure 2. Box-and-Whisker plot. The HAP (Iodine) value in the four phases with stable trend.

The scatter plots of correlation between HAP (Iodine) value and age in different age groups were shown in Figures 3A-3D. In group A for patients with ages <30 years, HAP (Iodine) value was positively associated with age (r=0.393, P<0.05), HAP= 1.110* age+689.54 2 mg/cm^3. A negative relationship between HAP (Iodine) value and age was observed in group B (30-49 years) (r=-0.298, P<0.05), HAP=-0.833* age+740.04 2 mg/cm^3. The value of HAP (Iodine) was negatively correlated with age in group C (50-69 years) (r=-0.361, P<0.05), HAP=-0.871* age+735.08 2 mg/cm^3. In group D (≥ 70 years), the value of HAP (Iodine) showed a negative relationship with age (r=-0.361, P<0.05), HAP=-0.662* age+723.44 2 mg/cm^3. In addition, we found the value of HAP (Iodine) was highly negatively related to age in the age ≥ 30 years group (r=-0.775，P<0.05), HAP= -0.939* age+742.66 2 mg/cm^3 (Figure 4).

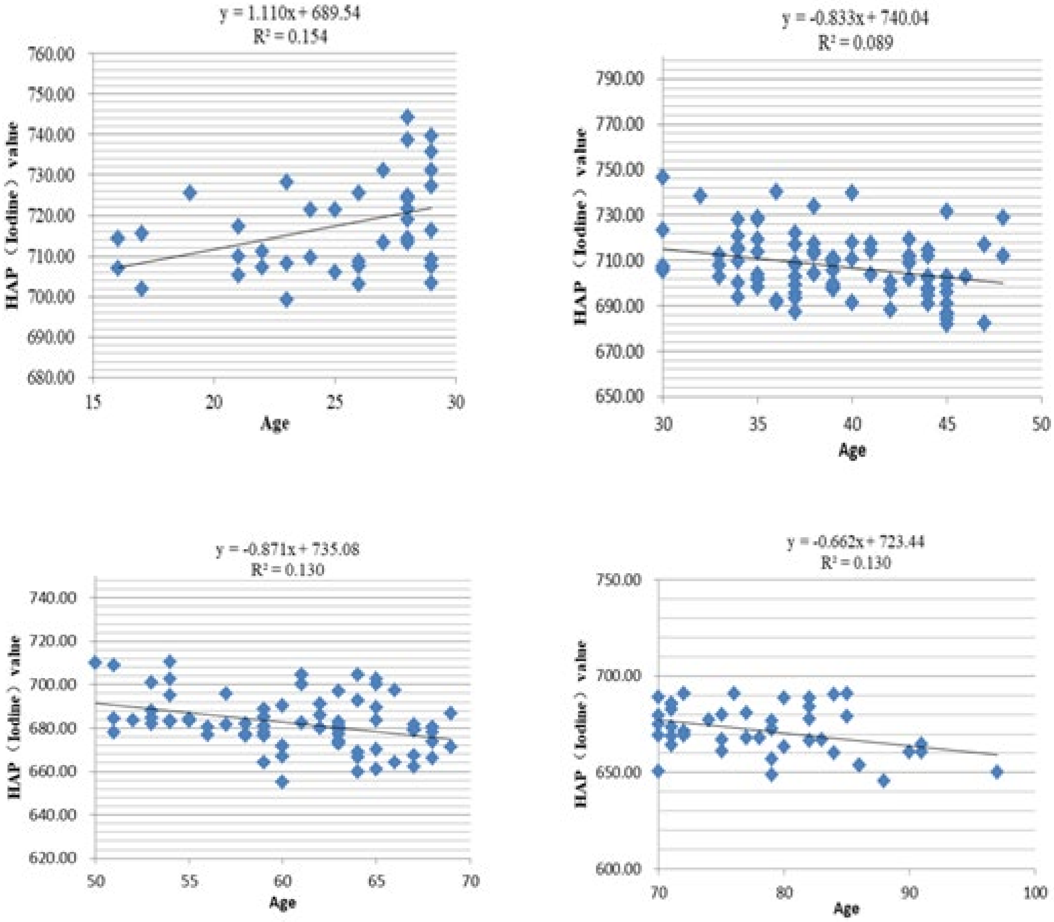

Figure 3. 3A: Scatter diagram between HAP (Iodine) value and age in group A; 3B: Scatter diagram between HAP (Iodine) value and age in group B; 3C: Age-related scatter diagram of HAP (Iodine) value in group C; 3D: Age-related scatter diagram of HAP (Iodine) value in group D.

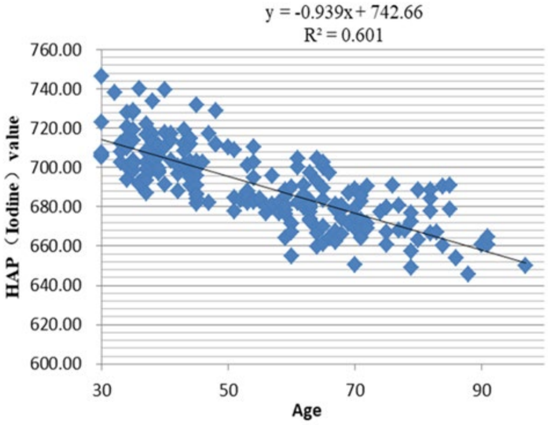

Figure 4. Scatter diagram between HAP (Iodine) value and age in the age ≥ 30 years group.

Discussion

The application of dual-energy spectral CT has broken the limitations conventional CT imaging to provide quantitative material composition analysis, which greatly expands the applications of CT technique in clinical practice and provides a better research platform for radiologists [18]. The material decomposition technique in dual-energy spectral CT is based on the fact that any substance can be expressed by the combination of other two basic materials in a corresponding proportion [19]. The measured value of the basis material pair can reflect the relative composition of materials in the tissue to make a relatively quantitative description of the relevant indicators [20]. Dual-energy CT has been proposed as an alternative for 3D volumetric assessment of bone mineral density [21]. Studies have shown that the density of HAP can indirectly reflect the changes of bones with age, thus provides a novel method for measuring BMD [22,23]. Dual-energy spectral CT can exclude the influence of cortical bone, and the measured value is more representative [24]. So far, HAP and water, HAP and fat are the two most common basis material pairs applied in the research of dual-energy CT imaging. In our study, we employed HAP and iodine to express vertebral bone mineral density in both unenhanced and enhanced images. In the contrast-enhanced CT scans, the contrast medium containing iodine will flow into the bones, increasing x-ray attenuation which will introduce phase-dependent attenuation value (CT number) measurement variation in the conventional CT imaging. Our study would potentially expend the database to survey population BMD using existing contrast-enhanced CT images.

Lumbar spine is the most common and earliest site where osteopenia occurs. Trabecular bone is more sensitive to bone mass reduction and lumbar vertebral body is rich in homogeneous trabecular bone. Therefore, lumbar vertebral trabecular bone is a common location for measuring bone mineral density [25,26], and L3-L5 are the sites prone to degeneration due to the anatomical and physical reasons. HAP is the main component of trabecular bone and its content determines bone mineral density of the vertebral body. In our works, the trabecular bone in the middle part of the third lumbar vertebral body without obvious pathological changes was selected as the measurement site of bone mineral density. ROIs were placed on the homogeneous trabecular bone and the abnormal areas were avoided as far as possible [17].

Our study also investigated the relationship between bone mineral density and age using HAP density values. HAP (Iodine) value was positively correlated with age for patients 30 years and younger, while negatively correlated with age for patients older than 30 years of age, indicating BMD peaked around the age of 30. The correlation between HAP density and age may be fitted to generate linear regression equation and to predict the HAP (Iodine) value threshold for diagnosing osteopenia and osteoporosis. Together, our results showed that HAP density values in the unenhanced and contrast-enhanced images had no statistically significant difference, and the HAP value in any contrast-enhanced phase would be suitable for representing BMD. The measurement of HAP (Iodine) density in bones based on dual-energy spectral CT material decomposition technique could provide a new way for evaluating bone mineral density during the enhanced phases. Material-specific measurements were an adequate alternative for the detection of patients with low BMD in routine clinical practice without additional osteodensitometry examination to save radiation dose and medical cost.

Some limitations of this study should be discussed. Firstly, the composition of trabecular bone is complex [marrow (mainly fat), water, collagen, and bone minerals] [26], only using HAP and iodine as basis material pair may decrease the accuracy. Thus, HAP and other components (fat, water, etc.) should also be included as basis material pairs to provide extra diagnostic evidence. Secondly, this was a preliminary study and patients had only undergone dual-energy spectral CT examinations. The HAP (Iodine) value as a surrogate measurement maybe not perfect tool for diagnosing osteoporosis. Thirdly, there was no detailed screening and grouping for the patient cohort, we did not separate male and female, BMD may be affected because of differences in gender, thus affecting HAP (Iodine) value [27], which can be used as the follow-up research content. In the future, other sensitive parts of bone alterations should also be introduced, such as thoracic vertebrae and femoral neck [28], to collect more data and establish a larger database of multiple basis material pairs for monitoring bone mineral density.

Conclusion

Dual-energy spectral CT material decomposition technique has opened a new field of application for measuring bone mineral density. HAP and iodine as basis material pair in dual-energy spectral CT can reflect the changes of vertebral BMD with age. The measured value is consistent in both the unenhanced and contrast-enhanced phases. Dual-energy spectral CT may provide greater flexibility regarding BMD assessment in clinical routine and reduce radiation exposure by avoiding the unenhanced examination. Meanwhile, HAP (Iodine) values for patients of different ages can be predicted according to the linear regression equation, which provides a reference for the clinical evaluation of bone mineral density.

Acknowledgement

None.

Conflict of Interest

All authors declare that they have no conflicts of interest.

References

1. Bousson, V, Bergot C, Meunier A and Barbot F, et al. “CT of the middiaphyseal femur: Cortical bone mineral density and relation to porosity.” *Radiology* 217(2000):179-87.
2. Pickhardt, PJ, Lee SJ, Liu J and Yao J, et al. “Population-based opportunistic osteoporosis screening: Validation of a fully automated CT tool for assessing longitudinal BMD changes.” *Br J Radiol* 92(2019): 20180726.
3. Berry, SD, Dufour AB, Travison TG and Zhu H, et al. “Changes in bone mineral density (BMD): A longitudinal study of osteoporosis patients in the real-world setting.” *Arch Osteoporos* 13(2018):124.
4. Oei, L, Koromani F, Rivadeneira F and Zillikens MC, et al. “Quantitative imaging methods in osteoporosis.” *Quant Imaging Med Surg* 6(2016): 680-698.
5. Gnudi, S, Sitta E and Fiumi N. “Bone density and geometry in assessing hip fracture risk in post-menopausal women.” *Br J Radiol* 80(2007): 893-7.
6. Sollmann, N, Franz D, Burian E and Loffler MT, et al. “Assessment of paraspinal muscle characteristics, lumbar BMD, and their associations in routine multi-detector CT of patients with and without osteoporotic vertebral fractures.” *Eur J Radiol* 125(2020):108867.
7. Stewart, KJ, Deregis JR, Turner KL and Bacher AC, et al. “Fitness, fatness and activity as predictors of bone mineral density in older persons.” *J Intern Med* 252(2002):381-8.
8. Sung, KH, Choi Y, Cho GH and Chung CY, et al. “Peripheral DXA measurement around ankle joint to diagnose osteoporosis as assessed by central DXA measurement.” *Skeletal Radiol* 47(2018): 1111-1117.
9. Matsumoto, K, Jinzaki M, Tanami Y and Ueno A, et al. “Virtual monochromatic spectral imaging with fast kilovoltage switching: improved image quality as compared with that obtained with

conventional 120-kVp CT." *Radiology* 259(2011): 257-62.

10. Ascenti, G, Siragusa C, Racchiusa S and Ielo I, et al. "Stone-targeted dual-energy CT: A new diagnostic approach to urinary calculosis." *Am J Roentgenol 195(2010):953-8.*
11. Son, W, Park C, Jeong HS and Song YS, et al. "Bone marrow edema in non-traumatic hip: high accuracy of dual-energy CT with water-hydroxyapatite decomposition imaging." *Eur Radiol* 30(2020):2191-2198.
12. Lv, P, Zhang Y, Liu J and Ji L, et al. "Material decomposition images generated from spectral CT: detectability of urinary calculi and influencing factors." *Acad Radiol* 21(2014):79-85.
13. Huang, HC, Srinivasan R, Sun Y and Kazakia GJ, et al. "Detection of lumbar spine osseous metastases using dual-energy CT: Phantom results and preliminary clinical validation." *Am J Roentgenol* 212(2019):402-410.
14. Van, Hamersvelt RW, Schilham AMR, Engelke K and Den Harder AM, et al. "Accuracy of bone mineral density quantification using dual-layer spectral detector CT: A phantom study." *Eur Radiol* 27(2017):4351-4359.
15. Zhou, S, Zhu L, You T and Li P, et al. "In vivo quantification of bone mineral density of lumbar vertebrae using fast kVp switching dual-energy CT: Correlation with quantitative computed tomography." *Quant Imaging Med Surg* 11(2021): 341-350.
16. Abdullayev, N, Neuhaus VF, Bratke G and Voss S, et al. "Effects of contrast enhancement on in-body calibrated phantomless bone mineral density measurements in computed tomography." *J Clin Densitom* 21(2018):360-366.
17. Marinova, M, Edon B and Wolter K. "Use of routine thoracic and abdominal computed tomography scans for assessing bone mineral density and detecting osteoporosis." *Curr Med Res Opin* 31(2015):1871-81.
18. Marinova, M, Edon B, Wolter K and Katsimbari B, et al. "Material separation using dual-energy CT: current and emerging applications." *Radiographics* 36(2016):1087-105.
19. Shinohara, Y, Sasaki F, Ohmura T and Itoh T, et al "Evaluation of lumbar intervertebral disc degeneration using dual energy CT virtual non-calcium imaging." *Eur J Radiol* 124(2020): 108817.
20. Zhang, D, Li X and Liu B. "Objective characterization of GE discovery CT750 HD scanner: Gemstone spectral imaging mode." *Med Phys* 38(2011):1178-88.
21. Mallinson, PI, Coupal TM, McLaughlin PD and Nicolaou S, et al. "Dual-Energy CT for the Musculoskeletal System." *Radiology* 281(2016):690-707.
22. Roski, F, Hammel J, Mei K and Baum T, et al. "Bone mineral density measurements derived from dual-layer spectral CT enable opportunistic screening for osteoporosis." *Eur Radiol* 29(2019): 6355-6363.
23. Wichmann, JL, Booz C, Wesarg S and Kafchitsas K, et al. "Dual-energy CT-based phantomless in vivo three-dimensional bone mineral density assessment of the lumbar spine." *Radiology* 271(2014):778-84.
24. WGIPDC. "Technical standardization for dual-energy x-ray absorptiometry." *J Clin Densitom* 7(2004):27-36.
25. La, Fontaine J, Shibuya N, Sampson HW and Valderrama P. "Trabecular quality and cellular characteristics of normal, diabetic, and charcot bone." *J Foot Ankle Surg* 50(2011):648-53.
26. Nickoloff, EL, Feldman F and Atherton JV. "Bone mineral assessment: New dual-energy CT approach." *Radiology* 168(1988):223-8.
27. Khadilkar, AV and Mandlik RM. "Epidemiology and treatment of osteoporosis in women: An Indian perspective." *Int J Womens Health* 7(2015):841-50.
28. Mao, SS, Li D, Luo Y and Syed YS, et al. "Application of quantitative computed tomography for assessment of trabecular bone mineral density, microarchitecture and mechanical property." *Clin Imaging* 40(2016):330-8.

How to cite this article: Liu, Yijun, Mingyue Z, Lei L and Zijing Z, et al. "Feasibility of Assessing Bone Mineral Density Based on Hydroxyapatite-(Iodine) Image Analysis in Contrast-Enhanced Dual-Energy Spectral CT Imaging" *J Neurol Disord* 10(2022):494.