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Opportunistic bone density screening for the abdominal radiologist using colored CT images: a pilot retrospective study

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Abstract

Purpose: The purpose of the study was to develop an accurate and reproducible method for detecting low spinal bone density on abdominal CT images.
Methods: For this IRB-approved HIPAA-compliant single-center retrospective study, nonenhanced CT images of the lower abdomen were obtained in 631 African-American participants. Mean attenuation of L3/L4 was associated with quantitative CT bone density (QCT) in a randomly selected training cohort ($N = 511$), and receiver operating characteristics analysis was used to identify the optimal mean attenuation threshold for differentiating normal from low bone density. Custom image processing software was used to generate grayscale and colored CT images of the midline spine, with green for normal and red for low bone density. Five radiologists independently assessed bone density at L3/L4 in a validation cohort ($N = 120$) using various methods: QCT, visual assessment of sagittal grayscale images (Grayscale), quantitative measurement of mean attenuation on a midline sagittal image (Attenuation), and visual assessment of a midline sagittal colored image (Color). Accuracy was calculated using the average QCT bone density as a reference standard. Inter-observer agreement was assessed using intraclass correlation coefficient (ICC).
Results: The optimal mean attenuation threshold for differentiating normal from low bone density at L3/L4 was 145 Hounsfield Units. The average accuracy of Grayscale, Attenuation, and Color methods was 58, 87, and 91% ($p < 0.001$), respectively. Inter-observer agreement was poor for Grayscale (ICC: 0.20; 95% CI 0.12, 0.28) and excellent for both Attenuation (ICC: 0.85; 95% CI 0.73, 0.91) and Color methods (ICC: 0.87; 95% CI 0.83, 0.90).
Conclusion: Detection of low spinal bone density using colored abdominal CT images was highly accurate and reproducible.

Key words: Osteoporosis—Bone density—Opportunistic screening—Computed tomography

Osteoporosis is a silent disease that is underdiagnosed and undertreated until a fracture occurs, with 1 in 2 women and 1 in 5 men > 50 years at risk for an osteoporosis-related fracture, with mortality rates of 20% in the first year [1–4]. Approximately 10 million Americans have osteoporosis and 33 million have low bone density, both contributing to 1.5 million annual fractures in the U.S [1–4]. There are significant healthcare and economic costs, morbidity, and mortality associated with osteoporotic fractures [1–6].

Screening for low bone density and osteoporosis is underutilized with more than half of insufficiency fractures occurring in patients that were never screened [1–4]. While dual energy X-ray absorptiometry (DXA) is a safe, reliable, noninvasive, and relatively inexpensive method for measuring bone density, DXA is underutilized [1–4, 7].

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Opportunistic screening for low bone density and osteoporosis using routine abdominal computed tomography (CT) images obtained for other purposes offers a potential solution to improve screening efforts [7–12]. There are approximately 74 million CT scans performed annually in the U.S [13]. Opportunistic screening using routine abdominal CT images is applicable to millions of patients and requires no additional cost, patient time, scanner equipment, or radiation exposure [7–12].

Quantitative CT (QCT) to measure spinal bone density is accurate but not a practical opportunistic screening method as it requires advanced post-processing software and is labor intensive and time consuming [1–4]. In clinical practice, many radiologists visually assess grayscale CT images on bone windows to subjectively assess bone density, though the accuracy and inter-observer agreement of this approach is not well characterized.

A recently proposed quantitative opportunistic screening method that utilizes routine abdominal CT images includes measurement of trabecular bone attenuation at L1 on a single sagittal image [7–12]. Despite being accurate and rapid, attenuation measurements of L1 are rarely used in clinical practice as this requires active engagement by the radiologist, multiple computer mouse movements and clicks, and additional time for interpretation of the quantitative information.

There is a need to develop a practical and passive opportunistic screening method to assess for low spinal bone density on routine abdominal CT scans obtained for other purposes, and we hypothesize that this may be accomplished by using color to indicate the spinal bone density status on CT images. Therefore, the objective of this study was to develop an accurate, reproducible, and rapid method for detecting low spinal bone density on abdominal CT images.

Methods

Patient cohort

For this Health Insurance and Portability Accountability Act-compliant institutional review board-approved single-center retrospective study, a post hoc secondary subanalysis of the Genetic Epidemiology Network of Arteriopathy (GENOA) study was performed. The GENOA study is a multi-institutional prospective longitudinal observational sibling cohort study [14]. For this subanalysis, 657 African American participants from Jackson, Mississippi who underwent nonenhanced multidetector CT imaging of the lower abdomen (including L3/L4 levels) between 2008 and 2010 were included. A clinical database captured age, gender, ethnicity, height, weight, body mass index, and medical history related to bone disease (sickle cell disease, presence or absence of spinal hardware, and presence or absence of vertebral body fractures). A minority of participants were excluded from analysis for the following reasons: missing abdominal images ($N = 2$), metallic spinal hardware in the lumbar spine at L3/L4 levels ($N = 12$), absence of the quantitative CT phantom in the axial images ($N = 4$), extreme degenerative sclerosis of the entire L3/L4 vertebra ($N = 5$), sickle cell bone changes in the spine ($N = 2$), or severe compression fracture deformity at L3/L4 ($N = 1$). The final full patient cohort ($N = 631$) was divided into a training cohort ($N = 511$ participants) and a validation cohort ($N = 120$ participants) using a random number generator to select patients. The size of the validation cohort was thought to be the maximal number of QCT bone density measurements that a single reader could complete in a day while maintaining high accuracy.

CT imaging protocol

All participants in the study underwent nonenhanced CT imaging of the lower abdomen with a General Electric (GE) Lightspeed 16 CT scanner (Fairfield, CT) at the University of Mississippi Medical Center. The scanner underwent routine quality assurance testing, including daily recalibration with a water phantom. The CT image acquisitions in the GENOA study were designed to assess the severity of aortic calcified atherosclerotic disease, and the field of view (FOV) for CT imaging therefore included L3 through the mid sacrum. The L1/L2 vertebra, which are typically used for QCT bone density analysis, were not routinely included in the FOV in order to exclude imaging of the kidneys and thereby reduce the number of incidental finding detected and reported in this population-based study. Therefore, bone density analysis focused on the L3/L4 vertebrae. The CT image acquisition protocol included the following parameters: patients in supine position with arms raised, 120 kVp, auto mA, pitch 1.375:1, rotation speed 0.8 s, beam collimator 20, table speed 27.5 mm/s, 35 cm FOV, 1.25 mm axial section thickness and interval and 3.0 mm sagittal section thickness and interval, standard smoothing kernel, and filtered back projection reconstruction. A QCT phantom from Image Analysis Inc. (Columbia, KY) was placed posterior to the patient. The QCT phantom was used for calibration and standardization of QCT bone density analysis and contained three compartments: a water attenuating compartment and two compartments with different concentrations of bone equivalent calcium hydroxyapatite.

CT attenuation measurements in the training cohort

After training and under supervision by an academic abdominal radiologist (A. S.) with 6 years of post-fellowship training experience, a medical student (B. L.)

measured the mean attenuation of the trabecular bone at L3/L4 on the sagittal images from the training cohort ($N = 511$). Philips IntelliSpace version 4.4.543.1 (Philips Clinical Informatics, Foster City, CA) was used to measure the mean attenuation on the CT image corresponding to the midline of the L3/L4 vertebral bodies and on the two contiguous slices to the left and two contiguous slices to right of the midline, for a total of 5 measurements. Circular regions of interest (ROIs) with a 2 cm diameter were placed in the anterior two-thirds of the trabecular portion of the vertebral bodies, with avoidance of the venous plexus, bone lesions, and endplate sclerosis related to degenerative changes. The mean attenuation values were recorded, and an average mean attenuation value for each vertebra was calculated.

QCT bone density measurements in the training cohort

After training and under supervision by an attending body radiologist (A. S.), a medical student (E. V.) performed 3-dimensional QCT bone density analysis at L3/L4 using QCT Pro Software version 5.1 (Mindways, Austin, TX) and using the QCT phantom as an internal reference standard. QCT measurements were made in the training cohort ($N = 511$) while blinded to the mean attenuation measurements. Using the QCT Pro Software, volumetric ROIs were placed in the anterior two-thirds of the trabecular portion of the vertebral bodies, with avoidance of the venous plexus, bone lesions, and endplate sclerosis related to degenerative changes. The QCT Pro software outputs images of all ROIs in 3 orthogonal views, which were checked by an attending body radiologist (A. S.) for accuracy, and measurement revisions were made in a small minority of patients as a part of the quality control process. The bone density at L3/L4 was recorded in mg/cm^3 and associated with the average mean attenuation measurements to identify the optimal average mean attenuation cut point (145 HU) for differentiating normal bone density (≥ 120 mg/cm^3) from low bone density (< 120 mg/cm^3) [4].

Color enhanced detection (CED) spine software

Color Enhanced Detection (CED) Spine Software version 0.50 (Jackson, Mississippi) was developed by an attending body radiologist (A. S.) in collaboration with software engineers from ImageIQ (Cleveland, Ohio). The CED Spine Software is post-processing imaging software that was designed to export paired grayscale and colored CT image of the spine ($N = 2$ images). Axial CT images are loaded into the software, and a single grayscale sagittal image of the central aspect of the spine is generated with 20 mm section thickness and a Gaussian smoothing algorithm applied. The 20 mm section thickness and smoothing algorithm are designed to increase volume averaging of the central trabecular bone in 3 orthogonal planes. A duplicate color image is generated by applying a color palette that assigns green color to normal bone density (pixel values with attenuation ≥ 145 HU) and red color to low bone density (pixel values > 20 and < 145 HU). The final grayscale and colored images are exported in digital imaging and communications in medicine (DICOM) format.

Validation study

The images from the validation cohort ($N = 120$) were de-identified and used to form four data sets for four different reading sessions. In order to reduce recall bias, reading sessions were separated by 2 weeks, the order of images was randomized between each reading session, and unique coded identifiers were used for each reading session. Five academic faculty radiologists ($N = 2$ neuroradiologists, $N = 2$ musculoskeletal radiologists, and $N = 1$ body radiologist) served as readers, and each reader independently assessed L3/L4 trabecular bone density in all participants ($N = 120$) using four different techniques. The time of assessment for each patient was recorded from the time of opening the study to the time the reader provided a final bone density assessment.

For the first reading session, readers performed subjective visual assessment of grayscale sagittal CT images, using OsiriX Lite (Pixmeo, Bernex, Switzerland) to view the images. The CT images were pre-windowed to standard bone windows (window length = 300, window width = 1500), and readers were allowed to scroll through the images and alter window settings as desired. Readers were instructed to assess the trabecular bone density at L3/L4 and subjectively characterize it as normal or low bone density, without making attenuation measurements.

For the second reading session, readers used OsiriX Lite to view images and measure the mean attenuation of the trabecular bone at L3/L4 on sagittal images with 3 mm section thickness. Readers were instructed to place a single circular ROI with a 2 cm diameter in the anterior two-thirds of the trabecular portion of the L3/L4 vertebral bodies, with avoidance of the venous plexus, bone lesions, and endplate sclerosis related to degenerative changes [9]. Readers were allowed to alter the size of the ROIs as needed to obtain the best possible measurements. Normal bone density was defined as mean attenuation ≥ 145 HU, and low bone density was defined as mean attenuation of < 145 HU.

For the third reading session, paired grayscale and colored images were prepared using CED Spine Software. Readers performed subjective visual assessment of paired grayscale and colored sagittal CT images using OsiriX Lite to view the images. Readers were instructed to assess the bone density at L3/L4 and subjectively

Table 1. Patient characteristics

	Full cohort ($N = 631$)	Training cohort ($N = 511$)	Validation cohort ($N = 120$)	p value*
Characteristics				
Age	68.5 (8.2)	68.6 (8.3)	68.0 (8.1)	0.464
Male	167 (26%)	136 (27%)	31 (26%)	0.861
African American	631 (100%)	511 (100%)	120 (100%)	1.000
BMI	32.4 (7.0)	32.4 (7.1)	32.5 (6.9)	0.859
QCT bone density				
L3 level (mg/cm^3)	129.4 (40.1)	130.0 (39.7)	126.9 (41.9)	0.452
L4 level (mg/cm^3)	128.3 (40.0)	129.0 (39.7)	125.7 (41.4)	0.427
QCT bone density category				
L3 level				
Normal bone density	365 (58%)	300 (59%)	65 (54%)	0.365
Low bone density	266 (42%)	211 (41%)	55 (46%)	
L4 level				
Normal bone density	359 (57%)	294 (58%)	65 (54%)	0.488
Low bone density	271 (43%)	216 (42%)	55 (46%)	

*p value comparison is between training and validation cohorts

characterize it as normal or low based on the predominant color (red or green) in the anterior two-thirds of the trabecular portion of the vertebral bodies. The intent of the grayscale image was to rapidly identify endplate sclerosis, which could confound bone density assessment by any technique.

For the fourth reading session, readers performed 3-dimensional QCT bone density analysis at L3/L4 using QCT Pro Software version 5.1 and using the QCT phantom as an internal reference standard. The purpose of this reading session was to gather the reference standard bone density measurements and was not an experimental session. Readers were instructed to place the volumetric ROIs in the anterior two-thirds of the trabecular portion of the vertebral bodies, with avoidance of the venous plexus, bone lesions, and endplate sclerosis related to degenerative changes. The bone density was recorded in mg/cm^3, and the average bone density among the five readers was used as the reference standard for assessment of accuracy. Normal bone density was defined as $\geq$ 120 mg/cm^3, and low bone density was defined as $<$ 120 mg/cm^3 [4].

Statistical analysis

Statistical analysis was performed by a Ph.D. biostatistician (S. L.). Mean, standard deviations, counts, and percentages were used as summary statistics. Pearson's correlation and simple linear regression slopes were used to describe the relationship between mean attenuation and QCT bone density. Receiver Operating Characteristics analysis using the Youden index was performed to identify the optimal cut point for differentiating normal from low bone density. Accuracy, sensitivity, specificity, positive predictive value, and negative predictive values were constructed using QCT bone density as the reference standard. Intraclass correlations were calculated using two-way random effects models. All analyses were completed with Stata v15.0.

Results

Patient characteristics

Patient characteristics are depicted in Table 1. The full cohort was elderly with a mean age of 68.5 years (range 40.1–90.5 years), predominantly female with only 26% (167/631) males, and obese with a mean BMI of 32.4. The average bone density of the full cohort was normal with a mean value of 129.4 mg/cm^3 at L3 and 128.3 mg/cm^3 at L4. The prevalence of low bone density was 42% (266/631) and 43% (271/631) at L3 and L4, respectively. The training ($N = 511$) and validation cohorts ($N = 120$) were similar with no statistical differences between any of the parameters assessed in Table 1.

Mean attenuation at L3/L4 was highly correlated with QCT bone density (r = 0.95/0.94, $p < 0.001$ for both) in the training cohort ($N = 511$). The optimal mean attenuation cut point for differentiating normal from low bone density was 145 HU (Fig. 1). Incidentally, the optimal mean attenuation cut point for differentiating osteoporosis from normal/low bone density was 95 HU.

A post-processing technique was developed to display normal vertebral body bone density as green (Fig. 2) and low bone density as red (Fig. 3). In the validation cohort ($N = 120$), the average accuracy, sensitivity, specificity, positive predictive value, and negative predictive value of various bone density assessment techniques for L4 bone density are depicted in Fig. 4. Results at L3 were similar (Appendix Fig. 6). The average accuracy among five readers for assessing bone density using visual assessment of grayscale CT images, quantitative measurements of mean vertebral attenuation, and visual assessment of colored CT images was 58, 87, and 91% ($p < 0.001$),

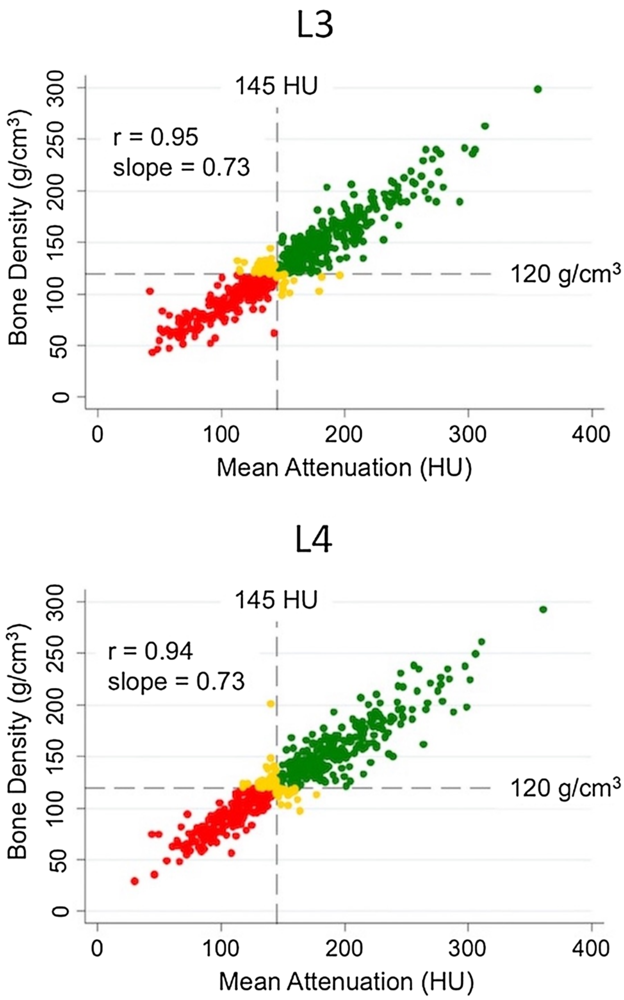

Fig. 1. Association of L3 (left) and L4 (right) mean attenuation and bone density in the training cohort ($N = 511$). Green color indicates patients who had mean attenuation ≥145 HU and corresponding normal bone density (≥120 mg/cm^3). Red color indicates patients who had mean attenuation < 145 HU and corresponding abnormal bone density (< 120 mg/cm^3). Yellow color indicates patients not meeting the above match between mean attenuation and bone density.

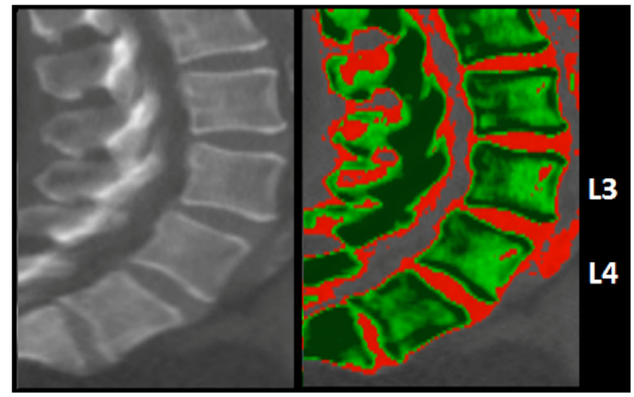

Fig. 2. 64-year-old female with normal done density (135 mg/cm^3) per QCT. Post-processed CT of the central aspect of the spine are displayed in grayscale and color, with predominantly green color in the anterior two-thirds of the trabecular portion of the L3/L4 vertebral bodies, indicting normal bone density.

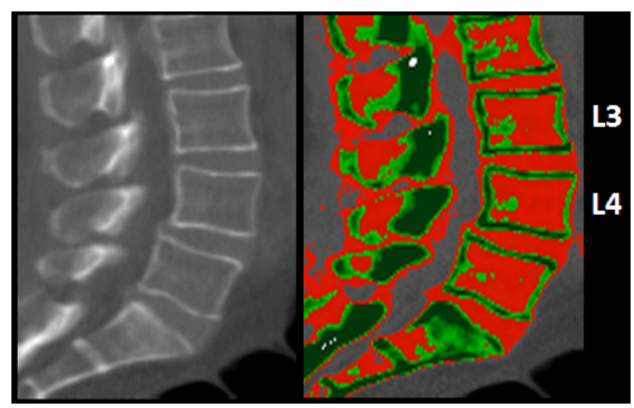

Fig. 3. 61-year-old female with low done density (102 mg/cm^3) per QCT. Post-processed CT of the central aspect of the spine are displayed in grayscale and color, with red color in the anterior two-thirds of the trabecular portion of the L3/L4 vertebral bodies, indicting low bone density.

respectively. Inter-observer agreement among five readers for assessing bone density in the validation cohort ($N = 120$) was poor with visual assessment of grayscale CT images (ICC: 0.20; 95% CI 0.12, 0.28) and excellent with both quantitative measurements of mean vertebral attenuation (ICC: 0.85; 95% CI 0.73, 0.91) and visual assessment of colored CT images (ICC: 0.87; 95% CI 0.83, 0.90). Mean time of bone density assessment using visual assessment of grayscale CT images, quantitative measurements of mean vertebral attenuation, and visual assessment of colored CT images were 8.4, 12.9, and 2.0 s ($p < 0.001$; Fig. 5), respectively.

Discussion

The most significant barrier to osteoporotic fracture risk reduction is failure to implement low bone density screening in appropriate populations [15–18]. Millions of patients at risk for low bone density undergo CT imaging each year. The ability to assess bone density on CT images obtained for other purposes in individuals who have not previously undergone screening for low bone density could have a wide impact on health around the world. CT images of the spine contain valuable information of both global and regional bone quality, and the information can be extracted with no additional patient cost or radiation [7–12].

The ideal opportunistic screening method for detecting low spinal bone density on routine CT images should be practical, passive, accurate, reproducible, and rapid.

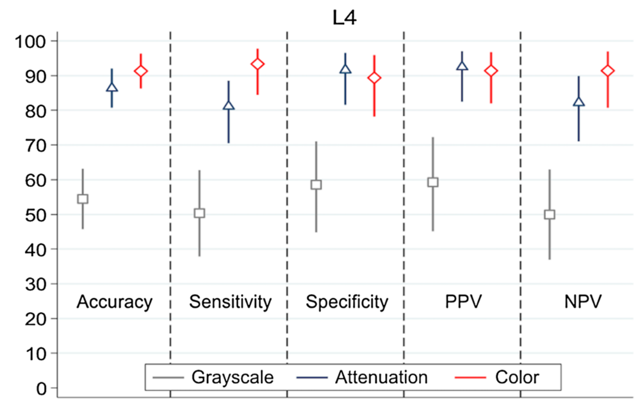

Fig. 4. Mean accuracy, sensitivity, specificity, positive predictive value (PPV), and negative predictive value (NPV) by bone density assessment techniques in the validation cohort (*N* = 120 participants; *N* = 5 readers). Bone density at L4 was assessed by visual assessment of grayscale CT images (Grayscale), quantitative measurements of mean vertebral attenuation (Attenuation), and visual assessment of colored CT images (Color).

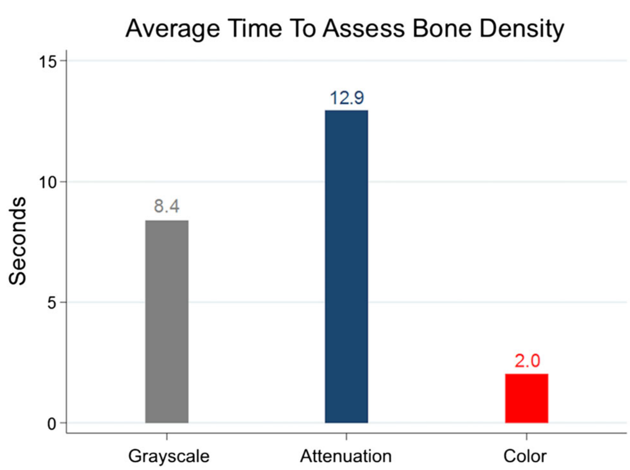

Fig. 5. Average time for each of the five readers used to assess bone density by visual assessment of grayscale CT images (Grayscale), quantitative measurements of mean vertebral attenuation (Attenuation), and visual assessment of colored CT images (Color).

The general principal guiding opportunistic bone density screening with CT is that mean attenuation of the vertebral bodies is directly related to bone density [7–12].

In our study, mean attenuation of the spine was highly correlated with bone density, and the optimal threshold for differentiating normal from low bone density was 145 HU. This threshold is higher than previous reports, likely related to the use of QCT as a reference standard in our study vs. DXA in comparable studies [7–12]. Of note, QCT may be a superior reference standard as QCT assessment of spinal bone density has several advantages as compared to DXA, including avoidance of confounders like body composition, calcified atherosclerotic aortic disease, and degenerative changes of the spine [19].

While it is simple and rapid to visually assess bone density on routine grayscale images, this study found that subjective visual assessment of bone density had both poor accuracy and poor inter-observer agreement. These findings suggest that subjective visual assessment of grayscale CT images to assess spinal bone density should not be performed for global or regional bone density assessment.

Conversely, use of a simple measurement of mean attenuation on routine sagittal reconstruction of the spine to differentiate normal from low bone density was accurate, had high inter-observer agreement, and was relatively rapid. The main problem with mean attenuation measurements as a method of opportunistic bone density screening is the need for active engagement of the radiologist, who is primarily focused on assessment of the images for another purpose or indication. In our academic radiology practice, active measurement of vertebral body bone density is rarely performed as a method for opportunistic bone density.

In our study, evaluation of colored CT images of the abdomen to detect low spinal bone density was highly accurate, had excellent inter-observer agreement, and required an average of 2 s to complete assessment. This method of assessment was practical and passive and met our goals for an ideal opportunistic bone density screening method. In the future, the reconstruction algorithm for coloring CT images could be performed at the scanner or at an offline automated processor so that the colored images would be available for immediate viewing, similar to how coronal or sagittal reconstructions are routinely generated at some center. The reconstruction algorithm used in this study was capable of straightening the spine, which would avoid problems with mild scoliosis or misalignment with the scanner. In order to avoid incorrect bone density assessment related to degenerative endplate sclerosis, the algorithm generated a grayscale image of the central aspect of the spine to allow the reader to rapidly detect this potential confounder and focus attention on the unaffected trabecular bone.

Using colored CT image reconstructions could improve screening efforts to identify low bone density or osteoporosis in both women and men. While this study focused on identification of low bone density and osteoporosis on nonenhanced CT images, the threshold could be altered to change sensitivity and specificity or to focus only on osteoporosis. The ability to adjust the threshold is important as future cost-effective analysis studies may identify a different threshold that is ideally suited for opportunistic bone density screening.

This study had several limitations. First, the study design was retrospective, and image analysis was performed in a research setting, not in a clinical practice setting. This is common for a pilot research study. Second, the patient cohort was entirely African American, limiting generalizability to other patient populations. However, QCT bone density was the reference standard and is not affected by race or gender, and this study benefited from a large patient cohort with different ages and a mix of males and females. Third, the L3/L4 vertebra were assessed in this study, while assessment of L1/L2 are the more traditional locations for QCT bone density analysis. We were limited by the constraints of the image acquisition methods used in this study. Fourth, our study did not assess repeatability of the techniques across a range of CT image acquisition parameters, reproducibility across multiple different CT scanners, or combine subjective assessment of abnormal bone density with quantitative measures of vertebral attenuation and subsequent conversion to numeric bone density. This was a pilot study, and a prospective evaluation overcoming many of these limitations is underway. Fifth, this study utilized nonenhanced CT images and did not assess the effect of intravenous contrast on opportunistic bone density screening with CT images.

In conclusion, detection of low spinal bone density using colored abdominal CT images is highly accurate, has very good inter-observer agreement, and is extremely rapid to perform. We believe the technique is practical and passive, requiring minimal effort to perform, and a prospective validation study is underway. These methods are currently applicable to nonenhanced CT images of the abdomen but may be adapted to thoracic CT images and to CT images with intravenous contrast in the future. Conversely, subjective visual assessment of spinal bone density on grayscale CT images had poor accuracy and poor inter-observer agreement, and we suggest that subjective visual assessment of grayscale CT images should not be used in clinical practice for either global or regional bone density assessment.

Compliance with ethical standards

IRB statement The study was approved by the institutional review board.

COI disclosure The study dates for data collection were from December 2011 to September 2015. AS. is the inventor of the technology and filed a U.S. patent in May 2017. The patent was assigned to Color Enhance Detection LLC. AS. and the University of Mississippi Medical Center have joint ownership in Color Enhanced Detection LLC. Manuscript preparations were performed from January through May of 2018. All other authors declare no relevant disclosures.

Appendix

See Fig. 6.

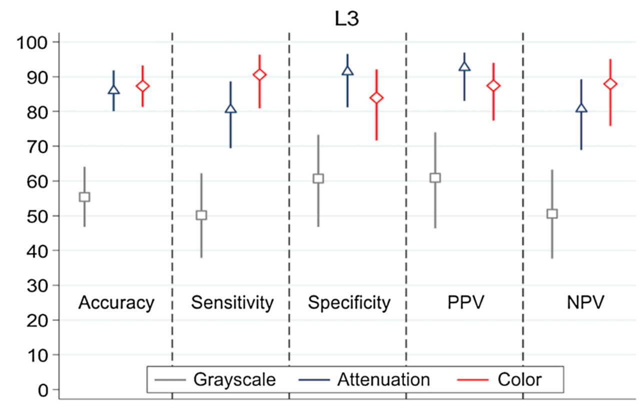

Fig. 6. Mean accuracy, sensitivity, specificity, positive predictive value (PPV), and negative predictive value (NPV) by bone density assessment techniques in the validation cohort ($N = 120$ participants; $N = 5$ readers). Bone density at L3 was assessed by visual assessment of grayscale CT images (Grayscale), quantitative measurements of mean vertebral attenuation (Attenuation), and visual assessment of colored CT images (Color).

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