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FULL PAPER

L1 vertebral density on CT is too variable with different scanning protocols to be a useful screening tool for osteoporosis in everyday practice

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Objective: To determine whether a single L1 density threshold can be used to screen all patients undergoing CT at a busy tertiary referral centre for those at risk of osteoporosis.

Methods: 200 patients, who had been randomly selected for an audit of CT reporting of incidental vertebral fractures, had their L1 density measured on 864 routine CT examinations. These had been performed with a variety of kVp and intravenous (i.v.) contrast protocols, reflecting the wide range of imaging indications.

Results: L1 density measured on thick axial, thin axial or sagittal images had an excellent intraclass correlation coefficient (0.996). For the same patients imaged twice within 6 months, there was mean intraexamination L1 density difference of 27.5 HU. Variability due to i.v. contrast medium administration resulted in a mean

difference of 24.5 HU. Mean difference due to acquisition kVp was 24.1 HU. Once matched for sex, age, kVp and i.v. contrast, there was a significant difference between the L1 density in patients with vertebral fractures compared to those without fractures (mean 30.19 HU).

Conclusion: There is significant variability in the L1 vertebral body CT density due to differences in acquisition variables such as kVp and timing post-i.v. contrast medium.

Advances in knowledge: Previous studies suggested that L1 CT density could be used to screen for osteoporosis. The current study cautions that it is not possible to define a single L1 density threshold for screening, due to the number of variables within a wide range of scanning protocols for different imaging indications in everyday practice.

INTRODUCTION

Osteoporosis is an important problem in the ageing population as low bone mineral density (BMD) can lead to fragility fractures that cause significant morbidity and an increased risk of mortality.¹ Despite increased efforts to promote screening, osteoporosis is often only identified following a fragility fracture.² However, early detection of osteoporosis can lead to prevention of fracture by early intervention with antiosteoporotic agents and falls management.³

The World Health Organisation definition of osteoporosis uses BMD measured by Dual Energy X-ray Absorptiometry (DXA)². However, recent developments in quantitative CT (QCT) have questioned the efficacy of the gold-standard DXA.⁴ Whereas DXA measures the density of two-dimensional data, superimposing the cortical and trabecular bone as well as overlying soft tissue, QCT measures BMD in three-dimensional specifically of the trabecular bone and without interference from overlying osteophytes and aortic

calcification. Therefore QCT gives a numerically different, arguably more accurate, assessment of BMD than DXA. Currently, QCT cannot be used to diagnose osteoporosis as QCT BMD thresholds for osteopaenia and osteoporosis have not been validated.⁴

More recently, there has been interest in the possibility of simply measuring vertebral body CT density in Hounsfield Units (HUs) as an indicator of BMD. Early studies showed that vertebral body density was well-correlated with BMD measured by DXA, first using multilevel vertebral body measurements^{5–8} and then, by a single L1 vertebral body density.^{9–11}

We have previously demonstrated excellent intra- and interobserver consistency in measurement of the L1 density on axial CT images and good correlation of the L1 density with the QCT BMD on a set of patients with highly controlled imaging parameters.¹² These patients were scanned using a single CT scanning system and a

uniform scanning protocol without intravenous (i.v.) contrast medium. However, in every day clinical practice, CT examinations are protocolled differently depending on the clinical question. Images may be acquired with or without i.v. contrast medium and at different times following contrast medium, *e.g.* arterial, portal, biphasic depending on the organ being examined. Patients may be imaged on different CT scanning systems depending on availability and at different kVp depending on the scanner, patient size and protocol. Images are then reformatted using different slice thicknesses before being read by the reporting radiologist.

We aimed to determine whether L1 density could be used as a simple screening tool for patients with osteoporosis in daily practice, screening all patients having CT imaging for any reason and with any scanning protocol. We considered the effect on L1 density in HU of slice thickness or using sagittal reconstructions, of different imaging parameters including kVp and the use and timing of contrast medium and the effect of using different scanning systems. We also assessed the effect of age and gender.

METHODS AND MATERIALS

Local ethical approval was acquired to retrospectively measure the L1 density on CT examination of patients identified in a departmental audit of the reporting of incidental vertebral fractures on CT of patients aged over 50 years. A maximum of 10 sequential patients had been audited per day for either CT chest, CT abdomen/pelvis or CT chest/abdomen/pelvis over three audit cycles. A total of 650 patients were audited from 2013 to 2015, of whom 117 had vertebral fractures (unpublished data).

All of the patients with vertebral fractures from the audit study were included in this project along with an equal number of sequential patients without vertebral fractures. Patients were excluded if there was no imaging of the L1 vertebra (sometimes not included on CT chest) or if there was marrow infiltration, myeloma or spinal metastases detectable on the CT imaging. The L1 density was measured for all available CT images for each patient. If the patient had DXA or QCT imaging, the T-score was recorded.

The trabecular density of the L1 vertebral body was measured in HU by a senior radiology trainee. Previously published work from our group showed excellent intra- and interobserver variability for measurements.¹² The centre of the L1 vertebral body was identified as the first non-rib-bearing vertebral body, at the level of the pedicles. An elliptical region of interest was drawn in the anterior two-thirds of the L1 vertebral body, avoiding the cortex by at least 1 mm and avoiding any cortical irregularities and posterior basilar veins. If there was fracture of the L1 vertebral body or a lesion such as a haemangioma in the L1 vertebral body, the L2 vertebral body was used instead.

The protocol of the CT imaging was recorded, including the scanning system, kVp, whether i.v. contrast was used and, when i.v. contrast was used, the timing of the subsequent imaging. The presence of vertebral fractures was also recorded.

For 100 consecutive patients, L1 density measurements were acquired from the thick axial (5 mm), thin axial (1 or 2 mm) and sagittal reformatted (3 mm thickness) images from the most recent examination. The area of the region of interest was also recorded. Subsequent analysis used L1 densities measured on the thick axial images. If images were obtained pre- and post-i.v. contrast medium, the identical section for L1 density measurement was selected.

Statistical analysis was performed using GraphPad and Stat-*s*To-*Do* online calculators. The intraclass correlation coefficient was used to analyse the correlation between the L1 density measured on the thick axial images compared to the thin axial images and sagittal images. Paired *t*-tests were used to test the Null hypothesis of no difference between size of the axial and sagittal ROI, L1 density measured at two different kVps or with/without contrast medium in the same patient. Mean L1 density of age-, sex-, kVp- and contrast-matched subsets of CT examinations were only included, if there were five or more examinations per subset.

RESULTS

Patients

200 patients were included in the study, of which 100 had vertebral fractures. L1 density was measured on 864 different CT images, including images acquired for the same patient on different dates and in different phases following i.v. contrast medium. The average age of the patients at the time of the study was 74.4 years (range 51–99 years) and 44% were male, 56% female. Images were acquired on a variety of CT scanning systems, at different kVps and with different contrast protocols (Tables 1–4). The majority of the examinations were performed following i.v. contrast medium (78%), the majority of which were performed in the portal phase (79% of post-contrast imaging) (Table 2). The kVp for image

Table 1. The number of L1 densities measured on images acquired with/without i.v. contrast medium and following the type and amount of i.v. contrast

Contrast	Type of contrast	Number of L1 densities
Non		194
i.v. contrast	All	670
	50 ml Niopam 300 (Bracco, UK)	3
	70 ml Niopam 300	392
	85 ml Niopam 300	36
	100 ml Niopam 300	193
	50 ml Omnipaque (GE Healthcare, Waukesha, WI)	1
	70 ml Omnipaque	31
	85 ml Omnipaque	8
	Unspecified	6

i.v., intravenous.

Table 2. Number of L1 densities measured on images acquired in different phases pre/post-i.v. contrast medium

Timing	Number of L1 densities
Pre contrast	194
Arterial phase chest	11
Arterial phase abdomen/pelvis	75
Aorta	2
Pulmonary arterial	45
Portal	532
Delayed	1
Biphasic	4

i.v, intravenous.

acquisition ranged from 80 to 140 kVp, however, the majority of images were acquired at 120 kVp (48%) and 100 kVp (30%) (Table 3).

L1 density may be measured on the thin or thick axial or sagittal CT images

The L1 density for 100 patients on their most recent CT study was measured using the thick (3–5 mm) axial, thin (1–2 mm) axial and sagittal (3 mm) images (Figure 1). There was very good agreement between the three L1 density measurements with an intraclass correlation coefficient of 0.966 [95% CI (0.954–0.976)]. The mean area of the region of interest for the axial images was significantly larger than that of the sagittal images (paired *t*-test $p < 0.0001$). The mean area of the region of interest was 361.7 mm² [95% CI (345.8–375.6 mm²)] for the axial images and 253.9 mm² [95% CI (242.7–265.2 mm²)] for the sagittal images.

Variability in L1 density in the same patient scanned on different days

To reduce differences due to age- or circumstance-related changes in bone marrow density, L1 densities for the same patients on different scan dates within 6 months were analysed. 129 patients had multiple scans within 6 months, with 470 different scans and a mean of 3.6 scans per patient. The mean of the difference in L1 density between scans was 27.5 HU, SD 20.8 HU [95% CI (23.8–31.1 HU)].

Variability due to contrast medium or timing of imaging

74 CT scans were performed pre- and post-i.v. contrast medium. The L1 density increased post-i.v. contrast in all patients (Figure 2). The mean of the maximum L1 density increase between pre- and post-contrast images was 24.5 HU, SD 12.4 HU [95% CI (21.62–27.38 HU)]. The paired *t*-test found the difference in L1 density pre- and post-i.v. contrast medium to be extremely statistically significant ($p < 0.0001$).

Of 43 patients who had CT imaging pre- and post-i.v. contrast medium in the arterial and portal phases, 70% had maximum L1 density on the portal phase imaging, however 30% had a higher L1 density on the arterial phase imaging. There was considerable

Table 3. Number of L1 densities measured on images acquired at different kVps

kVp	Number of L1 densities
80	10
100	262
120	411
130	137
140	44

variability in the effect of i.v. contrast medium between patients and in the same patient scanned on different dates. For example, in one patient who had 7 triple phase CT scans 3/7 had the greatest increase in L1 density in the arterial phase and 4/7 had the greatest increase in the portal phase.

Variability due to different kVp

To investigate the effect of kVp on the L1 density, patients with more than one post-contrast scan at different kVp within 2 years were analysed. Paired *t*-tests found that the L1 density was significantly different when the imaging was performed at different kVp (Table 5). The biggest difference was on comparing L1 densities at 100 kVp to 130 kVp when the mean difference was 24.13 HU (95% CI 13.45–34.8)].

Variability due to age and sex of patient

Males and females scanned at 120 kVp and post-i.v. contrast medium were subdivided into 10-year age groups and the mean L1 density decreased with age (Figure 3). There was a 45% decrease in L1 density for males and a 43% decrease for females

Table 4. Number of L1 densities measured on images acquired using different CT systems

CT system	Number of L1 densities
Somatom Definition Flash (Siemens Healthcare, Erlangen, Germany)	217
Somatom Definition AS (Siemens Healthcare, Erlangen, Germany)	62
Somatom Definition AS+ (Siemens Healthcare, Erlangen, Germany)	212
Sensation 4 (Siemens Healthcare, Erlangen, Germany)	1
Sensation 16 (Siemens Healthcare, Erlangen, Germany)	69
Sensation 64 (Siemens Healthcare, Erlangen, Germany)	148
Emotion 16 2007 (Siemens Healthcare, Erlangen, Germany)	127
Discovery 690 PET/CT (GE Healthcare, Waukesha, WI)	18
Biograph 6 (Siemens Healthcare, Erlangen, Germany)	10

Figure 1. Region of interest in L1 in (a) thick axial, (b) thin axial and (c) sagittal reformatted images.

between the 50–59 and 80–89 years groups. This averaged to a 1.7 HU decrease in L1 density per year.

Although L1 densities were lower in females than in males in all age groups, this was not statistically significant, likely due to the small number of patients analysed.

L1 density and vertebral body fractures

Once matched for sex, age, kVp and contrast, there is a significant difference between the L1 density in patients with vertebral fractures compared to those without fractures ($p = 0.0014$). The mean difference is 30.19 HU [95% CI (13.77–46.6 HU)]. Overall, the average L1 density was 129.5 HU in patients with no fracture and 99.3 HU in those with fractures.

L1 density and DXA results

37 patients had DXA T-scores and 25 of these patients had vertebral fractures (Figure 4). Of the fractured patients, only 14/25

were classed as osteoporotic by DXA. 5 patients with fractures were classified as normal by DXA T-score; 6 were classified as osteopaenic.

DISCUSSION

The CT density of the L1 vertebral body has previously been shown to be well-correlated with the BMD, whether measured by DXA⁹ or by QCT.¹² Low intra- and interobserver variability in L1 density measurements has also been previously demonstrated.^{12, 13} In this study, we found that the thickness or plane of sections used (axial or sagittal) to measure the L1 density do not significantly affect the L1 density result. There is very good correlation between CT L1 density measurements, whether they are measured using thick (3–5 mm) axial sections, thin (1–2 mm) axial sections or sagittal (3 mm) reformatted sections. This is supported by previously published work showing a correlation between L1 density measured on sagittal CT images and the DXA BMD.¹⁴

Figure 2. Increase in L1 density post-i.v. contrast medium. HU, Hounsfield Unit; i.v., intravenously.

Table 5. Paired *t*-test comparing L1 density in post-contrast images scanned at different kVp

Test kVp	Test kVp	<i>n</i>	Significance <i>p</i> =	Mean difference	95% CI
100	120	28	<0.0001	15.57	(9.04–22.10)
100	130	24	<0.0001	24.13	(13.45–34.8)
120	130	26	0.0005	14.92	(7.92–22.64)

We investigated the possibility of using the CT L1 density measurements as a screening tool to detect patients at risk of osteoporosis, to see if L1 density could be routinely measured on all CT examinations performed and those below a certain threshold referred for further osteoporosis investigation. Previous studies have investigated such a threshold in controlled patient populations, but such homogeneity in case-mix is not possible outside of a research protocol. We investigated whether an L1 density threshold could be used to screen all patients having a CT examination in our department, where a variety of CT scanning systems and CT protocols are in daily use depending on the clinical indication. We found that there is large variability in the L1 density measured for the same patient from different CT scanning systems performed within 6 months. The mean difference in L1 density for the same patient having two scans within 6 months was ± 27.5 HU. The main difference between CT scans for the same patient, were different scanning systems, different contrast protocols and different scan kVp.

The density of a bone phantom has previously been shown to be affected by the kVp and scanning system used¹⁵ with a 68% drop in CT density of the bone phantom at 140 kVp compared to 80 kVp. In our study, using post-contrast images of the same patient, L1 density was found to decrease with increasing kVp, decreasing by a mean of 24.13 HU when increasing from 100 kVp to 130 kVp. A recent study measuring multilevel lumbar vertebral density also found lower CT density for different patients with the same BMD scanned at 140 kVp compared to those with the same BMD scanned at 120 kVp.¹⁶

Figure 3. L1 density decreases with age but is not significantly different in males compared to females. All L1 densities measured on images acquired at 120 kVp post-i.v. contrast medium. Error bars show 95% confidence limits for the mean L1 density. HU, Hounsfield Unit; i.v., intravenously.

L1 densities measured post-i.v. contrast medium were on average 24.5 HU higher than those measured without i.v. contrast medium. This value is slightly higher than those of recent studies showing a mean increase of 18 HU in portal phase imaging¹⁷ and 11 HU.¹⁸ The effect of i.v. contrast varies depending on the exact timing of the scan and likely also depends on patient factors such as their cardiac function.

An attempt to set a single threshold for osteoporosis is also confounded by variability in L1 density between patients including factors such as sex and age. Although age-matched males had increased L1 densities compared to females in our study, this difference was not statistically significant, likely due to small numbers of matched patients scanned post-contrast and at 120 kVp. However, it has been well-documented previously that males have higher BMD than females.¹⁹ Our patients showed a statistically significant drop in L1 density with age, of approximately 1.7 HU per year between the age of 40 and 90 years. Age-related changes in BMD have been previously well-documented with QCT BMD suggesting a 1% decrease in BMD per year, increased to up to 6% per year in perimenopausal females¹⁹ and normative data for the density of all the lumbar vertebrae in mainly females of different ages have also been published.^{7,8}

Figure 4. L1 density compared to DXA or QCT BMD for 37 patients including those with (grey diamonds) and without (black squares) vertebral fractures. The WHO DXA thresholds are indicated for osteoporosis ($T < -2.5$) and osteopaenia ($-1 < T < -2.5$). BMD, bone mineral density; DXA, dual energy X-ray absorptiometry; HU, Hounsfield Unit; i.v., intravenously; QCT, quantitative CT.

Previously published thresholds of 160 HU for 90% sensitivity for osteoporosis and 110 HU for 90% specificity for osteoporosis⁹ are being used by other groups, but this may be inappropriate without reference to the CT protocol kVp or contrast medium used.^{10, 11, 13} Although the correlation between L1 density and BMD has been demonstrated in certain, defined conditions, threshold density levels cannot automatically be transferred to different patient populations, scanners and scan protocols.

Our study was limited by the lack of a gold standard for fracture risk. Of those patients who did not have a vertebral fracture, it is not possible to determine who is about to fracture or who is at increased fracture risk. A proportion of patients with low BMD and low L1 density will never have vertebral fractures. L1 density has previously been shown to be well-correlated with DXA and QCT BMD, however, DXA has inherent flaws as previously discussed and QCT has not been validated for fracture risk thresholds. It is not possible to determine truly “normative” data for L1 density without large number of patients and long term follow-up data would be required to equate L1 density to fracture risk, with age-, sex-, kVp- and contrast-specific stratification.

A further study limitation was that we did not specifically investigate density differences comparing different CT scanners. Most of the scanners were only used at one set kVp. The three Somatom Definition scanners had variable kVps from 80 to 140 kVp. It was not possible using our data to compare different scanners at the same kVp. However, scanner-specific difference in bone densities have previously been published.¹⁵

L1 density may be useful for specific questions using controlled patient and scan parameters, as in the case of the studies of L1 density and post-spinal fusion fracture risk²⁰ and success of spinal fusion.²¹ However, in our experience, L1 density cannot be used as a simple, general screening tool that can be quickly used by all general reporting radiologists. This may explain why the results of Buckens et al suggested lower diagnostic efficacy of measuring vertebral density, as this study included chest as well as abdomen/pelvis scans which would increase the variability of protocols. Specific details of the kVp and contrast protocols were not stated in this paper.¹¹

In conclusion, our data indicates that it would not be feasible to set a single L1 CT density threshold for general use when reporting CT imaging of patients in a general CT department running multiple CT scanning systems and using a variety of indication-specific scanning protocols. At a minimum, age-, sex- and departmental protocol-specific thresholds would need to be determined. It would, therefore, not be possible to introduce a single screening threshold for general radiologists as a routine screening tool for all CT scans performed. L1 density may be useful in subspecialty situations, where a well-defined subset of patients is scanned using one constant scanning protocol. Age and sex-specific, specialty-specific thresholds would need to be determined for each context of L1 density measurement.

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