Can bone scintigraphy play a role in identification and assessment of vertebral compression fractures?

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Research Article

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Posted Date: January 15th, 2024

DOI: https://doi.org/10.21203/rs.3.rs-3853167/v1

Can bone scintigraphy play a role in identification and assessment of vertebral compression fractures?

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Word count: 5718

ABSTRACT:

Purpose: This study aims to evaluate the role of bone scintigraphy (BS) in identifying and assessing the age of vertebral compression fractures (VCFs). **Methods:** A total of 190 patients with VCFs, eligible for vertebral augmentation surgery, underwent computed tomography (CT) and BS. The CT and scintigraphic patterns of 2966 vertebrae were compared. **Results:** The CT and BS findings were concordant in the majority of cases (95.5%), including 84.4% normal vertebrae, 6.4% acute VCFs, and 4.7% chronic VCFs. However, in 37 patients, 45 occult acute VCFs were only detected on BS and not on CT. Multivariate logistic regression analysis revealed that these patients were older and had lower bone density compared to the rest of the study population. Additionally, 40 patients had acute VCFs visible on CT but with no increased or low intensity uptake on BS. These cases were associated with a shorter time period between trauma and BS, a higher prevalence of male patients, and higher bone density. Acute VCFs with no increased uptake or low levels of uptake were found within six days of the trauma. **Conclusion:** BS provides valuable information about the age of VCFs, detects radiologically occult fractures, and can serve as a cost-effective alternative to MRI. To avoid missing acute VCFs, BS should be performed six days or more after the injury.

Keywords: Bone scintigraphy, Computed tomography, Vertebral compression fracture, Occult fracture, Osteoporosis

INTRODUCTION:

Vertebral compression fractures (VCFs) are one of the hallmark fractures of osteoporosis and are prevalent in the elderly population. The radiographic appearance of recent fresh VCFs and healed old VCFs can be similar. Further imaging studies are thus needed to determine the fracture's age for subsequent appropriate patient management. In acute, symptomatic VCFs, interventional procedures such as percutaneous vertebroplasty (VP), kyphoplasty (KP) or spine fusion surgery may be indicated (1).

Magnetic resonance imaging (MRI) is the imaging method of choice for determining a VCF's age (2,3). Acute fractures exhibit low signal intensity on T1-weighted sequences and high signal intensity on T2-weighted sequences. The abnormal signal gradually disappears within 2–4 months (4). Bone scintigraphy (BS) using Tc99m-MDP should be also considered as an effective method of determining the age of VCFs and therefore be utilized mainly when MRI is unavailable or contraindicated. An acute VCF presents as intense horizontal linear tracer uptake in a vertebral body. This pattern usually appears within the first 48 hours and decreases in intensity or fades over a period of 6 to 24 months (5). Blood pool scintigraphy performed early, up to 5 minutes after injection of Tc-99m MDP, can demonstrate areas of hyperemia, also indicating an acute process (6). Several studies compared the appearance of VCFs on MRI and BS with discordant results (7–9). Thus, it is not clear from the currently available literature data whether BS can safely replace MRI as a method of determining a fracture's age.

The aim of this study was to describe the patterns and temporal dynamics of VCFs on BS as related to the fracture type and age, and patient characteristics.

METHODS:

The study was conducted retrospectively and approved by the medical center's institutional review board (approval number 0038-20-NHR). The need for written informed consent was waived.

Study population:

The data of 200 consecutive patients admitted to our institution between March 2017 to April 2022 with suspected acute osteoporotic VCF in the thoracic and lumbar spine shown on CT were analyzed. Patients with non-osteoporotic fractures, systemic conditions affecting the skeleton (such as disseminated Multiple Myeloma) as well as technically inappropriate CT or BS were excluded. The data of 190 patients were eligible for further analysis.

Data collection:

Demographic and clinical information was collected from the patient's electronic hospital records and included age, gender, known diagnosis of osteoporosis, the presence of causative trauma and date of the trauma.

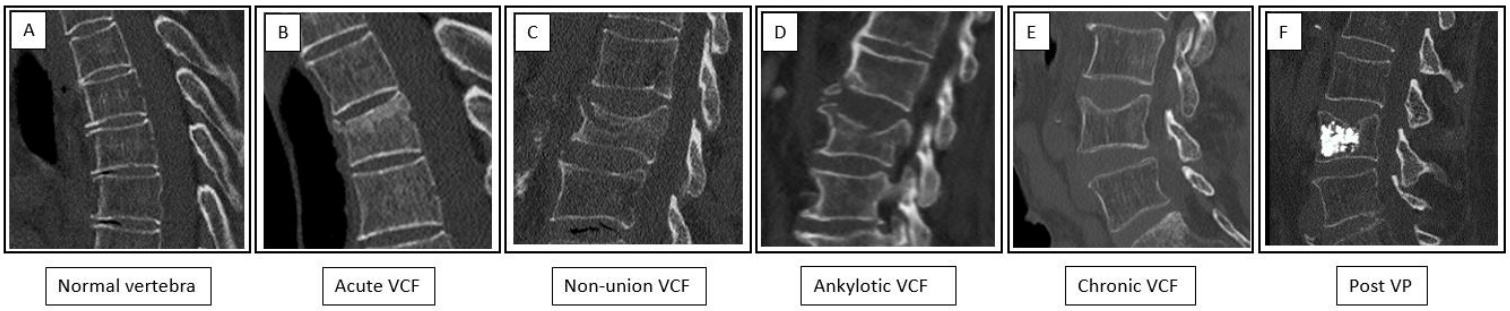
CT of the spine was acquired using one of two CT scanners (Philips Ingenuity 128 and Brilliance 64). MDCT parameters were as follows: tube voltage, 120 kV; tube current, 120–190 mA; slice thickness, 2 mm; detector collimation, 64 × 0.625 mm or 128 × 0.625 mm; gantry rotation time, 1; and pitch, 0.8. All CT data were reconstructed to 2-mm slice thickness with a 512 × 512 matrix using a soft-tissue kernel. No oral or intravenous (IV) contrast media were administered. Sagittal and coronal reformatted images with a slice

thickness of 2 mm were routinely created. In 161 patients, the CT included the thoracic and lumbar spine and in 29 patients only the lumbar spine. A total of 2966 vertebrae were scanned in 190 patients.

The CT images were reviewed by a radiologist for the presence of vertebral fractures at the time of admission. A spine surgeon retrospectively reviewed the CT images for the purpose of this study, defined the fractures as acute or chronic and classified them using the AOSpine Thoracolumbar Spine Injury Classification System (AO type) (10). Only A type (compression injury) and B type fractures (distraction injury) were included in the study. Characteristics of non-union of the fracture or a fracture in an ankylotic segment were also noted.

A description of the CT pattern was documented for each vertebra according to the following (figure 1): normal vertebra (A); acute VCF (B) displaying CT signs of loss of height or anterior wedge deformity with endplate irregularity, cortical incontinuity, step defects, increased density zone of impaction and soft-tissue edema or hematoma surrounding the vertebral body; non-union VCF (C) displaying non-healed fracture with an intravertebral cleft, also known as Kümmell disease, ankylotic VCF (D) displaying a transverse fracture in an ankylotic spine, termed as type B fractures in the AO classification; chronic VCF (E) displaying loss of height or anterior wedge deformity with smooth cortical borders; State after percutaneous vertebroplasty (Post VP) (F) displaying cement within the vertebral body.

Figure 1



Patterns of vertebrae appearance on sagittal spine CT
A Normal vertebra - retained height and continuous cortex
B Acute VCF showing a "step defect" in the anterior border and a "zone of impaction" caused by impaction of the trabeculae
C Non-union fracture – a non-healed fracture with an intervertebral cleft (white arrow)
D Ankylotic fracture – a transverse fracture in an ankylotic spine
E Chronic fracture showing loss of height and smooth cortical borders
F State after percutaneous vertebroplasty (Post VP) - chronic fracture with loss of height and hyperdense cement in the vertebral body

Bone density was estimated for each patient on CT. Hounsfield units (Hus) were measured by placing a region of interest (ROI) in the intramedullary area of a lumbar vertebral body, preferably L3, unless fractured. Values measured bellow 118HU were consistent with osteopenia (T-score of −1.0 to −2.5). Values below 93HU were consistent with osteoporosis (T-score of −2.5 or less) (11).

BS was performed using one of two gamma cameras (Infinia Hawkeye and Optima 640, GE Medical Systems) with a large field-of-view dual head single photon emission computed tomography (SPECT) system fitted with low-energy high-resolution collimators. Whole-body

planar acquisition was done using the continuous method in a 256 x 1024 matrix. SPECT images were obtained in a 128 x 128 matrix with 20% window centered at 140 keV and reconstructed with ordered subsets expectation maximization (OSEM), using 2 iterations. Early planar imaging of the spine and pelvis was performed 5-10 minutes after IV administration of 20-25 mCi (~740 MBq) of Tc99m-MDP (Jubilant Draxlmage Inc, Canada) and late whole body planar images and SPECT of the thoracic and lumbar spine were performed 2-4 hours after injection. Early BS of the spine was performed in 185 patients (97%). All patients underwent late planar whole body imaging and SPECT of the thoracic and lumbar spine with 2 field of views (FOVs). A total of 3230 vertebrae were scanned. All BS were reviewed by a board certified nuclear medicine physician and findings on planar and SPECT images were documented for each vertebra. For early images the presence or absence of increased increased blood pool was recorded. For late images a visual score of the uptake pattern was documented according to the following: low intensity uptake, slightly above that of adjacent normal vertebra; intermediate intensity uptake, above that of adjacent normal vertebra but below uptake in the sacroiliac joint (SIJ) or anterior superior iliac spine (ASIS); high intensity uptake, similar or above uptake in the SIJ or ASIS.

Evaluation of BS was performed with knowledge of findings on CT which were used to accurately define the location of fractures and distinguish between uptake caused by other etiologies such as osteophytes and degenerative changes.

Statistical analysis:

Data were analyzed using SPSS 27.0 for Windows. Normally distributed data were presented as means ± standard deviation and analyzed using unpaired student t test. Percent values were presented to express categorical distribution, and a value of $p < 0.05$ was considered statistically significant.

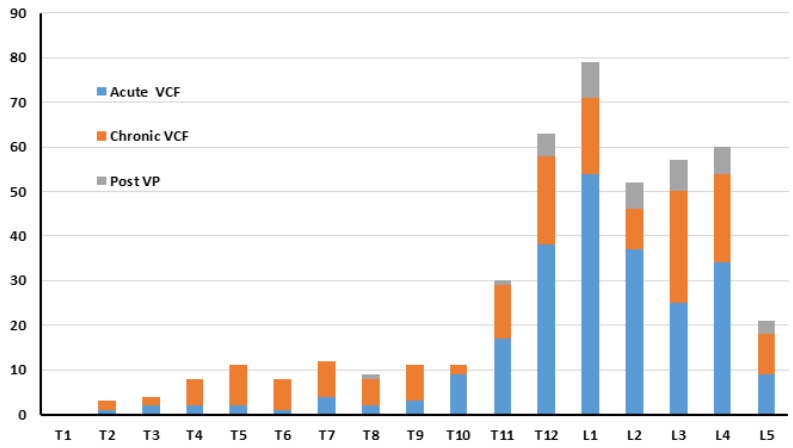
RESULTS:

Two hundred consecutive patients were initially included. Ten patients were excluded from further analysis due to technically inappropriate or missing imaging studies or to etiology of fractures secondary to malignancy or multiple myeloma. The final study population of 190 patients included 130 women (68.4%) and 60 men (31.6%) with a mean age of 75 years ±11.2 years, range 36-98 years. Forty-three patients had documented osteoporosis. In 108 patients (56%) a trauma event with a specific date was recorded, 19 patients (10%) had a known history of recent trauma within the previous two weeks but could not recall the exact date, and 63 patients (33%) had no history of a trauma event. In patients with a recorded trauma date, the mean time between the trauma and hospitalization was 6.1 ±10.7 days, range 0-61, and the mean time between the injury and BS was 8.3 ±10.5 days, range 0-62. The patients underwent spine CT within the first 48 hours of admission. BS was usually acquired 48 hours after the CT except in four cases whose study was performed on the same day or a day before the CT. The mean time interval between CT and BS was 3.1 ± 4.8 days, range -1-33.

On CT, 84 patients (44.2%) had a single acute VCF, 48 patients (25.2%) had two VCFs, 26 patients (13.7%) had three acute VCFs and 32 patients (16.8%) had more than three acute VCFs, with the highest number of 11 acute VCFs in a single patient. VCFs were observed in 439 vertebrae on CT, including 240 who had radiologic patterns of acute VCFs (54.7%), 162

chronic VCFs (36.9%) and 37 post VP VCFs (8.4%). Most of the VCFs were located between T11 and L4, with L1 being the most common location (figure 2). Among the acute VCFs, 49 were non-union and 16 were ankylotic fractures.

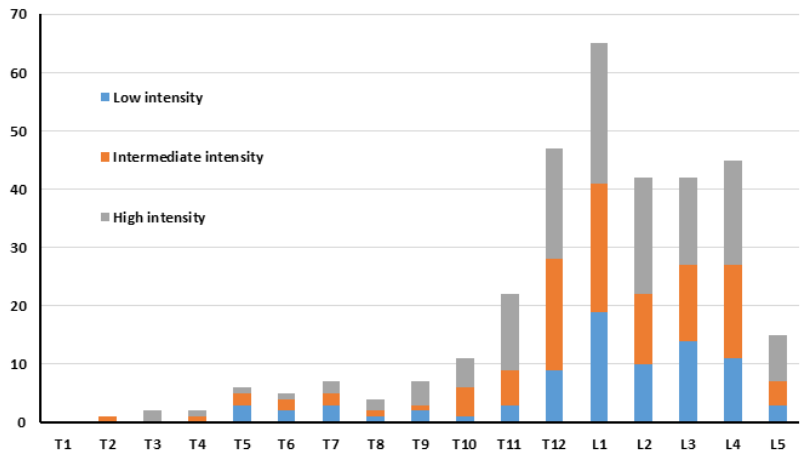
Figure 2:



The CT measured mean bone density was 61.2 ±32, range -21-164. Values above 118HU, considered normal, were found in 10 patients (5.2%). Values of 93 to 118HU, consistent with osteopenia, were found in 17 patients (8.9%), and below 93HU, consistent with osteoporosis, were found in 163 patients (85.7%). The mean bone density in women was significantly lower compared to men (55.6HU ±31 compared to 73.3HU ±31, $p<0.001$) and lower values were found with increasing age of the patients ($r=-0.368$, $p<0.001$).

On BS, increased uptake consistent with a vertebral fracture was observed in 323 vertebrae. The uptake intensity was low in 81 (25%) vertebrae, intermediate in 107 (33%) and high in 135 (42%) vertebrae. Most of the vertebrae with abnormal uptake were seen in the thoraco-lumbar region (figure 3).

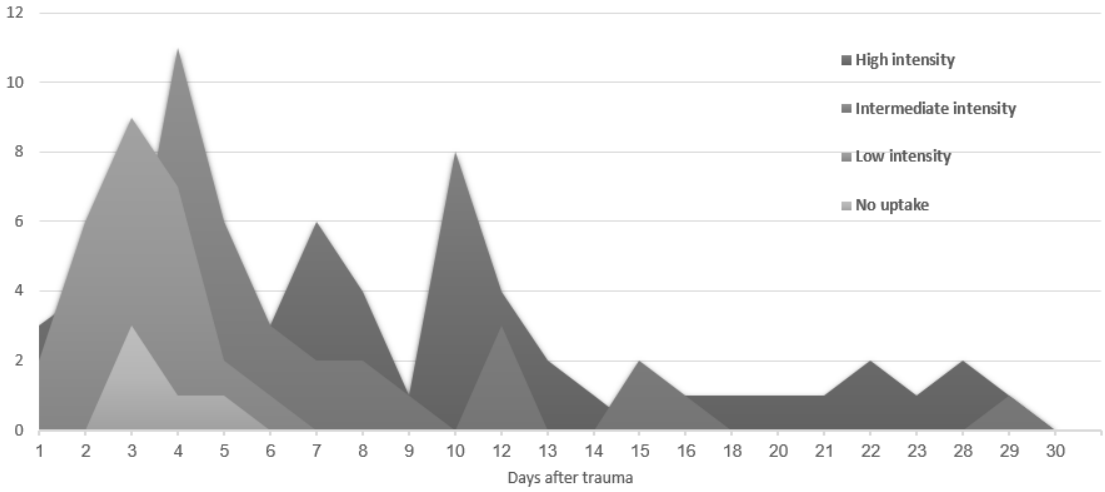
Figure 3:



On early BS, increased blood pool was observed in 193 vertebrae (60%). On late BS, vertebrae showing hyperemia on early studies had higher uptake intensities; 121 vertebrae (63%) had high intensity uptake, 60 (31%) had intermediate and 12 (6%) had low-level uptake. Increased late tracer uptake without hyperemia was found in 130 vertebrae (40%), with lower uptake intensities; 14 vertebrae had high intensity uptake (11%), 47 had intermediate (36%) and 69 had low intensity uptake (53%). Hyperemia was more prevalent in the lower thoracic and lumbar spine (T11 to L5, 63%) compared to high and mid-thoracic spine (T1 to T10, 42%).

In a subgroup of 108 patients with a known date of the traumatic event and 132 acute VCFs according to CT, BS uptake intensity was compared to the time period elapsed since the trauma. Acute VCFs with no increased uptake were found up to five days after trauma, and VCFs with low intensity uptake were seen up to six days after trauma. Acute VCFs with intermediate and high intensity uptake were seen from the first day after trauma up to 38 and 62 days, respectively (figure 4).

Figure 4:



Increased uptake in ribs, sacrum and pelvis, consistent with acute fractures, were seen in a majority of the patients (160, 84%) on BS. Single rib fractures were observed in 28 patients,multiple rib fractures in 63 patients, sacral fractures in 55 and pelvic fractures in 14 patients.

Comparison of CT and bone scintigraphy findings:

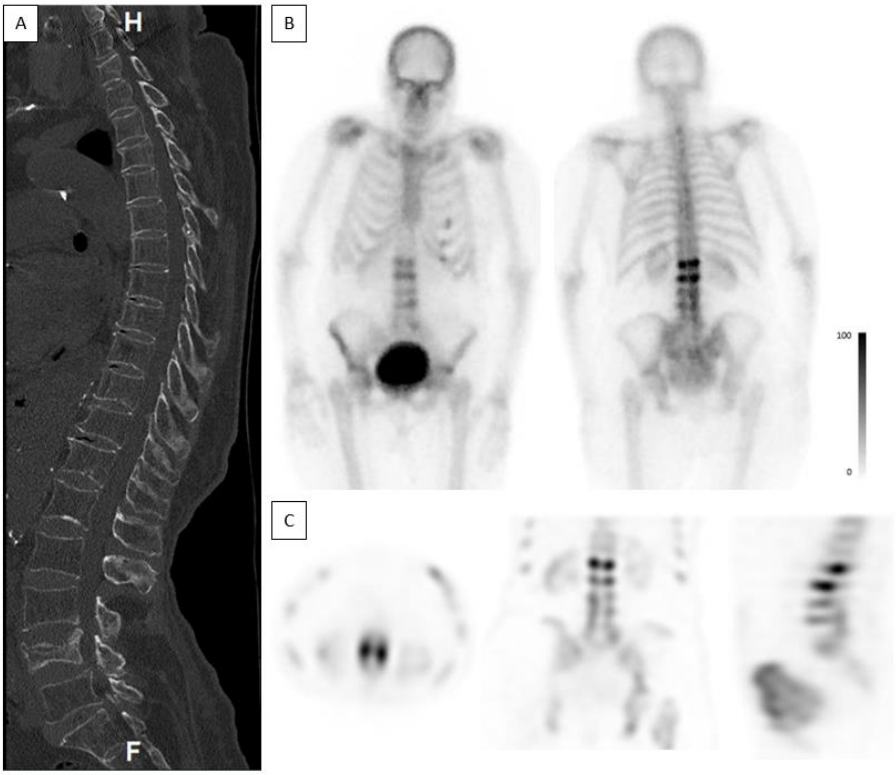
The imaging patterns of CT and BS were compared in 2966 vertebrae. Table 1 and figures 5-7 demonstrate the different combined patterns of CT and BS.

Table 1: Prevalence of combined CT and BS patterns (n=2966):

CT pattern	**BS uptake intensity (0-3)***	**Number (%)**
Normal	0	2504 (84.4)
Normal	1	3 (0.1)
Normal	2	6 (0.2)
Normal	3	14 (0.5)
Acute VCF	0	7 (0.2)
Acute VCF	1	43 (1.4)
Acute VCF	2	79 (2.7)
Acute VCF	3	111 (3.7)
Chronic VCF	0	117 (3.9)
Chronic VCF	1	23 (0.8)
Chronic VCF	2	15 (0.5)
Chronic VCF	3	7 (0.2)
Post VP	0	15 (0.5)
Post VP	1	12 (0.4)
Post VP	2	7 (0.2)
Post VP	3	3 (0.1)
Non-union VCF	0	2 (0.1)
Non-union VCF	1	6 (0.2)
Non-union VCF	2	22 (0.7)
Non-union VCF	3	19 (0.6)
Ankylotic VCF	0	3 (0.1)
Ankylotic VCF	1	4 (0.1)
Ankylotic VCF	2	8 (0.3)
Ankylotic VCF	3	4 (0.1)

* 0-No increased uptake, 1-Low intensity uptake, 2-Intermediate uptake, 3-High intensity uptake

Figure 5



Occult fractures

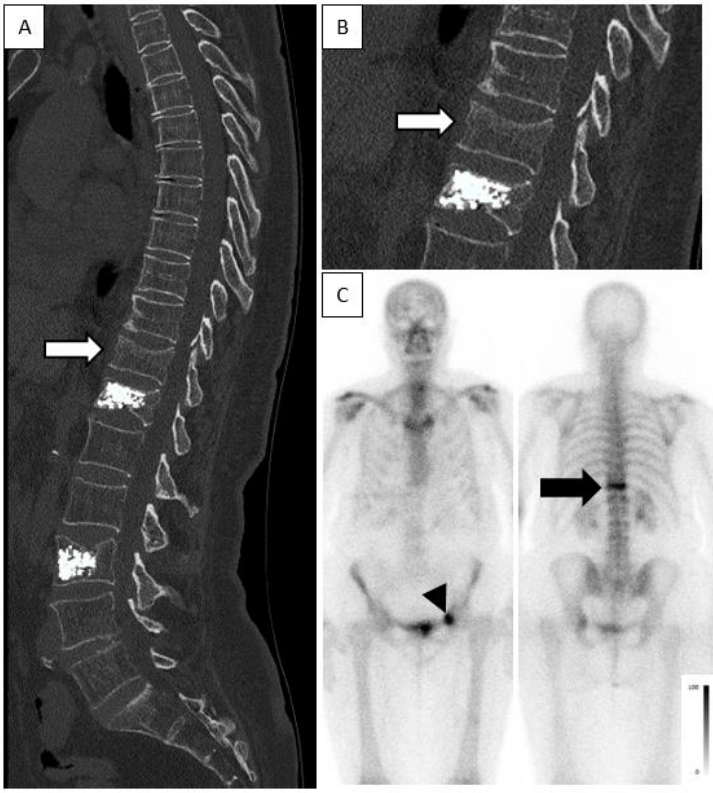
A 78 year old female complaining of back pain, without known trauma. CT was acquired on the day of admission and bone scintigraphy was performed 2 days after the CT.

A – Sagittal spine CT shows a non-union fracture in L4. No other fractures are demonstrated. Bone density measured in L3 was 7HU, consistent with severe osteoporosis.

B - Planar anterior and posterior bone scintigraphy shows high intensity uptake in L2 and L3 suggestive of acute fractures.

C – Axial, coronal and sagittal SPECT show high intensity uptake in L2 and L3.

Figure 6



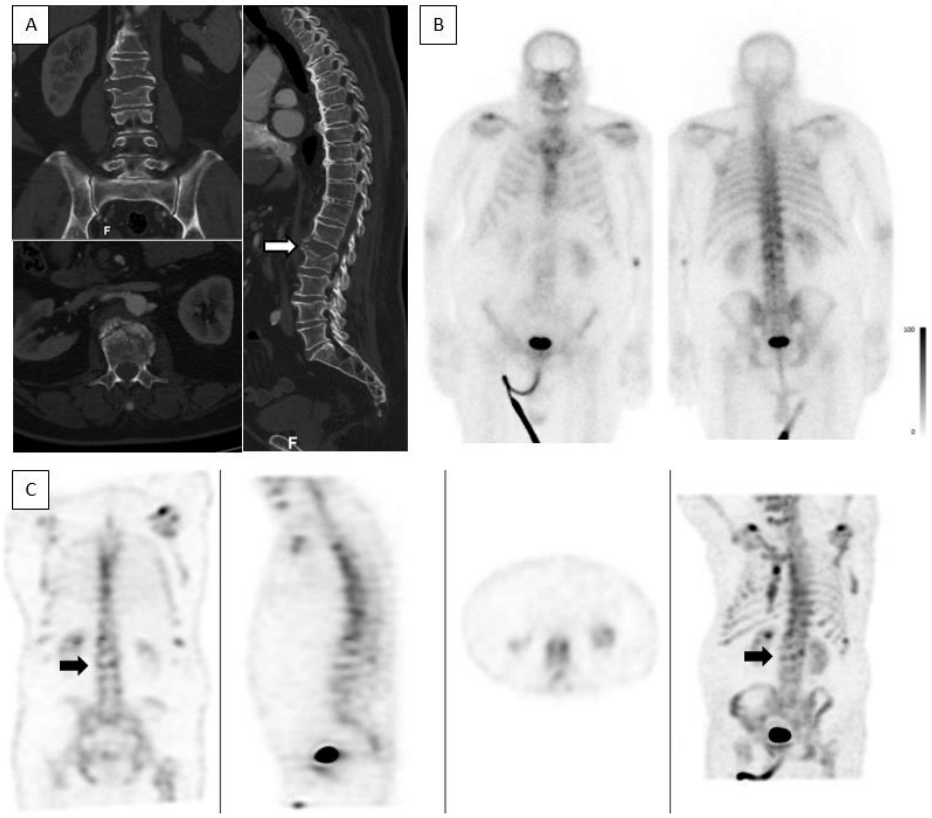
High intensity uptake in an acute fracture, no uptake in chronic fractures post-vertebroplasty

A 77 year old female after trauma. CT was acquired on the day of injury and bone scintigraphy was performed 3 days after the injury.

A and B – Sagittal spine CT (enlarged in B) show an acute fracture in T11 (white arrow) and chronic fractures after vertebroplasty in T12 and L3.

C - Planar anterior and posterior bone scintigraphy show high intensity uptake in T11 (black arrow) indicating an acute fracture and no increased uptake in T12 and L3, consistent with chronic fractures. Note also, high intensity uptake is seen in the anterior aspect of the left acetabulum (black arrow head), consistent with an acute fracture.

Figure 7



Low intensity uptake in an acute ankylotic VCF
A 72 year old male. CT was acquired on the day of injury and bone scintigraphy was performed 3 days after the injury.
A – Coronal, axial and sagittal spine CT show an acute ankylotic fracture in L2 and a fracture involving an osteophyte in L1 (white arrow).
B - Planar anterior and posterior bone scintigraphy do not show any increased uptake in L2.
C – Coronal, sagittal, axial and MIP SPECT show only low intensity uptake in L2 (black arrow).

Normal vertebrae – In the group of vertebrae with normal appearance on CT, most had no increased uptake on BS (2504/2527, 99%). Increased uptake was seen in 23 (0.9%) vertebrae that appeared normal on CT, consistent with the diagnosis of an acute radiologically occult fracture (figure 5). This pattern combination was observed in 17 patients. Multivariate logistic regression analysis of these patients indicated that an increase in age (OR = 0.913, 95% CI [0.840, 0.993], p = 0.035) and a decrease in bone density (OR = 0.969, 95% CI [0.939, 1.000], p = 0.052) were associated with a decrease in the odds of detection of a VCF on the CT. Notably, these associations remained statistically significant even after controlling for gender and the time elapsed between the trauma and scanning. Gender and time elapsed from trauma had no significant impact on the likelihood of detection of an occult fracture.

Acute VCFs – Most vertebrae with acute fractures on CT had increased uptake on BS (233/240, 97%), with 79 and 111 showing intermediate and high intensity uptake respectively (figure 6) and 43 showing low intensity uptake (figure 7). In seven acute VCFs, no increased uptake was seen on BS. The pattern combination of acute VCF with no increased or low intensity uptake was observed in 40 patients. The clinical characteristics of these patients were compared to the group with intermediate or high intensity uptake. In univariate analyses, the time elapsed between the trauma and BS was significantly shorter in these patients (4.62 ±6.18 vs. 9.68 ±11.48 days, p=0.026) and male gender was more

prevalent (31.7% vs. 16.2% ;p=0.015). Bone density was higher, but not statistically significant (69.90 ±34.92 vs 58.87 ±30.98, p=0.053). Multivariate logistic regression analysis also found a significant difference in the time span elapsed from the traumatic event to BS, with a shorter time period in the low uptake group (OR = 0.908, 95% CI [0.822, 1.003], p=0.057). No association was found with patient's age.

Hyperemia was seen in the early BS images in 157 acute VCFs (65%). In 83 acute VCFs (35%), no hyperemia was observed.

In non-union VCFs, high intensity uptake was more prevalent (84%), while in ankylotic VCFs, low intensity uptake was more prevalent (37%).

Chronic VCFs – Among 162 vertebrae with chronic fractures according to CT, most did not display increased uptake (117, 72%). Low intensity uptake was observed in 23 (14%) and high and intermediate intensity uptake was seen in 15 and 7vertebrae (9% and 4%) respectively. The pattern combination of chronic VCF and high intensity uptake was observed in 20 patients. Multivariate analysis of these patients' clinical characteristics showed significantly lower bone density (43.55 vs. 63.26 HU, p=0.009) and a trend towards female gender that was not statistically significant (p=0.092).

Post VP - Most vertebrae in this group showed no increased (15, 40%) or low intensity uptake (12, 32%) and few demonstrated intermediate and high intensity uptake (7, 19% and 3, 8% respectively).

DISCUSSION:

The present study identified and characterized 2966 vertebrae in 190 patients with 439 VCFs. The study population was mostly elderly and female. Only 5% of the patients had normal bone density, estimated using spine CT, and over 85% had osteoporosis according to these measurements. Most patients (55.8%) had more than one VCF, with 16.8% of them having three or more VCFs. In some cases, a combination of acute and chronic fractures was found. Most of the fractures were located in the thoraco-lumbar area.

In most patients CT results were sufficient to determine whether a vertebra was normal or had either acute or chronic VCF, but in 37 (19.5%) patients BS added important information related to the fracture that could influence patient management. Radiologically occult fractures were seen in 23 normal-appearing vertebrae and in 22 vertebrae with the appearance of chronic fractures. These occult fractures were amenable for surgical intervention, which could potentially improve pain relief and facilitate patient mobilization (1). The phenomenon of radiologically occult fractures, also known as "VCFs without radiologic collapse", has been described in several studies. Pham et al. described 16 osteoporotic subjects with acute, severe back pain but no evidence of VCF on lateral spine radiograph. MRI or BS showed findings consistent with acute fractures in an anatomic distribution correlating with the clinical pain. The subjects were followed-up prospectively with radiographic changes consistent with VCFs developing in 80% of subjects by the end of the study (12). Additional studies and reviews have described these phenomena on radiographs (13–17) but not on CT. Our study demonstrated that occult fractures may also be present and missed on diagnostic, high resolution CT or may be present in a vertebra with imaging characteristics of a chronic fracture. In a multivariate logistic regression analysis,

occult fractures in normal-appearing vertebrae on CT were associated with an increase in age and a decrease in bone density. This could be explained by the lower visibility of cortical disruption and impaction of the trabeculae in osteoporotic vertebrae, that have thinner and less dense trabeculae and cortex. The patient's gender and the time elapsed between the traumatic event and scanning had no significant impact on the likelihood of detection of an occult fracture on BS.

Increased radiotracer uptake in vertebral fractures begins to show up on BS in the osteoblastic activity once the healing process starts, usualy during the initial hours after injury. In many cases, fractures can be seen on BS earlier than on radiographs or even CT, mainly in rib and sacral fractures. In the seminal study by Matin et al. from 1979, the appearance of various fractures on BS over time was reported in 204 patients (19). In this study, 80% of all fractures showed abnormal uptake by 24 hours, and 95% by 72 hours after injury. Only in two patients, both over the age of 65 years, there was no increased uptake on BS in a known acute fracture by 72 hours. A week after the injury, BS was abnormal in 58 out of 59 patients, with only an 80-year-old woman with osteoporosis and an impacted hip fracture, showing no abnormalities on BS. While this study suggests that in the elderly population, scintigraphic abnormalities may appear later than in younger patients, it did not focus on vertebral fractures and had only a limited number of elderly patients. Another study by Spitz et al. from 1992 investigated the appearance of fractures on BS in 480 patients, including 123 fractures in the thoracic and lumbar spine and 357 fractures in other bones, including the radius, scaphoid, femoral neck, pelvis and shaft of long bones (20). In 18 patients, repeated scanning was conducted during the initial 24 hours after injury. All acute fractures showed increasing accumulation of Tc-99m MDP at the fracture site in those 24 hours and within 2 weeks after injury, but the magnitude of the increase was markedly different in different bones. Spine fractures showed the latest and slowest accumulation of Tc-99m MDP, with some fractures appearing only 10 to 12 days after the injury. The authors suggest that these findings are related to the amount of callus formation found in fractures adjacent to joints compared to vertebral fractures, and that similar behavior can be seen in skull fractures that show minimal uptake on BS and almost no callus formation on radiographs. Multiple-regression analyses did not find any correlation between the time of appearance of the fracture and the patient's age and gender, in contrast to Matin et al's study. The authors concluded that the rate of accumulation of Tc-99m MDP is only dependent on the fracture site, with slower accumulation in the spine and the shafts of long bones. To the best of our knowledge, the appearance of vertebral fractures over time on BS was not investigated in recent years. Present study investigates only vertebral fractures in mostly elderly patients. Most of the scans were conducted 48 hours after the spine CT, which was usually performed on the first or second day of admission. The mean time elapsed between the known trauma and BS was 8.3 days. Intermediate and high intensity uptake could be seen in fractures dating from 24 hours to 62 days after injury, demonstrating that higher intensities of uptake can appear soon after injury and persist for a long period of time. Acute fractures with no increased or low intensity uptake could only be seen within the first six days after injury (figure 4). In the group of patients with low intensity uptake in acute fractures, the time elapsed between the traumatic event and BS was significantly shorter, with an average time of 4.6 days compared to 9.7 days in patients with intermediate and high intensity uptake (P=0.026). Significant correlation was also found to male gender and a non-significant trend towards higher bone density. No association was found with the patient's age. These data show that the time of appearance of increased

tracer uptake does not necessarily dependent only on age, as suggested by Matin et al. or only on the timing of BS and the fracture location, as suggested by Spitz et al., but is influenced by multiple factors. The higher prevalence of males in the group of patients with low-grade uptake was surprising, considering the smaller number of males in our study population (33%). We also observed a higher prevalence of ankylotic fractures and a tendency towards ankylotic spine in this group, but this was not statistically significant. Since ankylosing spondylitis occurs more in males (21), this may explain their higher prevalence in this group. Further study of this population is needed to elucidate the reasons for the lack of appearance of fractures on BS.

According to orthopedic guidelines, MRI is considered the gold standard method for determining the acuity of a VCF, while the combination of CT and BS are reserved for claustrophobic patients or for MRI incompatibility (patients with a pacemaker, cochlear implant, etc.) (2,3,22). Some guidelines refer to MRI and BS equally as "advanced imaging" that can reliably confirm the presence and location of acute VCFs that may be amenable to treatment (23). Results of present study demonstrate that in clinical scenarios when MRI is unavailable in the acute setting of hospitalized patients, a combination of spine CT and BS can be used for detecting and establishing the age of vertebral fractures. While BS is considered a sensitive method for detecting acute fractures and for determining a fracture's age (5,24) several studies report discordance between results of MRI and BS concerning the establishment of the age of VCFs. A study by Masala et al. found that MRI and BS are concordant for fractures up to 4 months old (7). Kim et al. found an overall concordance of only 55% between the methods. The concordance for single level VCFs was very high (96%) with a significant drop in concordance in 2 level (50%) and 3 level fractures (only 36%) (8). In a study by Dafydd et al. from 2014 the overall concordance was of 63%, with almost twice as many acute or subacute fractures found on BS (9). These studies suggest that acute fractures appear on BS for a longer period of time than on MRI. In multilevel fractures, the different VCFs probably have different ages, with older fractures not apparent on MRI but still seen on BS. Therefore, it can be assumed that the information regarding the temporal dynamics is not equivalent in BS and MRI. Despite the discordance between the methods, BS were found to be a useful method for location of the painful vertebra before surgical treatment (25-28). Most of these studies had a small number of up to 44 patients, none of them used an early blood pool phase, and SPECT/CT was used only in a single study. To the best of our knowledge, this is the first study comparing imaging patterns of VCFs in BS and CT at varying time points. In our study, an early blood pool phase scan was acquired in 97% of the patients, and all studies included SPECT of the thoracic and lumbar spine. The majority of acute VCFs, 65%, showed hyperemia. The fact that 83/240 (35%) of these fractures demonstrated no hyperemia may be explained by relatively older aged fractures. The early blood pool images are characterized by low resolution and unfavorable target-to-background ratios. In the thoracic spine, vertebral hyperemia is often obscured by uptake in the mediastinum. Therefore, it might be concluded that although hyperemia can be considered a definite sign of acute fracture, its sensitivity is low and its absence should not rule out an acute VCF. SPECT studies are known to increase the sensitivity and specificity of BS (18). In current study, SPECT images were very helpful in detecting low intensity uptakes that would have been missed using only planar images, as shown in figure 7. They were also paramount for determining the exact location of the fractures and were easier to compare to the recently-performed spine CT. The combined viewing of the SPECT and CT images was helpful in differentiating uptakes caused by degenerative changes vs. true fractures. If spine

CT is not acquired prior to the bone scintigraphy in patients with suspected acute VCF, SPECT/CT should be performed when available.

In an attempt to detect radiologically occult acute VCFs using only CT, efforts aiming at the implementation of machine learning and artificial intelligence tools are planned in continuation of the present research project. Preliminary results indicate that applying these methods to CT images may potentially detect occult fractures invisible to the human eye.

The imaging patterns observed in the current study may be extrapolated in the future, after additional research, to other bone imaging scintigraphy methods such as F18-fluoride positron emmission tomography (PET) or PET/MR.

Our study was limited by using retrospective data. Even more definite data may have been gained by repeating BS at decided time points during the first week after injury but this was not clinically feasible. Estimation of osteopenia and osteoporosis in our patient population was performed using an opportunistic method applied to the previously acquired spine CT. Although this method was investigated and found to accurately represent mineral bone density (11), using dual x-ray absorptiometry would have been more precise.

In conclusion, BS in the setting of vertebral compression fractures in the elderly population, adds valuable information on the fracture's age, can detect occult fractures and subsequently affect patient management. The ideal timing of the scan should be considered, as in some cases no increased uptake or only low-intensity uptake was demonstrated in acute fractures up to six days after trauma. Further research is needed to elucidate the causes of the late uptake appearance in these cases.

ACKNOWLEDGEMENTS:

We are gratefull to Mr. Basem Hijazi for experimental design and statistical analysis.

STATEMENTS AND DECLARATIONS:

The authors declare that no funds, grants, or other support were received during the preparation of this manuscript.

Financial interests: Author A is a medical consultant to GE HealthCare. Authors B to D declare they have no financial interests. Author E reseaved a research grant, and lecturer honorarium from Medtronic LLC, USA and is an AO Spine examiner reimbursement and lecturer honorarium, AO, Switzerland.

Elite Arnon-Sheleg and Nimrod Rahamimov contributed to the study conception and design. Elite Arnon-Sheleg lead the data collection and analysis and wrote the manuscript. Daniel Weiner, Saeda Haj and Alon Rod contributed to data collection and analysis. All authors read and approved the final manuscript.

This study was performed in line with the principles of the Declaration of Helsinki and was approved by the medical center's institutional review board (approval number 0038-20-NHR). The need for written informed consent was waived.

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