Imaging in Osteoporosis: An update.

Karen M. Knapp[1], Robert Meertens[2], Richard Seymour[3]

1. Associate Professor in Musculoskeletal Imaging, College of Medicine and Health, University of Exeter, Exeter, UK

2. Senior Lecturer in Medical Imaging, College of Medicine and Health, University of Exeter, Exeter, UK

3. Consultant Radiologist, Radiology, Torbay Hospital, Torbay and South Devon NHS Foundation Trust., Torquay, UK

Corresponding author:

Dr Karen Knapp
Medical Imaging
South Cloisters
St Luke's Campus
Heavitree Road
Exeter
Devon
EX1 2LU

Telephone: 01392 724133
Email: K.M.Knapp@exeter.ac.uk

Abstract

Osteoporosis is characterised by low bone mineral density and micro-architectural deterioration of bone leading to an increased risk of low trauma fractures, associated morbidity and mortality. This article describes the advances in imaging of osteoporosis including opportunistic identification of low bone density and vertebral fractures. A recap of the imaging required in the diagnosis and management of osteoporosis is also covered since it is important to include imaging within the patient pathway, especially where vertebral fractures are suspected. Additional imaging modalities such as magnetic resonance imaging are important to aid differential diagnosis where the cause of the fracture is unclear. Clinicians reviewing imaging examinations, radiographers and radiologists reporting these must be vigilant for the presence of osteoporosis and play a major role in ensuring these patients have their risks highlighted so that they are put onto the appropriate pathway for diagnosis and treatment. Fracture liaison services provide a robust system for ensuring appropriate capture and follow-up of patients at risk of osteoporosis.

Key words: Osteoporosis, Imaging, Fracture, Diagnosis

Introduction

One in two women and one in five men over the age of 50 will sustain a fracture, most of which are attributable to osteoporosis[1]. Osteoporosis is characterised by reduced bone density and micro-architectural deterioration of bone; it is a common metabolic bone disease in the elderly population resulting in an increased risk of fracture[2]. Patients with osteoporosis-related fractures describe osteoporosis as a frequently invisible disability which negatively impacts on their life and can have a life changing impact, including the need to cease working or give up enjoyable activities which are not compatible with their risk of fracture[3]. Osteoporosis is a major public health issue in the UK, although trends in fracture incidence between 1990 and 2012 demonstrate no significant changes in fracture incidence in those aged 50 and over[4]. However, there is an increased incidence of clinical vertebral fractures in women reported over the same period, which may be as a result from improvements in diagnosis and reporting[4]. Appropriate diagnosis, therapeutic intervention and monitoring remains a key priority to reduce the burden of osteoporosis-related fractures. This paper will discuss the use of imaging in the opportunistic diagnosis, differential diagnosis and monitoring of osteoporosis.

Patients presenting with fragility fractures

Osteoporosis can lead to fractures anywhere in the skeletal system, although fractures of the wrist, hip and vertebrae are the most commonly seen.[5] Patients presenting with low trauma fragility fractures or those who have notable x-ray osteopenia should be referred for a DXA scan[6]. Figures 1a and 1b demonstrate a Colles' fracture with marked x-ray osteopenia. X-ray osteopenia can be identified by reduced cortical thickness with an associated appearance of reduced density and more prominent trabeculation being visualised on a radiograph, frequently providing less contrast between the bone and soft tissues than when compared to radiographs of normal density bone[7]. Whilst osteoporosis may be suspected from these radiographic findings, this is not a reliable way of making the diagnosis and projection radiography is not indicated for the assessment of osteoporosis in the absence of the requirement for fracture diagnosis. Projection radiography remains the first line imaging choice in many incidents where there is clinical suspicion of a fracture such as vertebral or appendicular fracture. However, in the case of a cervical spine fracture, computed tomography (CT) is recommended in the first instance due to the difficulties of interpretation of radiographs in the elderly population[8]. Some patients who have clinical signs and

symptoms of a fracture, but without radiographic confirmation may have and occult fracture. These are of particular importance in the hip, where identifying the fracture quickly to ensure the patient reaches theatre with twenty-four hours is of utmost importance[9]. In this case the ideal pathway providing the greatest diagnostic accuracy is to perform an magnetic resonance imaging (MRI) scan (figure 2), where the bone marrow oedema associated with the occult fracture can confirm its presence[10]. In patients who are not suitable for MRI, or where MRI is not available, CT can be used as an alternative, though has a marginally poorer accuracy[10,11]. Post imaging, the most effective way of ensuring patients presenting with a fracture are referred for a DXA and have appropriate assessment for osteoporosis is via a fracture liaison service[12].

Diagnosis

Dual energy x-ray absorptiometry (DXA) remains the most widely accepted method for the assessment of osteoporosis[13]. While the UK currently does not have a screening programme for osteoporosis[14], the SCOOP study has demonstrated that screening is a cost effective tool for preventing fractures in older women aged between 70 and 85 years using a combination of FRAX and bone mineral density (BMD) measurements[15]. Identification of patients who need bone assessment can be aided by tools such as FRAX and QFRACTURE which also independently predict fracture risk using modelling based on clinical risk factors[16 17,18]. Early diagnosis allows treatment for osteoporosis before a fragility fracture has occurred and NICE recommends considering assessing the risk of fragility fracture in all women aged 65 years and over and all men aged 75 years and over as well as patient with clinical risk factors over 50 years with and in those younger than 50 years with major risk factors[19]. Falls history should also be considered alongside bone mineral density and clinical risk factors when deciding on therapeutic intervention, since it provides a further independent risk factor for fracture[20].

Vertebral fracture assessment

Dual x-ray absorptiometry scanners can also be utilised for vertebral fracture assessment (VFA), as demonstrated in figure 3. VFA provides a lateral image of T4 to L4, and has a significantly reduced dose compared to a thoraco-lumbar projection radiography series[21]. It has been reported to have a high degree of accuracy for diagnosing fracture and in practice can increase the identification of vertebral fractures and altered patient management in

those with unknown fractures[22,23]. The presence of a vertebral fracture can lead to pain, deformity and loss of function, but importantly is also a strong predictor of future fracture[24]. Vertebral fracture diagnosis remains suboptimal and many sufferers have multiple fractures prior to diagnosis[25]. Using VFA in practice has been demonstrated to increase the number of patients diagnosed with osteoporosis and requiring therapeutic intervention[26 25].

If a vertebral fracture is identified on a VFA scan, then radiographs are required to differentiate between non-fracture deformities such as Scheuermanns' disease or degenerative changes, or to examine for another pathology causing the fracture, for example Paget's disease of bone or malignancy[27]. Further imaging may be required where other underlying pathology is suspected and MRI, CT, Nuclear Medicine or PET-CT may be used depending on the pathology suspected. MRI and PET-CT in combination have been demonstrated to have high sensitivity and specificity for benign and malignant lesions in the spine, with 100% accuracy in the former[28]. Figures 4a and 4b demonstrate a vertebral fracture resulting from metastatic disease.

Vertebral fractures where the patient continues to have pain despite optimal pain management[29], should be investigated using clinical examination and or imaging to confirm the pain is at the site of the fracture. Magnetic resonance imaging can be particularly useful if considering a vertebroplasty or kyphoplasty[30]. However, a recent Cochrane review reported moderate to high quality evidence that vertebroplasty has little benefit for treating acute or subacute vertebral fractures in routine clinical practice when compared to a sham procedure[31]. Patients with osteoporosis suffering from low back and pelvis pain should have sacral insufficiency or stress fractures considered as part of their differential diagnosis. These occasionally also occur in the final trimester of pregnancy and postpartum in younger women. Computed tomography or MRI provide better sensitivity and specificity, with MRI being considered the current gold standard for sacral insufficiency fractures[32].

Differential diagnosis

The presence of apparent osteoporosis on a DXA measurement, with or without fracture, may not provide the definitive diagnosis. Vitamin D deficiency is becoming increasingly prevalent among the elderly population within the UK and therefore osteomalacia should be ruled out by blood tests, particularly in those who are immobile and do not go outside often[33]. There are occasionally some findings in osteomalacia which are not seen in osteoporosis. A "Looser's zone" or pseudofracture, may be seen in osteomalacia along with reports of bone pain and muscle weakness[34], which are not typical symptoms of osteoporosis[35].

Multiple myeloma can cause lytic lesions, which improve with chemotherapy[36] but the x-ray appearance may also be one of diffuse osteopenia, mimicking osteoporosis. There should be a low index of suspicion for this condition and patients with suspected Multiple Myeloma may be screened by blood tests looking for anaemia, abnormal protein levels and raised plasma viscosity and further assessment of urine for Bence Jones protein and plasma electrophoresis where diagnosis is strongly suspected. Finally, occasional anatomical anomalies are visualised on DXA scans which may or may not impact on the BMD results. If these are unexplained, then further imaging may be required to investigate these.

Opportunistic identification of low bone mineral density and vertebral fractures

Around 30% of vertebral fractures are asymptomatic and do not come to clinical attention or are undiagnosed at the point patients present with pain[3,37]. This has resulted in an interest in opportunistic identification of vertebral fractures from imaging undertaken for other clinical reasons. This includes CT, MRI and radionuclide or PET scans as well and projection radiographs. Multi-planar sagittal reconstructions (Figure 5) of CT scans enable easier visualisation of vertebral fractures than the traditional axial slices and education for all clinicians to look for and report vertebral fractures is a key requirement for improving outcomes in patients with osteoporosis and vertebral fractures [37,38]

Further opportunistic identification of low bone mineral density comes from CT scans using asynchronous techniques. Traditionally, CT measurements of BMD have required the patient to be scanned with a phantom within the field of view. However, asynchronous BMD measurement using CT means that a phantom can be scanned weekly and the Hounsfield numbers of bone compared to the phantom, yielding a bone mineral density measurement for patients who are having CT scans for potentially unrelated reasons [39,40 41]. This technology is still developing an evidence-base and it is not currently used in general clinical practice, however, it affords opportunities for the future to improve the identification of those at risk of fragility fractures.

Emerging computer aided detection technologies aiming to better identify and classify incidental vertebral fractures from CT and projection radiography, as well as estimating osteoporotic risk based on cortical thickness of commonly performed imaging such as orthopantomography (OPG) are developing. Although these currently remain predominately

in the research phase, they may potentially help in the future to address the high miss rate of these clinically important findings that are predictive of future osteoporotic fracture [33] [34].

Longitudinal monitoring

A diagnosis of osteoporosis requires the consideration of therapeutic intervention in line with national and local guidelines and in line with clinical decision making in relation to the clinical history of the patient[42] [43]. The monitoring of treatment responses in patients can assist with adherence and compliance, which is currently poor for those taking bisphosphonates[44,45]. However, the use of DXA in treatment monitoring is often sub-optimal, with time intervals between 18 to 24 months to reliably measure changes as a result of therapeutic interventions [46]. Biochemical markers of bone turnover are an appropriate alternative where available and can detect treatment response much more rapidly than DXA, with a reliable result just three months post commencing treatment[47]. Monitoring of BMD five to ten years post commencing treatment is of particular use when considering a drug treatment holiday for patients on bisphosphonates to prevent the over suppression of bone turnover. Further monitoring may be required during the treatment holiday when an increase in bone turnover markers and a reduction in BMD may signal the requirement to recommence treatment[48].

Bisphosphonates have been demonstrated to be effective at increasing BMD and reducing fractures by approximately 50% over 2 years of use[49]. However, as the longevity of bisphosphonates has increased, adverse events in long-term users, generally of greater than five years have been reported. Atypical fractures of the femora (figure 6) in men and women have been reported in a number of studies. These fractures share a common appearance, with periosteal thickening as often seen in stress fractures. The fractures also tend to be transverse and in the upper third of the femur[50] [51]. Projection radiography is the most common method for diagnosing these fractures and additional imaging is rarely required; the important thing is for radiologists and physicians to be aware of the imaging findings and to suspect the condition when patients on bisphosphonate therapy present with new hip, groin or thigh pain. Bilateral atypical femoral fractures also occur in a proportion of cases and a low threshold for imaging the contra-lateral femur in cases of incomplete or complete atypical femoral fracture is recommended [52,53] [54]. If there is doubt on radiographic images MRI or radionuclide imaging may be helpful.

Osteonecrosis of the jaw (ONJ) is a rare, but notable complication of those on long term and especially high dose bisphosphonates, such as those with metastatic bone disease[55]. Imaging for this is required to ascertain the extent and differentiate from metastatic disease. Nuclear medicine scintigraphy provides the ability for early diagnosis and other imaging may include dental radiographs, orthopantomographs (OPG's), MRI and CT to investigate the extent and assist in differential diagnosis of ONJ[56].

Conclusion

In conclusion, imaging plays an integral role in the diagnosis and management of osteoporosis, osteoporotic fractures and the complications associated with bisphosphonate treatment. Opportunistic identification of vertebral fractures and low bone mineral density is increasing and these are likely to become standard practice in the future. Additional imaging modalities such as MRI can aid differential diagnosis where the cause of the fracture is unclear and it is important to include imaging within the patient pathway where vertebral fractures are suspected. Radiographers and radiologists reporting imaging examinations have a duty to identify and report vertebral fractures as such and highlight the need for osteoporosis assessment. Fracture liaison services provide an evidence-based provision to ensure that patients presenting with fractures are directed into osteoporosis services.

References

1. Van Staa TP, Dennison EM, Leufkens HGM, Cooper C. Epidemiology of fractures in England and Wales. *Bone* 2001; **29**(6): 517-22.
2. Leali PT, Muresu F, Melis A, Ruggiu A, Zachos A, Doria C. Skeletal fragility definition. *Clinical cases in mineral and bone metabolism : the official journal of the Italian Society of Osteoporosis, Mineral Metabolism, and Skeletal Diseases* 2011; **8**(2): 11-3.
3. Arnold J, Ewings P, Handel L, et al. Fragile: Please handle with care. *Radiography* 2018; **24**: S9-S10.
4. van der Velde RY, Wyers CE, Curtis EM, et al. Secular trends in fracture incidence in the UK between 1990 and 2012. *Osteoporosis international : a journal established as result of cooperation between the European Foundation for Osteoporosis and the National Osteoporosis Foundation of the USA* 2016; **27**(11): 3197-206.
5. Gehlbach S, Saag KG, Adachi JD, et al. Previous fractures at multiple sites increase the risk for subsequent fractures: the Global Longitudinal Study of Osteoporosis in Women. *Journal of bone and mineral research : the official journal of the American Society for Bone and Mineral Research* 2012; **27**(3): 645-53.
6. Rabar S, Lau R, O'Flynn N, Li LL, Barry P, Guideline Dev G. Risk assessment of fragility fractures: summary of NICE guidance. *Br Med J* 2012; **345**.
7. Jergas MaG, H.K. Radiology of Osteoporosis. . Third Edition ed: Amsterdam; Boston: Elsevier Academic Press; 2008. .
8. National Institute for Health and Care Excellence (NICE). Spinal injury: assessment and initial management. NICE guideline [NG41]; 2016.
9. NICE. CG124 Hip fracture: The management of hip fracture in adults. . NICE; 2011.
10. Hakkarinen DK, Banh KV, Hendey GW. Magnetic resonance imaging identifies occult hip fractures missed by 64-slice computed tomography. *The Journal of emergency medicine* 2012; **43**(2): 303-7.
11. Jordan R, Dickenson E, Westacott D, Baraza N, Srinivasan K. A vast increase in the use of CT scans for investigating occult hip fractures. *Eur J Radiol* 2013; **82**(8): e356-9.
12. Physicians RCo. Fracture Liaison Service Database (FLS-DB) clinical audit. FLS forward: Idnetifying high-quality care in the NHS for secondary fracture prevention. London: Royal College of Physicians, 2017.
13. Blake GM, Fogelman I. The role of DXA bone density scans in the diagnosis and treatment of osteoporosis. *Postgrad Med J* 2007; **83**(982): 509-17.
14. Kanis JA, McCloskey EV, Johansson H, et al. European guidance for the diagnosis and management of osteoporosis in postmenopausal women. *Osteoporosis International* 2013; **24**(1): 23-57.
15. Turner DA, Khioe RFS, Shepstone L, et al. The Cost-Effectiveness of Screening in the Community to Reduce Osteoporotic Fractures in Older Women in the UK: Economic Evaluation of the SCOOP Study. *Journal of bone and mineral research : the official journal of the American Society for Bone and Mineral Research* 2018; **33**(5): 845-51.
16. Hippisley-Cox J, Coupland C. Derivation and validation of updated QFracture algorithm to predict risk of osteoporotic fracture in primary care in the United Kingdom: prospective open cohort study. *BMJ (Clinical research ed)* 2012; **344**: e3427.
17. Premaor M, Parker RA, Cummings S, et al. Predictive Value of FRAX for Fracture in Obese Older Women. *Journal of Bone and Mineral Research* 2013; **28**(1): 188-95.
18. Hillier TA, Cauley JA, Rizzo JH, et al. WHO Absolute Fracture Risk Models (FRAX): Do Clinical Risk Factors Improve Fracture Prediction in Older Women Without Osteoporosis? *Journal of Bone and Mineral Research* 2011; **26**(8): 1774-82.
19. National Institute for Health and Care Excellence (NICE). Osteoporosis: assessing the risk of fragility fracture. Clinical guideline [CG146]; 2012.

20. Edwards MH, Jameson K, Denison H, et al. Clinical risk factors, bone density and fall history in the prediction of incident fracture among men and women. *Bone* 2013; **52**(2): 541-7.
21. Diacinti D, Guglielmi G. Vertebral morphometry. *Radiologic clinics of North America* 2010; **48**(3): 561-75.
22. Kuet KP, Charlesworth D, Peel NFA. Vertebral fracture assessment scans enhance targeting of investigations and treatment within a fracture risk assessment pathway. *Osteoporosis International* 2013; **24**(3): 1007-14.
23. Diacinti D, Guglielmi G, Pisani D, et al. Vertebral morphometry by dual-energy X-ray absorptiometry (DXA) for osteoporotic vertebral fractures assessment (VFA). *Radiol Med* 2012; **117**(8): 1374-85.
24. Puisto V, Heliovaara M, Impivaara O, et al. Severity of vertebral fracture and risk of hip fracture: a nested case-control study. *Osteoporosis international : a journal established as result of cooperation between the European Foundation for Osteoporosis and the National Osteoporosis Foundation of the USA* 2011; **22**(1): 63-8.
25. de Klerk G, Hegeman JH, Bronkhorst P, van der Palen J, van der Velde D, Duis HJ. The (a)-Symptomatic Vertebral Fracture: A Frequently Discovered Entity With Clinical Relevance in Fracture Patients Screened on Osteoporosis. *Geriatric orthopaedic surgery & rehabilitation* 2012; **3**(2): 74-8.
26. Mrgan M, Mohammed A, Gram J. Combined Vertebral Assessment and Bone Densitometry Increases the Prevalence and Severity of Osteoporosis in Patients Referred to DXA Scanning. *J Clin Densitom* 2013.
27. Schousboe JT, Vokes T, Broy SB, et al. Dual-energy X-ray absorptiometry technical issues: The 2007 ISCD Official Positions. *J Clin Densitom* 2008; **11**(1): 92-108.
28. Aggarwal A, Salunke P, Shekhar BR, et al. The role of magnetic resonance imaging and positron emission tomography-computed tomography combined in differentiating benign from malignant lesions contributing to vertebral compression fractures. *Surgical neurology international* 2013; **4**(Suppl 5): S323-6.
29. NICE. TA279 Percutaneous vertebroplasty and percutaneous balloon kyphoplasty for treating osteoporotic vertebral compression fractures NICE; 2013.
30. Graziotti PJ, Graziotti CR, Sangster AM. Significance of preoperative MRI in establishing levels of augmentation for percutaneous vertebroplasty. *Journal of pain research* 2013; **6**: 359-65.
31. Buchbinder R, Johnston RV, Rischin KJ, et al. Percutaneous vertebroplasty for osteoporotic vertebral compression fracture. *The Cochrane database of systematic reviews* 2018; **11**: Cd006349.
32. Longhino V, Bonora C, Sansone V. The management of sacral stress fractures: current concepts. *Clin Cases Miner Bone Metab* 2011; **8**(3): 19-23.
33. Mavroeidi A, Aucott L, Black AJ, Fraser WD, Reid DM, Macdonald HM. Seasonal variation in 25(OH)D at Aberdeen (57 degrees N) and bone health indicators--could holidays in the sun and cod liver oil supplements alleviate deficiency? *PloS one* 2013; **8**(1): e53381.
34. Reginato AJ, Falasca GF, Pappu R, McKnight B, Agha A. Musculoskeletal manifestations of osteomalacia: report of 26 cases and literature review. *Seminars in arthritis and rheumatism* 1999; **28**(5): 287-304.
35. Zhao Y, Liu Y, Zheng Y. Osteoporosis and related factors in older females with skeletal pain or numbness: a retrospective study in East China. *The Journal of international medical research* 2013; **41**(3): 859-66.
36. Roux S, Bergot C, Fermand JP, Frija J, Brouet JC, Mariette X. Evaluation of bone mineral density and fat-lean distribution in patients with multiple myeloma in sustained remission. *Journal of bone and mineral research : the official journal of the American Society for Bone and Mineral Research* 2003; **18**(2): 231-6.
37. Adams JE. Opportunistic Identification of Vertebral Fractures. *J Clin Densitom* 2016; **19**(1): 54-62.
38. Adams J CEM, Clunie G, Griffin J, Groves C, Javaid K, Jones T, Layland S, Pearson A, Peel N, Sahota O, Salem K, Sayer J, Stephenson S, Wakefield V. Clinical Guidance for the Effective

Identification of Vertebral Fractures. National Osteoporosis Society: National Osteoporosis Society; 2017.
39. Pickhardt PJ, Bodeen G, Brett A, Brown JK, Binkley N. Comparison of femoral neck BMD evaluation obtained using Lunar DXA and QCT with asynchronous calibration from CT colonography. *J Clin Densitom* 2015; **18**(1): 5-12.
40. Therkildsen J, Thygesen J, Winther S, et al. Vertebral Bone Mineral Density Measured by Quantitative Computed Tomography With and Without a Calibration Phantom: A Comparison Between 2 Different Software Solutions. *J Clin Densitom* 2018; **21**(3): 367-74.
41. Lee SJ, Anderson PA, Pickhardt PJ. Predicting Future Hip Fractures on Routine Abdominal CT Using Opportunistic Osteoporosis Screening Measures: A Matched Case-Control Study. *AJR American journal of roentgenology* 2017; **209**(2): 395-402.
42. Compston J, Bowring C, Cooper A, et al. Diagnosis and management of osteoporosis in postmenopausal women and older men in the UK: National Osteoporosis Guideline Group (NOGG) update 2013. *Maturitas* 2013; **75**(4): 392-6.
43. National Institute for Health and Care Excellence (NICE). Bisphosphonates for treating osteoporosis. Technology appraisal guidance [TA464]; 2017.
44. Olsen KR, Hansen C, Abrahamsen B. Association between refill compliance to oral bisphosphonate treatment, incident fractures, and health care costs-an analysis using national health databases. *Osteoporosis international : a journal established as result of cooperation between the European Foundation for Osteoporosis and the National Osteoporosis Foundation of the USA* 2013.
45. Vieira HP, Leite IA, Araujo Sampaio TM, et al. Bisphosphonates adherence for treatment of osteoporosis. *Int Arch Med* 2013; **6**(1): 24.
46. Knapp KM, Welsman JR, Hopkins SJ, Fogelman I, Blake GM. Obesity increases precision errors in dual-energy x-ray absorptiometry measurements. *Journal of clinical densitometry : the official journal of the International Society for Clinical Densitometry* 2012; **15**(3): 315-9.
47. Wheater G, Elshahaly M, Tuck SP, Datta HK, van Laar JM. The clinical utility of bone marker measurements in osteoporosis. *Journal of translational medicine* 2013; **11**(1): 201.
48. Chiha M, Myers LE, Ball CA, Sinacore JM, Camacho PM. Long Term Follow Up of Patients on Drug Holiday from Bisphosphonates: Real World Setting. *Endocrine practice : official journal of the American College of Endocrinology and the American Association of Clinical Endocrinologists* 2013: 1-16.
49. Murad MH, Drake MT, Mullan RJ, et al. Clinical review. Comparative effectiveness of drug treatments to prevent fragility fractures: a systematic review and network meta-analysis. *The Journal of clinical endocrinology and metabolism* 2012; **97**(6): 1871-80.
50. Cakmak S, Mahirogullari M, Keklikci K, Sari E, Erdik B, Rodop O. Bilateral low-energy sequential femoral shaft fractures in patients on long-term bisphosphonate therapy. *Acta orthopaedica et traumatologica turcica* 2013; **47**(3): 162-72.
51. Thompson RN, Phillips JR, McCauley SH, Elliott JR, Moran CG. Atypical femoral fractures and bisphosphonate treatment: experience in two large United Kingdom teaching hospitals. *The Journal of bone and joint surgery British volume* 2012; **94**(3): 385-90.
52. LeBlanc ES, Rosales AG, Black DM, et al. Evaluating Atypical Features of Femur Fractures: How Change in Radiological Criteria Influenced Incidence and Demography of Atypical Femur Fractures in a Community Setting. *Journal of bone and mineral research : the official journal of the American Society for Bone and Mineral Research* 2017; **32**(11): 2304-14.
53. Leclerc JT, Michou L, Vaillancourt F, Pelet S, Simonyan D, Belzile EL. Prevalence and Characteristics of Atypical Periprosthetic Femoral Fractures. *Journal of bone and mineral research : the official journal of the American Society for Bone and Mineral Research* 2018.
54. Black DM, Abrahamsen B, Bouxsein ML, Einhorn T, Napoli N. Atypical Femur Fractures - Review of epidemiology, relationship to bisphosphonates, prevention and clinical management. *Endocrine reviews* 2018.

55. Hinchy NV, Jayaprakash V, Rossitto RA, et al. Osteonecrosis of the jaw - Prevention and treatment strategies for oral health professionals. *Oral oncology* 2013; **49**(9): 878-86.
56. Vassiliou V, Tselis N, Kardamakis D. Osteonecrosis of the jaws: clinicopathologic and radiologic characteristics, preventive and therapeutic strategies. *Strahlentherapie und Onkologie : Organ der Deutschen Rontgengesellschaft [et al]* 2010; **186**(7): 367-73.

Figure 1a Postero-anterior wrist radiograph demonstrating a Colles' fracture and x-ray osteopenia

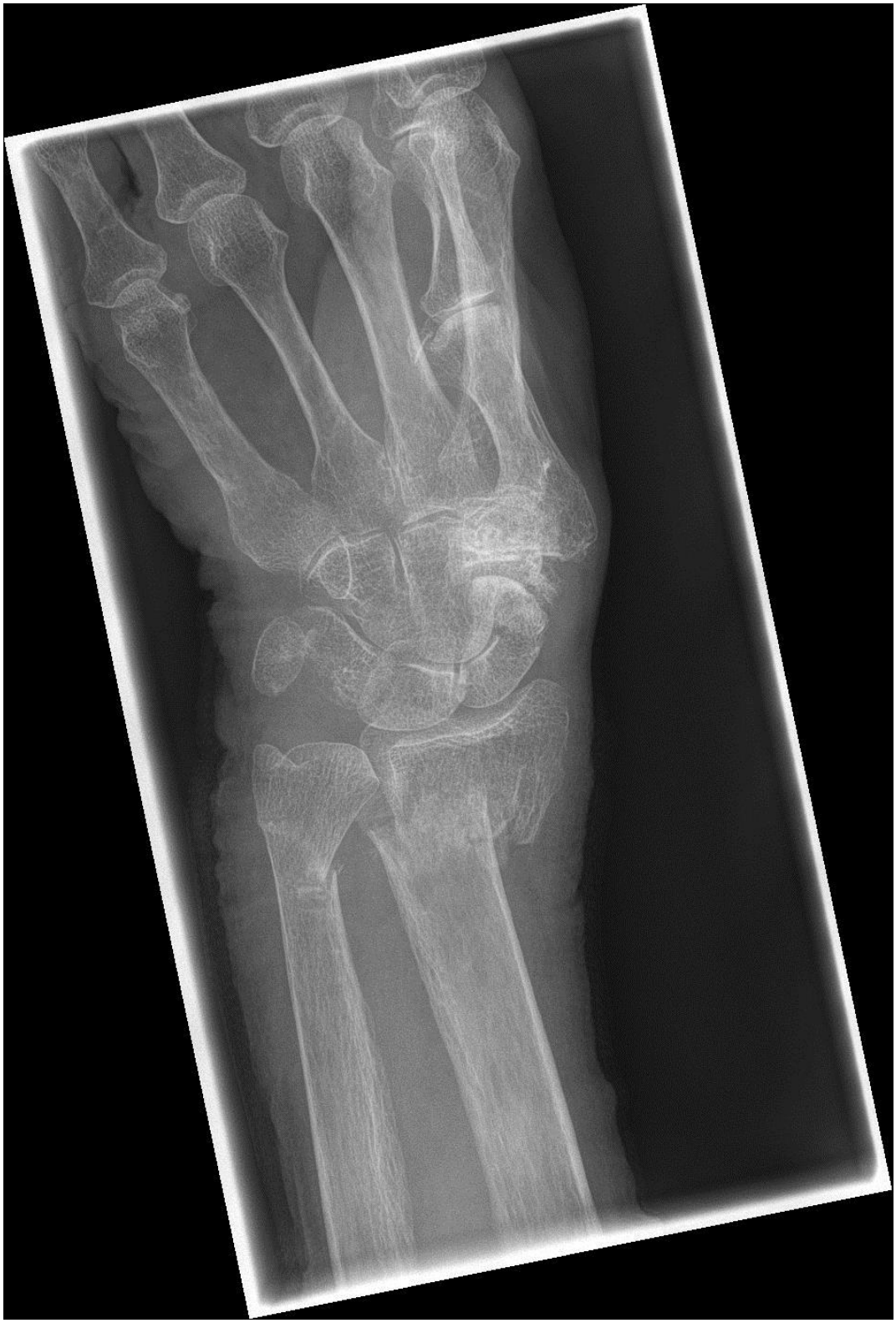

Figure 1b Lateral wrist radiograph demonstrating a Colles' fracture and x-ray osteopenia

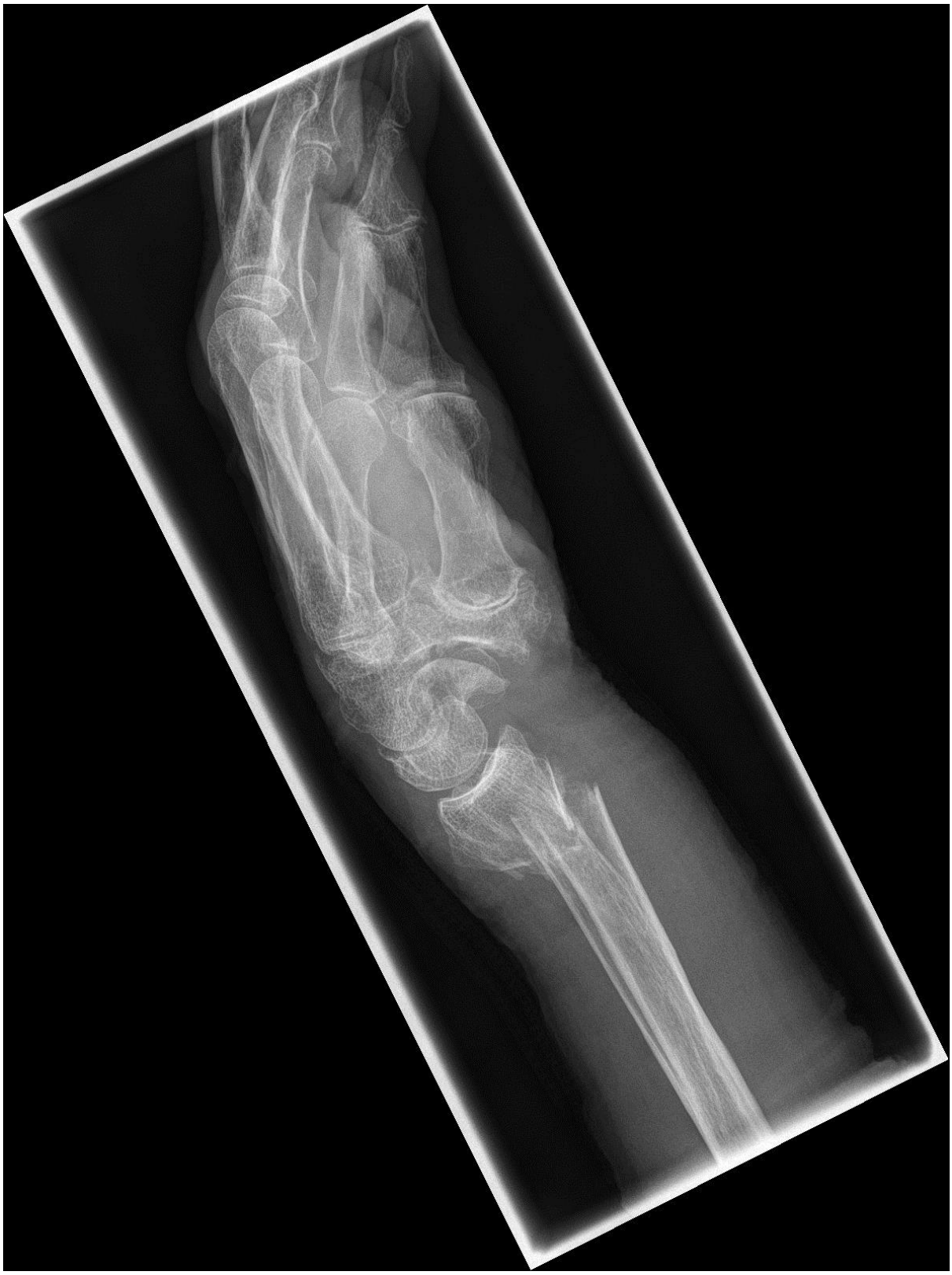

Figure 2: MRI showing occult femoral neck fracture

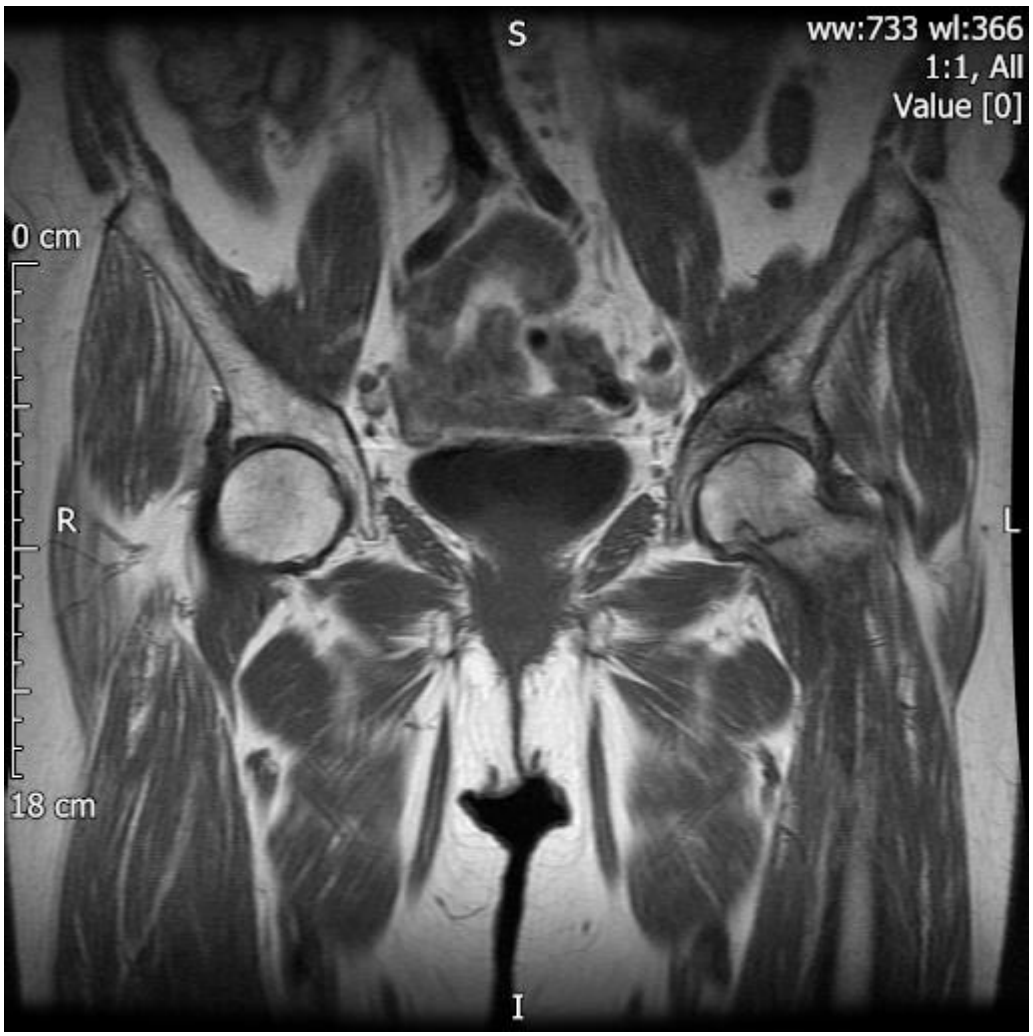

Figure 3: GE Lunar Prodigy dual energy lateral vertebral assessment scan, utilising morphometric software to indicate fracture presence and grade.

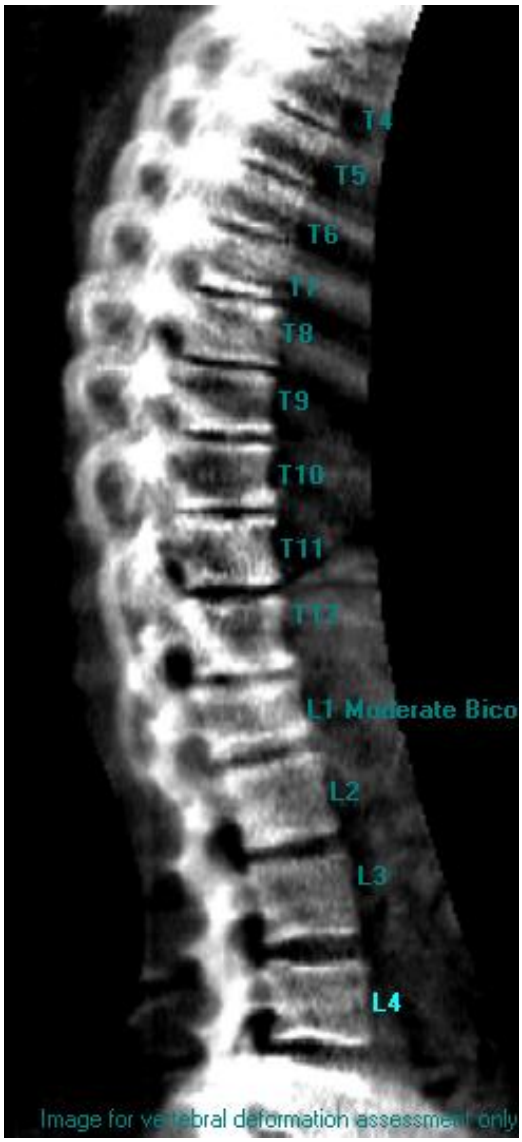

Figure 4a: MRI of vertebral fracture from metastasis

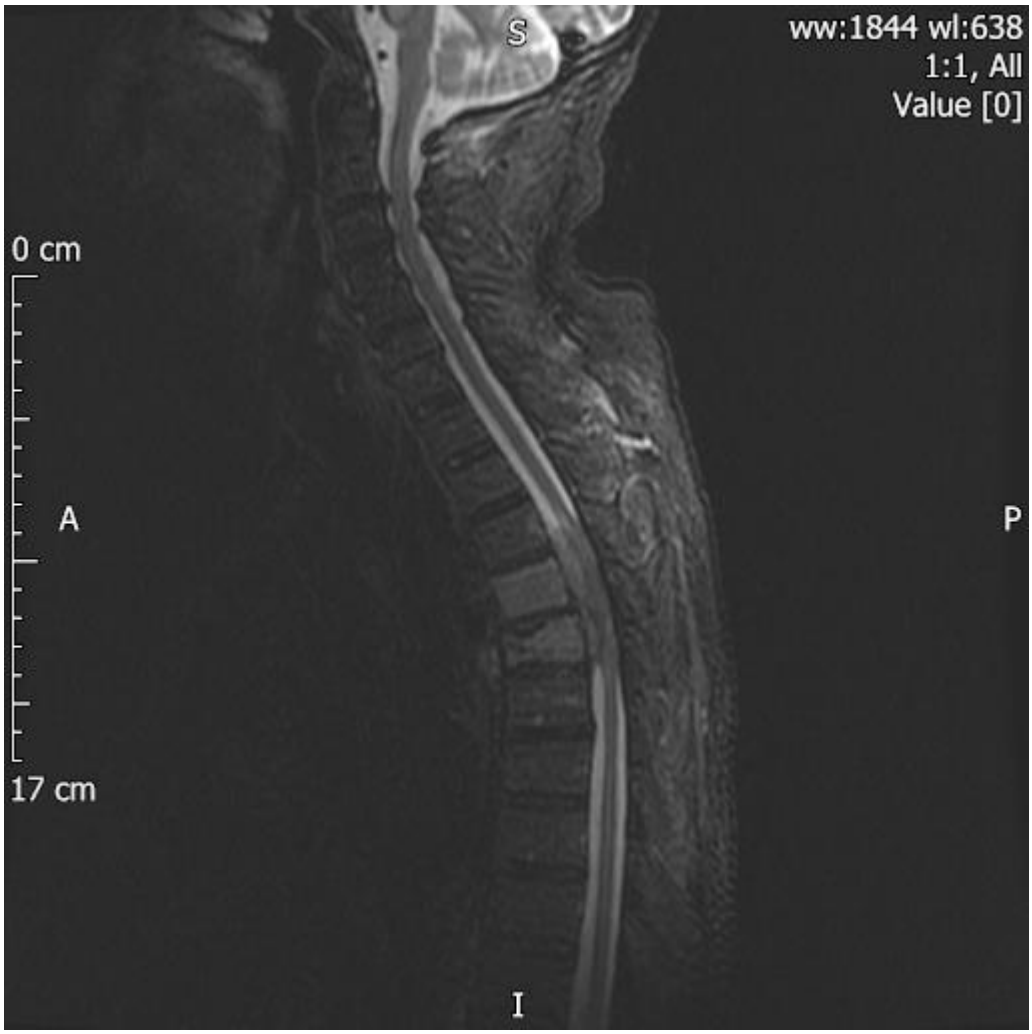

Figure 4b: MRI of vertebral fracture from metastasis

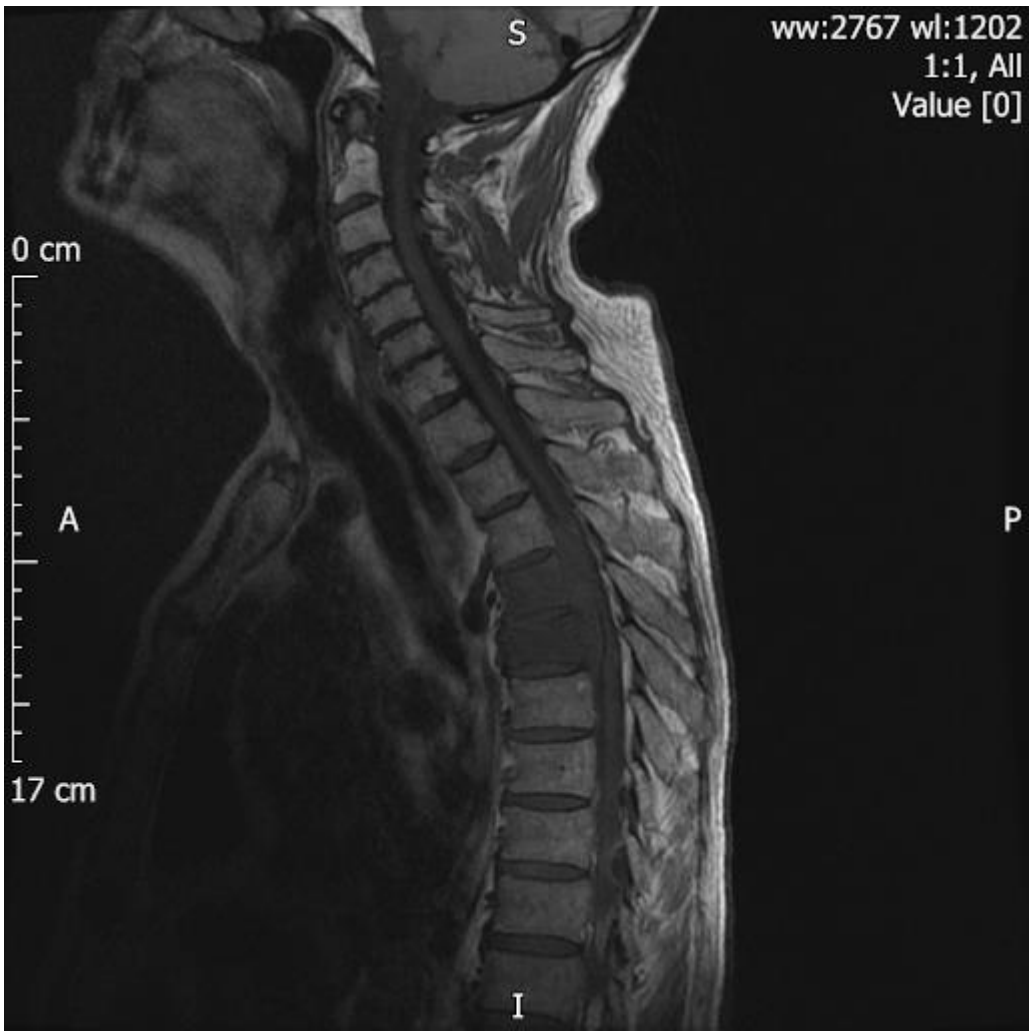

Figure 5 Sagittal multi-planar reconstruction of a CT scan demonstrating an incidental finding of osteoporosis related vertebral fractures at T6 and T8.

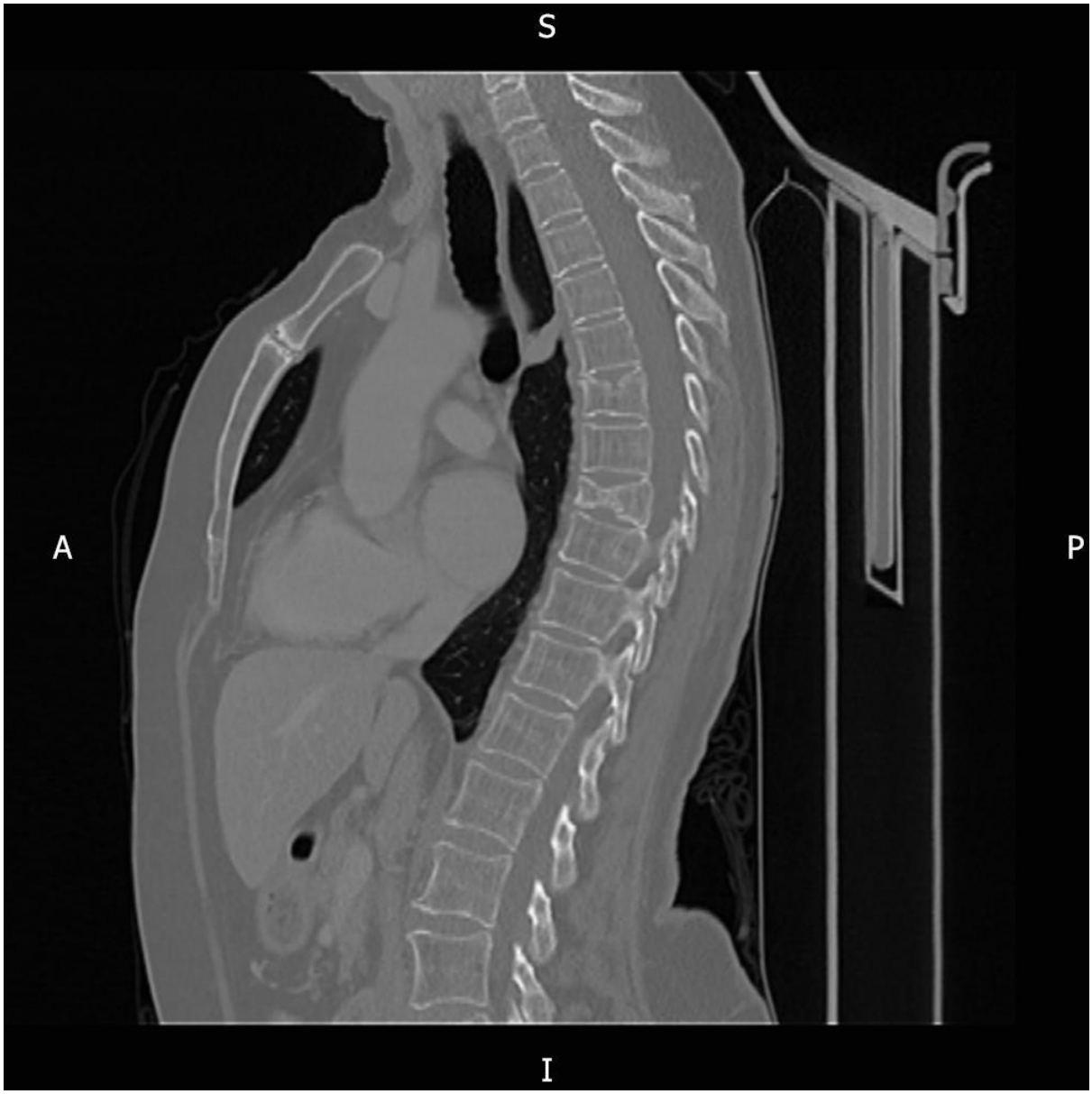

Figure 6: Radiograph of an atypical femoral fracture