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**ABSTRACT**

**Dual-energy X-ray absorptiometry (DXA) is currently the gold standard by which bone mineral density (BMD) is measured. It can be used for the diagnosis, prognosis and monitoring of osteoporosis. Currently, a DXA T-score of  $\leq -2.5$ , or BMD less than or equal to 2.5 standard deviations (SDs) below that of the young-adult mean, is used to diagnose osteoporosis in postmenopausal women and men age 50 years and older. A T-score  $< -1.0$  but  $> -2.5$  signifies Osteopenia or low bone mass, whereas a T-score  $\geq -1.0$  indicates normal bone density. The relative risk of fracture can be calculated as approximately  $2^{T\text{-score}}$ . When a patient has been treated, the change in BMD can be used to show whether there has been a significant improvement or not. Finally, the Z-score, or number of standard deviations of BMD compared to that of an adult of the same age and sex, if less than  $-2$ , can give a clue that there are secondary causes to the bone loss. However, the DXA scan must be done as precisely and accurately as possible, and there may be artefacts that interfere with accurate interpretation.**

**Keywords: BMD; T-scores; LSC;**

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**DIAGNOSIS OF OSTEOPOROSIS USING DXA BMD**

There have been many ways that bone mineral density (BMD) can be quantified, ranging from plain X-rays, to the earlier single-photon absorptiometry and more recent quantitative CT scans. Dual-energy X-ray absorptiometry (DXA) is currently the gold standard by which BMD is measured. Decisions in the management of osteoporosis are based largely on DXA, as most large-scale studies of epidemiology and drug treatment have been done using this modality. DXA measures BMD using a two-dimensional calculation of the amount of calcified bone present in the region of interest, set in  $g/cm^2$ .

**Use of DXA T-scores**

In 1994, the **World Health Organization (WHO)** set criteria for the diagnosis of osteoporosis in postmenopausal Caucasian women,<sup>1</sup> as shown in Table 1. **T-scores**, based on the number of standard deviations above or below the **young-adult mean**, are used. These definitions have now been extended to apply to all **postmenopausal women**, and **men aged 50 years and**

**above.** Only **central DXA** measurements, i.e. in the **lumbar spine, femoral neck and total hip**, should be used. In certain situations, where there have been operations or artefacts at the spine and bilateral hip, or if the patient is too obese for the DXA table, the 33 percent radius (also called 1/3 radius) may be utilised, especially in the management of hyperparathyroidism. The lowest of the 3 central T-scores is used to make the BMD diagnosis, as osteoporosis is a systemic disease and not confined to one particular part of the skeleton.

The WHO and **International Society of Clinical Densitometry (ISCD)**<sup>2</sup> have further recommended to DXA manufacturers that femoral neck and total hip T-scores of non-Caucasians and males should also be based on the NHANES III database, which is comprised largely of Caucasian postmenopausal women, but this has not been adopted universally for all Singaporean DXA reports. Lumbar spine T-scores are based on local reference data. In NUH, this is of Singaporean Chinese females and males age 30–35 years.

**Table 1: WHO Criteria for the Diagnosis of Osteoporosis**

Diagnostic Criteria	Diagnostic Thresholds in DXA T-scores (Standard Deviations compared to young-adult mean)
Normal	$\geq -1$
Osteopenia or Low Bone Mass	$< -1$ but $> -2.5$
Osteoporosis	$\leq -2.5$
Severe Osteoporosis	$\leq -2.5$ with fragility fracture

These WHO criteria were chosen on the basis of the prevalence of fragility fractures in the general population of postmenopausal Caucasian women: that a similar number of women would be labeled with osteoporosis on the basis of a low bone mass in a DXA scan as the number of women who would suffer from fragility fractures. However, it must be pointed out that a T-score of  $\leq -2.5$  is found only in approximately 2/3 of all the women who suffer a fragility fracture,<sup>3</sup> as **DXA BMD measures only bone mass** and does not detect microarchitectural deterioration or poor bone quality. Most women who suffer a fracture have T-scores indicating osteopaenia and some, especially those with diabetes mellitus, even have normal BMD. Hence, a good DXA result does not exclude osteoporosis.

**Use of DXA Z-scores**

**Z-scores** are based on the number of standard deviations compared to the mean in **Age- and sex-matched people of the local population**. A Z-score  $< -2.0$  indicates that a search for secondary causes of osteoporosis needs to be initiated.

In **premenopausal women** and **men below age 50 years**, T-scores cannot be used to diagnose osteoporosis. However, **Z-scores  $< -2.0$**  can be used to identify people with low bone mass or “below expected bone mineral density” (Table 2).

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**Table 2: Diagnosis of Low Bone Mass in Premenopausal Women and Men below age 50 years**

Diagnostic Criteria	Diagnostic Thresholds in Z-scores (Standard deviations in age- and sex- matched means)
≥-2.0	Within expected BMD
<-2.0	Lower than expected BMD

A single DXA scan captures the result at one moment of life, and if the BMD result is low, more tests and a follow-up scan must be done to ascertain whether this is a result of a low peak bone mass achieved, e.g. due to childhood illness such as asthma requiring the use of glucocorticoids, or whether there is ongoing bone loss. In younger adults, the diagnosis of osteoporosis cannot be confidently made on the basis of a low BMD, but the presence of **fragility fractures**, especially if recurrent, will strengthen the diagnosis. An exception to using Z-scores is in peri-menopausal women, who already experience significant bone loss leading up to complete amenorrhoea. In these women close to menopause, T-scores can be used.

### Analysing Technical Details of BMD DXA Scans

Before using the results of a DXA scan, the scan must be scrutinised to confirm that it has been properly done, and any artefacts that may affect the results noted. It is advisable for the technologist performing the DXA scan and the clinician interpreting the scan to undergo formal training, such as those organised by the ISCD.

The **spine** should be central in the image. Check that the **intervertebral markers** have been properly placed, especially in patients with scoliosis, and that the **vertebrae are correctly outlined and labelled**. Lumbar vertebrae 1–4 are commonly used for analysis, as L5 has potential interference from the pelvis. The shape of L1 to L3 is U-shaped or Y-shaped, whereas L4 looks like a block H or X. L5 is shaped like the block letter I (with short side arms) lying on its side. These shapes will help decide the L1–L4 vertebrae for analysis, especially when there are 6 lumbar vertebrae or if the ribs come off T11 instead of the more usual T12. Each vertebra should have increasing Bone Mineral Content (BMC) from L1 to L4, with BMD increasing from L1 to L3; BMD may decline a little in L4 in comparison to L3 despite higher BMC, as the vertebral body in L4 is larger. If the **BMD of any particular vertebra is abnormally high or low** and not within 1 SD of adjacent vertebrae, it may that the vertebra is affected by a **vertebral fracture** or other structural change, and that vertebra should be removed from the calculation of the T-score. A minimum of 2 vertebrae are required for accurate analysis. In addition to vertebral fractures, the presence of **osteophytes** and **artefacts** such as calcifications in the pancreas, aorta or posterior spinal ligaments, and radio-dense objects such buttons, zippers and calcium tablets, will also artificially elevate the DXA T-score and Z-score.

For the **hip**, the region of interest box should be placed accurately and should not include the pelvis. As the hip is less affected by osteophytes, hip T-scores are usually more accurate and lower than that of the spine. The lesser trochanter is a posterior structure and should not be overly protruberant. Inadequate internal rotation results in a factitious increase in

T-score. Both the femoral neck and total hip T-scores are of interest, although the femoral neck BMD reading is that used in the calculation of FRAX™.

It can be seen that the T-score derived from the L2–L4 vertebrae (-1.2) is higher than the T-scores of the hip (-3.1 and -2.9) due to the presence of large osteophytes in the spine. L1 was excluded as there was a known history of vertebral fracture.

### DXA BMD for the Prognosis of Fracture Risk

The **relative risk (RR) of a fragility fracture is in the order of  $2^{T\text{-score}}$** , as compared to an adult of the same sex and race with a T-score of zero. For e.g., a 60-year-old Chinese woman with a T-score of -3.0 in the spine will have an approximate RR of  $2^3$ , or an 8-fold higher risk of fracture than a 60-year-old Chinese woman with a T-score of 0.

In the FRAX™ algorithm, entering the actual DXA BMD result of the femoral neck helps to generate a more accurate **absolute risk of a fragility fracture** in terms of major fractures and hip fractures than when BMD is not used. Do note that in doing so, a T-score is generated that is slightly different from that on the DXA report, as FRAX™ uses a database of primarily Caucasian postmenopausal women.

### DXA BMD for the Monitoring of Progress

Serial DXA scans that have been performed similarly each time can give information whether there has been a change beyond the measurement error of the machine and operator, or **Least Significant Change (LSC)**. In Figure 2, the change in BMD between 2015 and the baseline scan in 2002 was an increase of 0.108 g/m<sup>2</sup> or 13.9 percent\*, and since the change was beyond the LSC, as marked by the asterisk, there appears to have been a clinically significant increase in the BMD, which may have been due to pharmacological treatment, or the worsening of osteoarthritis. Do note that in the interim period, there was a change of the DXA machine (#) and, although both machines had been standardised to NHANES III, there was still individual variation. Using the same machine yields more reliable results. Between 2015 and the most recent scan in 2013, there was a change in BMD of 0.06 g/cm<sup>2</sup> or 0.7 percent on the same DXA machine, meaning no significant clinical change, as it is within the LSC.

The corresponding changes from baseline and from the most recent scan in the hip scan in Figure 3 was -1.9 percent (no significant change) and -6.6 percent\* (significant deterioration). This patient, who had been adherent to her oral medication respectively, would warrant a closer look in terms of excluding a secondary cause of bone loss, as well as consideration of a more potent parenteral pharmacological agent for treating her osteoporosis.

Change in BMD with treatment occurs faster in the spine than in the hip, due to its higher trabecular and lower cortical bone content. Changes in T-scores should not be used in monitoring, as the change may not be beyond the LSC.

When a patient has been commenced on pharmacological treatment, it is good to see an increase in BMD beyond the LSC. No significant change is also acceptable and does not mean the medication is not working. However, a reduction in BMD beyond the LSC is concerning, and the clinician must find out whether there is a medication adherence issue or whether there are secondary causes of bone loss that have not been addressed.

It is recommended that **DXA scans should not be done more than once a year**, unless a very drastic impact on BMD is expected, such as from high-dose glucocorticoid treatment or oestrogen- or androgen-deprivation therapy. A DXA scan may be performed one year after starting a new treatment, but if there is good improvement and T-scores remain fairly low, then it is reasonable to repeat the DXA two-yearly thereafter.

**TRABECULAR BONE SCORE (TBS)**

The DXA machine can use software to analyse the patterns of “holes” in the bone density of vertebral bodies in a semi-quantitative measure of bone quality, to generate a Trabecular Bone Score (TBS). Hence, using the TBS can modify the results in FRAX™ calculations.

**Vertebral Fracture Analysis (VFA): Using DXA to Diagnose Vertebral Fractures**

Using lower radiation than a conventional spine X-ray, a lateral view of the spine can be taken with the DXA machine, and the diagnosis of a vertebral fracture can be made, based on the Genant classification (Figure 5).

**Safety of DXA**

DXA is safe. The radiation dose used in one region of a DXA scan is approximately one-tenth of a chest X-ray, or one-hundredth of a mammogram, or that sustained from exposure to natural radiation during a long-distance airplane flight.

**CONCLUSION**

DXA is the current gold standard in the measurement of BMD or bone mass. It is useful to diagnose osteoporosis and osteopaenia or low bone mass, particularly in those who have not yet suffered fragility fractures. It can give an estimated relative risk of fracture, and in conjunction with FRAX and other risk calculators, it can give an estimated absolute fracture risk in the major bones and in the hip. Hence, DXA aids the clinician in the decision whether to treat with just lifestyle changes, or with medications. The progress of the patients on treatment can be monitored precisely with DXA as well.

Figure 4: TBS

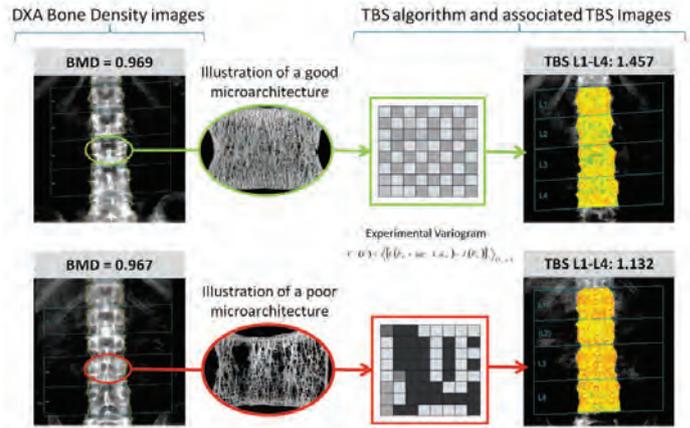
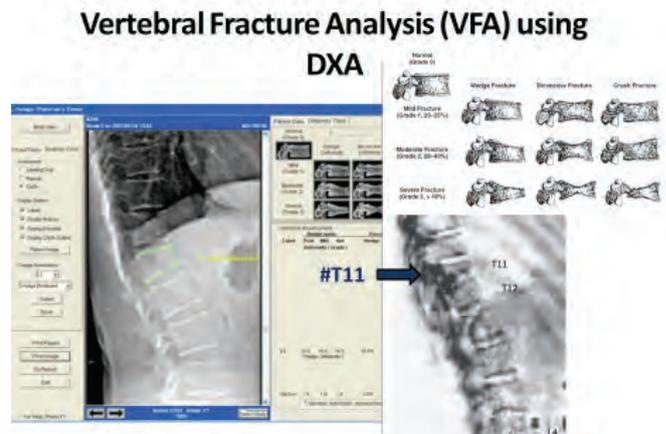


Figure 5: Vertebral Fracture Analysis Using DXA



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**LEARNING POINTS**

- **DXA T-scores of -2.5 or less in the spine, hip and 1/3 radius can be used to diagnose osteoporosis in postmenopausal women and men age 50 and above. DXA Z-scores of less than -2.0 in premenopausal women and men below age 50 are used to identify those with below expected bone density. However, a one-time BMD result alone cannot be used to make the diagnosis of osteoporosis in young adults, unless a fragility fracture is present.**
- **The spine is more prone to the development of silent fractures, osteoarthritis and other artifacts, resulting in an artificial elevation of the T-score of the spine.**
- **In monitoring BMD, the change in BMD must be beyond that of the Least Significant Change (LSC) to be clinically significant. The use of changes in T-scores alone are not recommended.**

**Figure 1: Patient 1's Scan Shows Clearly the Vertebral Shapes Expected in a DXA Spine Image for L1-L5**

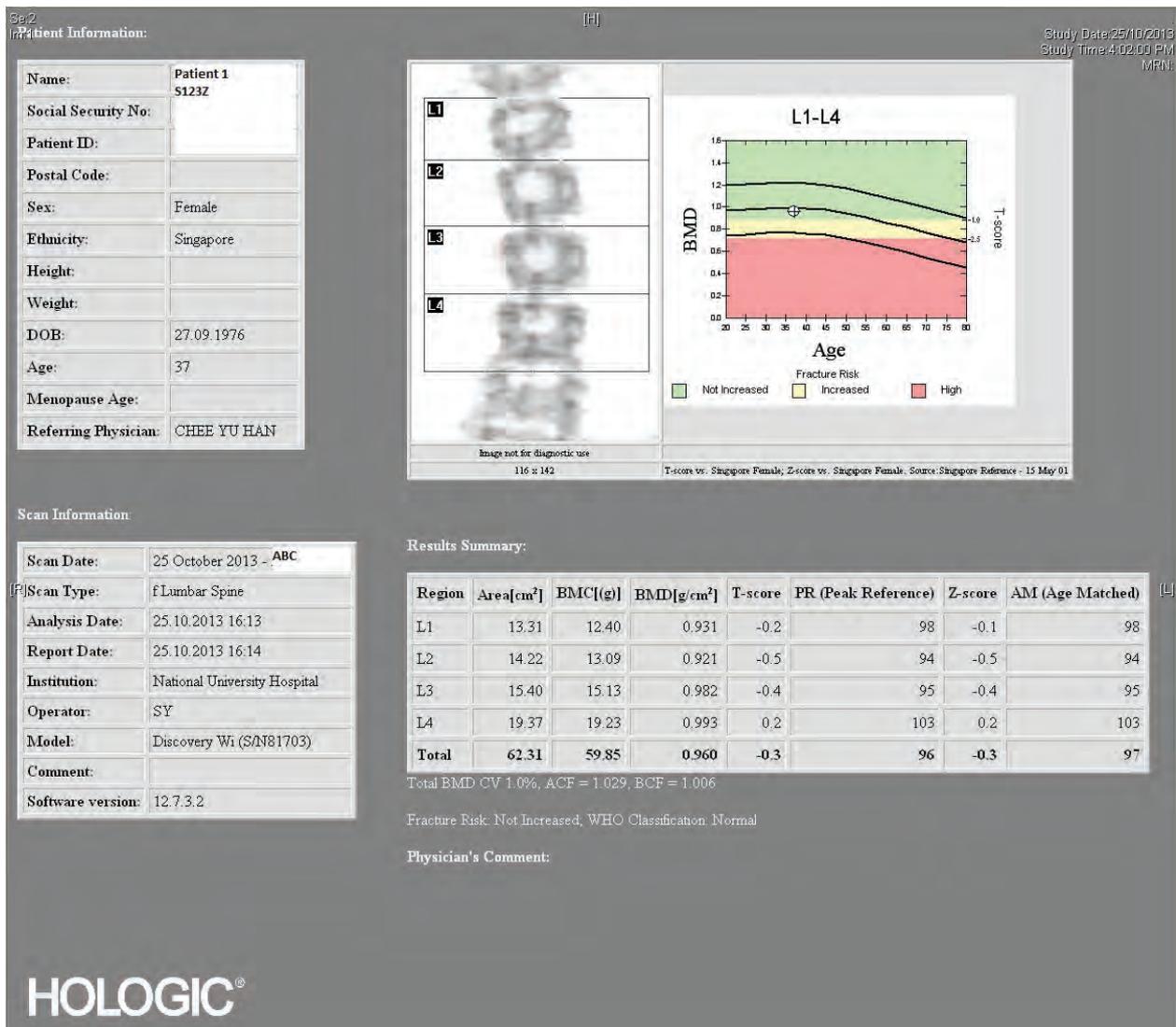


Figure 2: DXA Spine Result of Patient 2

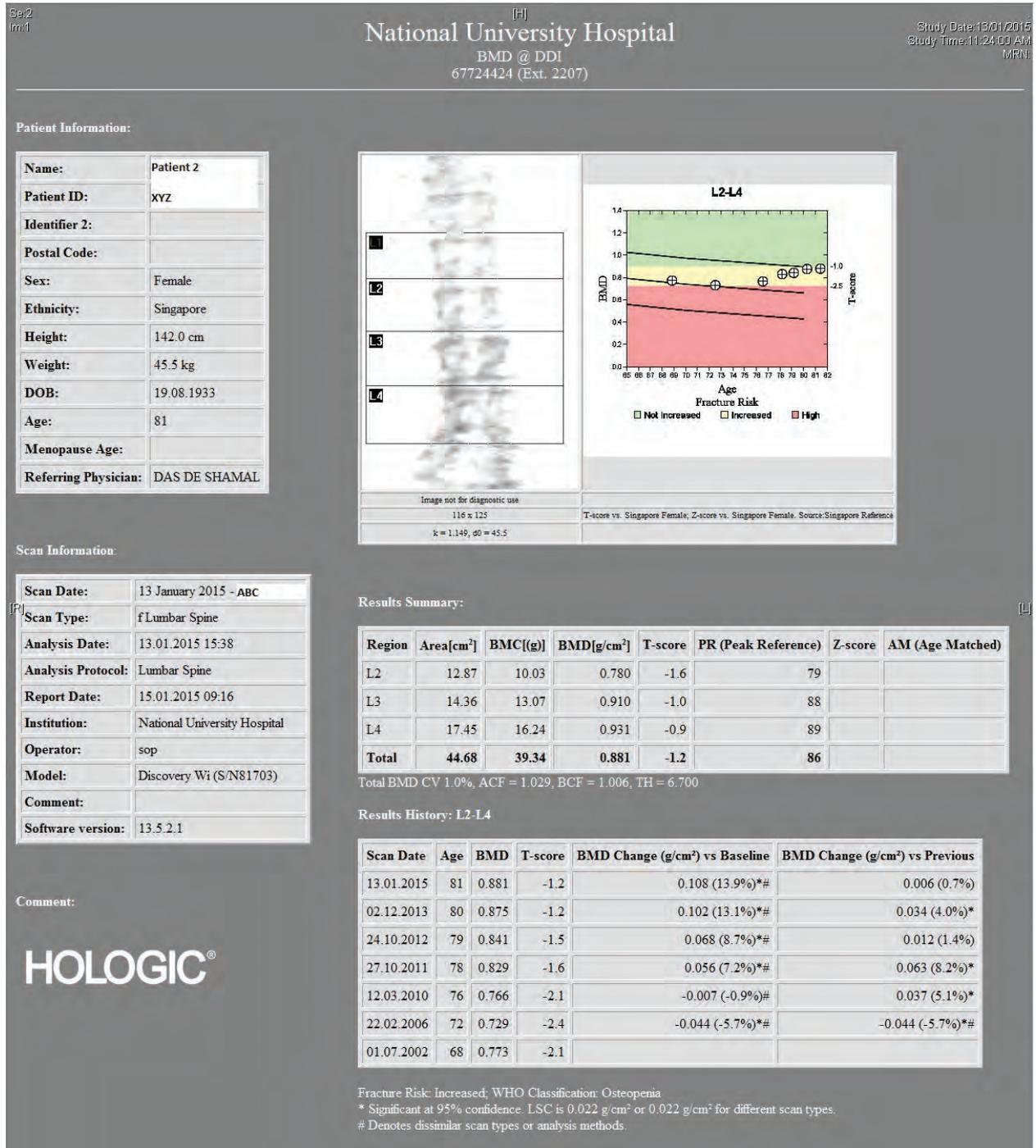


Figure 3: DXA Hip Results of Patient 2

