DXA
When to order?
How to interpret?

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Clinical Utility of Bone Densitometry (DXA)

- Diagnosis
  - WHO T-score classification
- Prognosis
  - Facilitates fracture risk assessment
- Monitoring
  - Requires knowledge of precision and least significant change (LSC)

WHO Classification of Postmenopausal Osteoporosis

- Published in 1994 by a working group of the WHO
- Intended to assess the prevalence of the disease in a population
- Evaluated postmenopausal Caucasian females using DXA of spine, hip or forearm
- Results were expressed as a standard deviation from the mean predicted bone mass in young adult Caucasian females (which was later expressed as a T-score)

World Health Organization. Technical Report Series 843, WHO, Geneva.1994.

WHO Classification for Postmenopausal Osteoporosis

The T-score compares an individual's BMD with the mean value for young normals and expresses the difference as a standard deviation score

	T-score (SD)
Normal	Equal to -1.0 or higher
Low Bone Mass (Osteopenia)	Between -1.0 and -2.5
Osteoporosis	Equal to -2.5 or lower
Severe Osteoporosis	Equal to -2.5 or lower with fracture

World Health Organization. Technical Report Series 843; WHO, Geneva.1994.
Kanis JA et al. J Bone Miner Res. 1994;9:1137.

Why the WHO Chose a T-score of -2.5

- “Such a cutoff value identifies approximately 30% of postmenopausal women as having osteoporosis using measurements made at the spine, hip, or forearm. This is approximately equivalent to the lifetime risk of fracture at these sites.”

Kanis JA, et al. J Bone Miner Res. 1994; 9:1137.

Caveats of Diagnosis Based on BMD

- Diagnosis of osteoporosis by DXA is based on the WHO classification as a T-score of -2.5 or below
  - Some patients with T-score –2.5 or below do not have osteoporosis
  - Some patients with T-score above –2.5 may be diagnosed with osteoporosis
- T-scores may differ at different skeletal sites
- Patients with a diagnosis of osteoporosis may have substantially different fracture risk
- Diagnosis of osteoporosis does not explain etiology

Advantage of T-score Instead of BMD

- If there were only one type of densitometer and one skeletal site to measure bone density, absolute BMD criteria would be preferable
- Multiple devices exist that use different approaches to BMD measurement
- Theoretically, T-score provides a way of using the same diagnostic criteria for all devices and skeletal sites

Limitations of 1994 WHO Classification

- **Not intended as treatment guidelines**
- Definitions do not necessarily apply to other populations (e.g., men, non-Caucasians, premenopausal women)
- Does not recognize that a presumptive diagnosis of osteoporosis can be made by a low-trauma (fragility) fracture regardless of the patient's BMD
- Does not differentiate between osteoporosis and other causes of low BMD

T-score Equal to or Lower Than –2.5 is Not Always Due to Osteoporosis

Examples of Non-Osteoporotic Causes of Low BMD

- Osteomalacia
- Genetic disorders, e.g., osteogenesis imperfecta
- Renal bone disease
- Multiple myeloma/other malignancies
- Marrow infiltrative diseases, e.g., mastocytosis

T-score Calculation

- Number of standard deviations patient's BMD is above or below average BMD of young-adult reference population
- T-score = $$\frac{\textbf{BMD patient} - \textbf{BMD young-normal reference}}{\textbf{SD young-normal reference}}$$
- Used for diagnosis
- If low, does not necessarily imply prior bone loss

Z-score Calculation

- Number of standard deviations patient's BMD is above or below average BMD of age-matched reference population

- Z-score = $\dfrac{\textbf{BMD patient} - \textbf{BMD age-matched reference}}{\textbf{SD age-matched reference}}$

- Not used for diagnosis
- There is no evidence to support a specific cut-point to evaluate for secondary causes*
- Secondary causes should always be considered as clinically indicated

*Tannenbaum. J Clin Endocrinol Metab. 2002;87(10):4431

Central DXA for Diagnosis: Skeletal Sites to Measure

- Measure BMD at both lumbar spine and hip in all patients
- Measure forearm BMD when:
  - Lumbar spine and/or hip cannot be measured or interpreted
  - Hyperparathyroidism
  - Very obese patients (over the weight limit for DXA table)

Central DXA for Diagnosis: Spine Region of Interest

- Use L1-L4 for spine BMD measurement
- Use all evaluable vertebrae and only exclude vertebrae affected by structural change or artifact; use 3 vertebrae if 4 cannot be used, and 2 if 3 cannot be used
- BMD-based diagnostic classification should not be made using a single vertebrae
- Lateral spine should not be used for diagnosis

Central DXA for Diagnosis: Hip Region of Interest

- Use femoral neck or total proximal femur whichever is lowest
- BMD may be measured at either hip
- Do not use Ward's area or the greater trochanter for diagnosis
- Mean hip BMD can be used for monitoring with total hip preferred ROI

Central DXA for Diagnosis: Forearm Region of Interest

- Use 33% radius (sometimes called one-third radius) on the non-dominant forearm as alternative site
- Other forearm ROIs are not recommended

Central DXA Diagnosis of Osteoporosis

- Diagnosis is based on the lowest site (lumbar spine, femur neck/total femur or one-third radius) provided:
  - Measurements are technically valid
  - Low bone mass is not due to some other pathology

Why Measure Spine **AND** Hip?

- Diagnosis is based on the lowest BMD site
- Spine-hip discordance
- Fracture prediction
- Spine BMD for spine fractures
- Hip BMD for hip fractures
- Monitoring response to therapy
- May lose the ability to continue to monitor an individual site (osteoarthritis, hip fracture)
- Serial changes at different sites may vary

Causes of Discordance

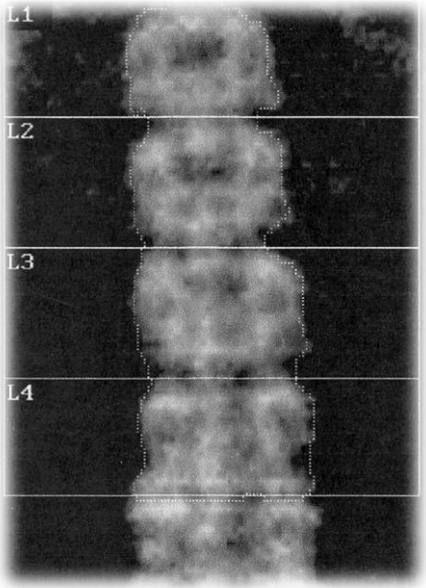
- Peak adult bone mass and rate of bone loss are not the same throughout skeleton
- In postmenopausal women, the initial rate of bone loss is greater in cancellous bone than cortical bone
- Some disorders affect mostly cortical bone (e.g., hyperparathyroidism)
- Artifacts (e.g., degenerative disease, fractures)

Discordance in a Patient Taking Glucocorticoids

L1-L4

- T-score −2.4
- WHO diagnosis

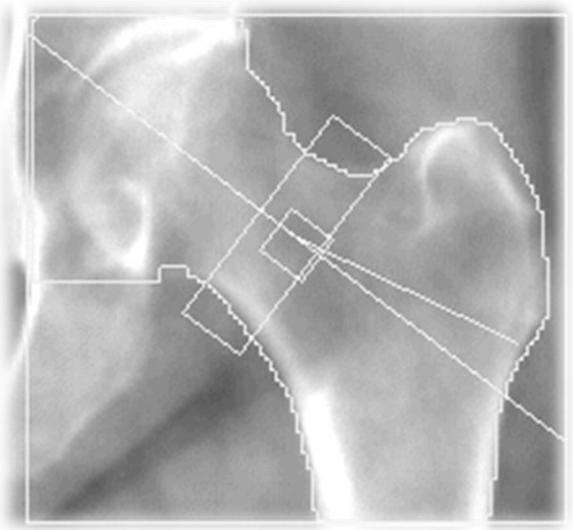
LOW BONE DENSITY (OSTEOPENIA)



Total Hip

- T-score −0.5
- WHO diagnosis

NORMAL



Why DXA Systems and Data are Not Interchangeable: **Same Manufacturer**

- May use different acquisition methods
  - E.g., pencil vs. fan beam
- May use different software
- May use different young-normal databases
- Inter-device variability ± 2%

Why DXA Systems and Data are Not Interchangeable: **Different Manufacturers**

- Use different methods for dual energy production
- Use different methods of X-ray detection
- Are calibrated differently
- Use different edge detection software
- May use different regions of interest
- Use different young-normal databases
- Inter-device variability ± 5%-7%

WHO Classification should be limited to Specific Populations, Skeletal Sites and Devices

Original Derivation of 1994 WHO Classification

- Only postmenopausal Caucasian women
  - Not men, premenopausal women, children
  - Not other racial or ethnic groups
- Only PA spine, hip and forearm DXA
  - Not lateral spine, heel, finger, etc
- Only for central DXA and forearm
  - Not peripheral DXA (other than forearm)
  - Not for QCT, QUS, RA, etc

Indications for BMD Testing

Category	USPSTF	NOF	AACE	ACR	ACOG	OSC	ISCD	ABRASSO	NOGG†	DVO
♀ ≥ 65	✓	✓	✓	✓	✓	✓	✓	✓		✓ >70
♀ with risk factors	✓ *	✓ >50	✓	✓	✓	✓	✓	✓		✓
♂ with risk factors		✓ >50		✓	✓	✓	✓	✓		✓
♂ ≥ 70		✓				✓>65	✓	✓		✓ >80
Monitor		✓	✓	✓	✓	✓	✓	✓		✓

*In postmenopausal women; indicated if estimated 10 year risk calculated using FRAX clinical risk factors only (no BMD)

†Note: NOGG recommends BMD based on estimated fracture risk

Relative Contraindications for Central DXA

- Pregnancy
- Recent contrast study (generally less than 72 hours)
  - Spine measurement only
- Recent nuclear medicine scan
- Extensive orthopedic instrumentation
- Body weight greater than table limit
  - Solution: Measure the forearm

Diagnosis in Premenopausal Women (age 20 and older)

- WHO classification should not be applied to healthy premenopausal women
- For women prior to menopause, Z-scores, rather than T-scores, are preferred. This is particularly important in children.
- A Z-score of -2.0 or lower is defined as "below the expected range for age" and a Z-score above -2.0 is "within the expected range for age."
- The diagnosis of osteoporosis in premenopausal women should not be made on the basis of densitometric criteria alone

Diagnosis in Perimenopausal Women

- The WHO diagnostic criteria may be applied to women in the menopausal transition
- BMD measurement is indicated for women during the menopausal transition who have clinical risk factors for fracture such as low body weight, prior fracture or high-risk medications

Simonelli, C., et. al., J Clin Densitom; 2008; 11:109-122

Skeletal Sites to Measure for Diagnosis in Children

- Patients should have spine and total body less head (TBLH) BMC and areal BMD measured
- The total hip is not a reliable site for measurement in growing children due to significant variability in skeletal development and lack of reproducible regions of interest

Gordon C, et. al., J Clin Densitom; 2008; 11:43-58

Diagnosis in Children and Adolescents

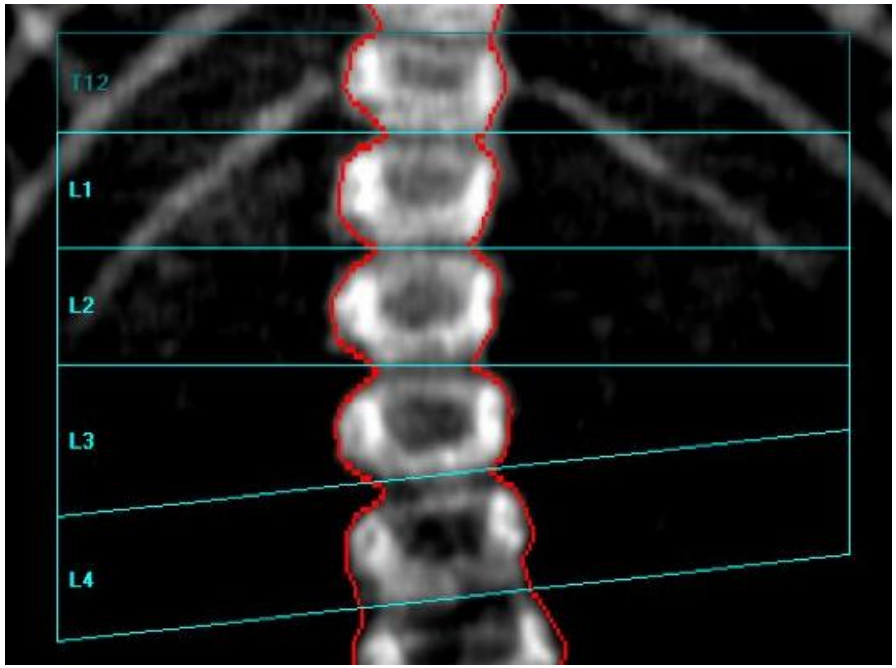
Males and Females Ages 5-19

- Should NOT be made on the basis of densitometric criteria alone
  - The diagnosis of osteoporosis requires the presence of both a clinically significant fracture history and low bone mineral content or bone mineral density
  - Clinically significant fracture history is defined as:
    - Long bone fracture of the lower extremities, and/or
    - Vertebral compression fracture, and/or
    - Two or more long-bone fractures of the upper extremities
- Low BMC or BMD is defined as a Z-score ≤ -2.0 adjusted for age, gender and body size as appropriate

Rauch F, et. al., J Clin Densitom; 2008; 11:22-28

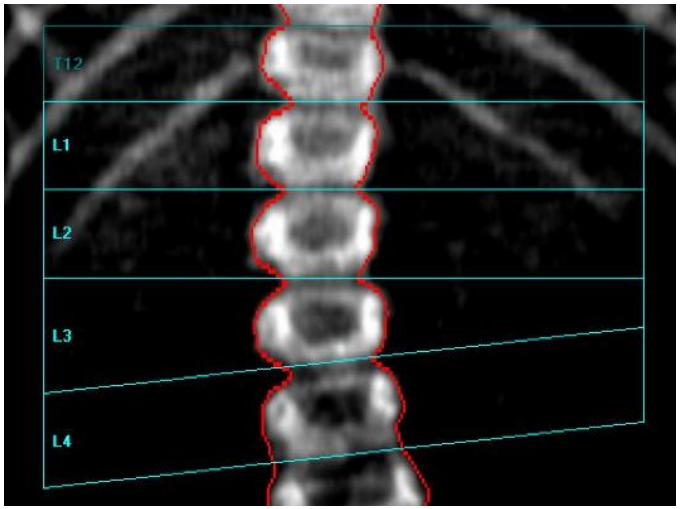
Your Patient Has a T-score of -5.0

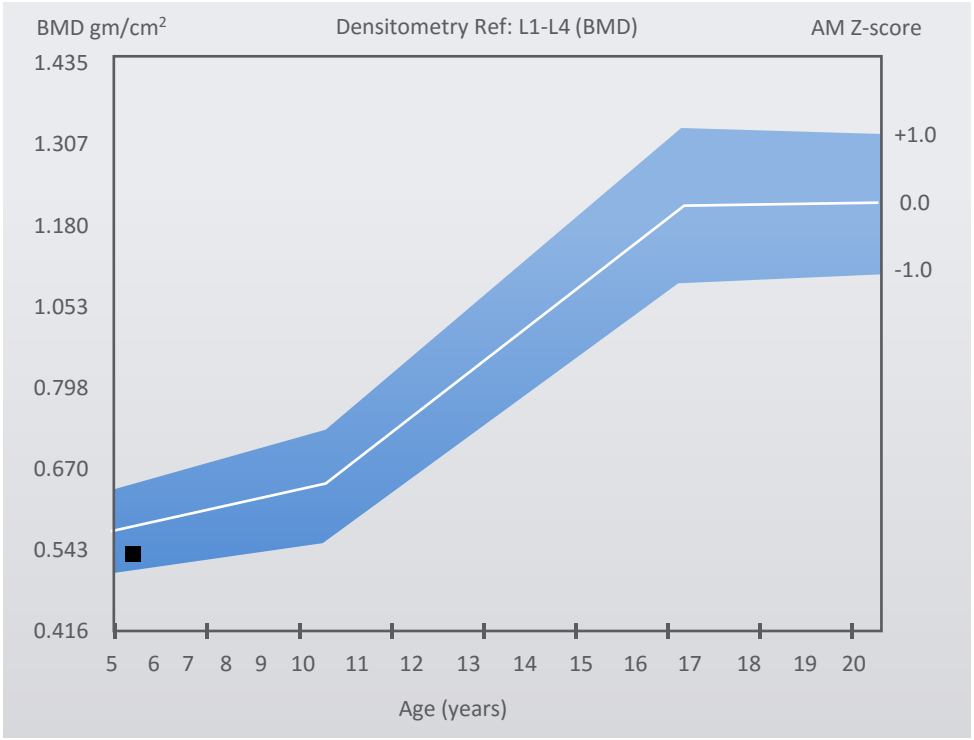
Is Osteoporosis Treatment Needed?



Densitometry			
	Region	BMD (g/cm^2)	YA T-score
	L1	0.583	-4.6
	L2	0.517	-5.7
	L3	0.653	-4.6
	L4	0.584	-5.1
	L1-L2	0.548	-5.1
	L1-L3	0.585	-4.9
	L1-L4	0.585	-5.0

No, This Patient is a Five Year Old Girl!





Region	BMD (g/cm²)	AM Z-score
L1	0.583	0.0
L2	0.517	-2.0
L3	0.653	0.0
L4	0.584	-1.0
L1-L2	0.548	-0.8
L1-L3	0.585	-0.6
L1-L4	0.585	-0.7

The Z-score is -0.7: this is normal for age

T-scores are not appropriate in children

Summary: Children and Adolescents

Males and Females Ages 5-19

- Osteoporosis diagnosis requires both low bone mineral content or bone mineral density and a clinically significant fracture history
- T-scores should not be used and should not appear on DXA printouts in children
- Terminology such as “low bone density for chronologic age” may be used if the Z-score is –2.0 or lower

Diagnosis in Men

Influence of Sex on BMD

- Using DXA
  - Young men have areal BMD ~10% higher than women
  - Mostly because men have generally have larger bones
- Male T- and Z-scores were historically based on male reference data resulting in T-scores which, at the same BMD, differed depending on sex

Male Female

How to Derive T-scores in Men Has Been Controversial

- WHO T-score based on data for postmenopausal Caucasian women
- Previously ISCD Official Position was to use a:
  - Female database to derive T-scores in women
  - Male database to derive T-scores in men
- Basic question: at a given BMD, does the fracture risk differ between men and women?
  - If the fracture risk is the same for men and women, then the T-score should be the same
    - And thus the database to derive the T-score should be the same

ISCD Now Recommends Using a Female Reference to Derive T-scores in Males

- Consequences
  - T-scores improve by roughly 0.3 to 0.5[1]
  - Fewer men with osteoporosis by T-score
    - However, many with osteopenia/low bone mass will still qualify for treatment based on FRAX[2]

[1]Wiemann L, et. al, J Clin Densitom, 2007; 10:244-248.
[2]Leslie and Majumdar, J Clin Densitom, 2013; in press

Diagnosis in Men: ISCD Position

- Use a uniform Caucasian (non-race adjusted) female reference for men of all ethnic groups.*
- Age 50 and older
  - T-scores are preferred
  - The WHO densitometric classification is applicable
- In men younger than age 50
  - Z-scores, not T-scores are preferred
  - A Z-score of -2 or lower is defined as "below the expected range for age" and a Z-score above -2 is "within the expected range for age"
  - Osteoporosis cannot be diagnosed on the basis of BMD alone

*www.iscd.org/official-positions

ISCD Position
Technologies Other Than Central DXA

The WHO classification system cannot be applied to T-scores from measurements other than DXA at the:

- Femoral neck
- Total hip
- Lumbar spine
- One-third (33%) radius

Baim, S., et. al. J Clin Densitom; 11:75-91, 2008.

Summary: Application of WHO Classification for Diagnosis

	WHO 1994	ISCD 2013
Postmenopausal Caucasian women	Yes	Yes
Postmenopausal women other ethnic groups	No	Yes*
Premenopausal women	No	No
Men younger than age 50	No	No
Older men all ethnic groups	No	Yes*
Other technology or sites	No	No

*Use female Caucasian database

DXA Interpretation: Examples

Central DXA Interpretation: Printouts Have Common Features

- Patient demographics
- Image of skeletal site
- Graph (age vs. BMD)
- Numerical results

Image

Graph

Demographics

Results
T- and
Z-scores

Name:
Patient ID:
DOB:

Sex: Female
Ethnicity: Hispanic
Menopause Age: 34

Height: 57.4 in
Weight: 105.0 lb
Age: 55

Referring Physician:

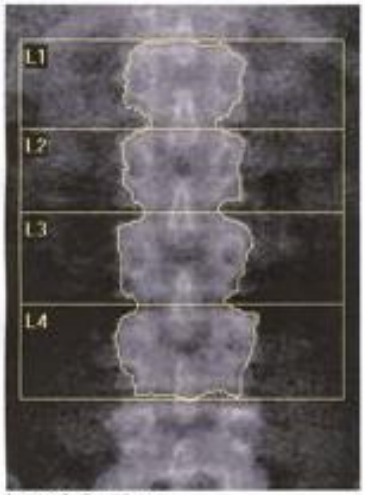


Image not for diagnostic use
k = 1.160, d0 = 47.4
116 x 126

Scan Information:

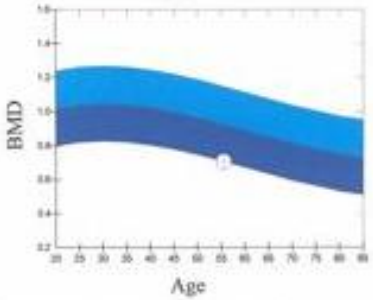
Scan Date: ID:
Scan Type: f Lumbar Spine
Analysis: 11:09 Version 11.2:7
Lumbar Spine
Operator:
Model:
Comment:

DXA Results Summary:

Region	Area (cm^2)	BMC (g)	BMD (g/cm^2)	T-Score	PR (%)	Z-Score	AM (%)
L1	11.19	6.93	0.619	-2.8	67	-1.8	76
L2	11.43	7.60	0.665	-3.3	65	-2.2	73
L3	13.66	10.68	0.782	-2.7	72	-1.6	81
L4	14.40	10.49	0.728	-3.5	65	-2.4	74
Total	**50.68**	**35.69**	**0.704**	**-3.1**	**67**	**-2.0**	**76**

Total BMD CV 1.0%, ACT = 1.033, BCF = 1.086, TH = 6.689

Total



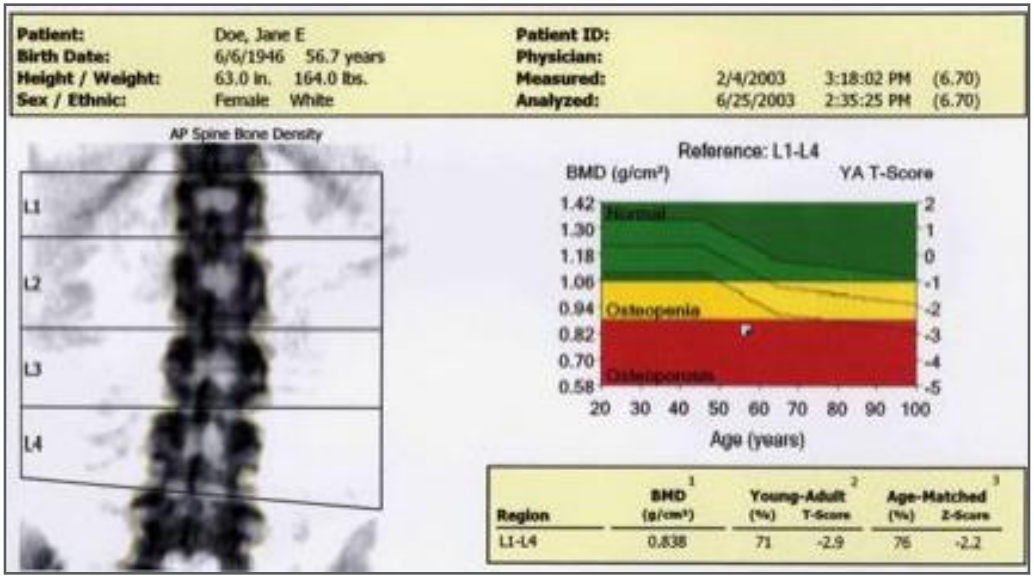
Reference curve and scores matched to Hispanic Female

Source: T-Score not adjusted for ethnicity per ISCD

Physician's Comment:

Demographics

Image



Graph

ANCILLARY RESULTS [AP Spine]

Region	BMD[1] (g/cm²)	Young-Adult[2] (%)	T-Score	Age-Matched[3] (%)	Z-Score	BMC (g)	Area (cm²)	Width (cm)	Height (cm)
L1	0.820	73	-2.6	78	-2.0	7.7	9.4	3.5	2.70
L2	0.806	67	-3.3	72	-2.7	10.8	13.4	3.6	3.71
L3	0.907	76	-2.4	80	-1.8	11.3	12.5	3.8	3.24
L4	0.820	68	-3.2	73	-2.6	12.0	14.6	4.1	3.53
L1-L2	0.812	71	-2.8	75	-2.2	18.5	22.8	3.5	6.41
L1-L3	0.845	72	-2.7	77	-2.1	29.8	35.3	3.6	9.65
L1-L4	0.838	71	-2.9	76	-2.2	41.8	49.9	3.8	13.18
L2-L3	0.855	71	-2.9	76	-2.3	22.1	25.8	3.7	6.95
L2-L4	0.842	70	-3.0	75	-2.4	34.1	40.5	3.9	10.48
L3-L4	0.860	72	-2.8	76	-2.2	23.3	27.1	4.0	6.77

Results

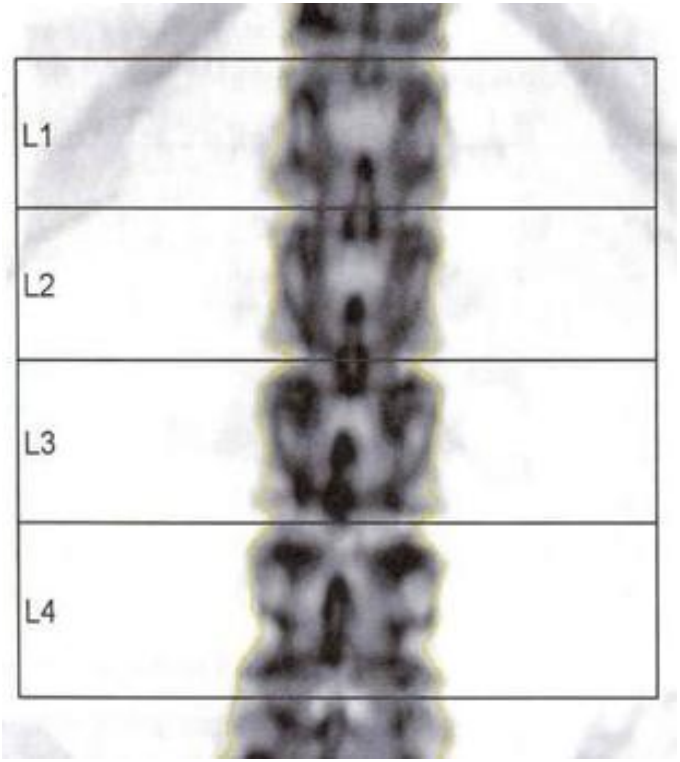
Central DXA Interpretation Principles

- Check demographics
- Review the image
  - Evaluate positioning, edge placement, labeling, artifacts
- Exclude vertebral bodies or regions/sites if artifacts
- Utilize the lowest T-score for diagnosis
  - Spine (L1-L4)
  - Hip (neck or total femur) not Ward's area or trochanter

DXA Image

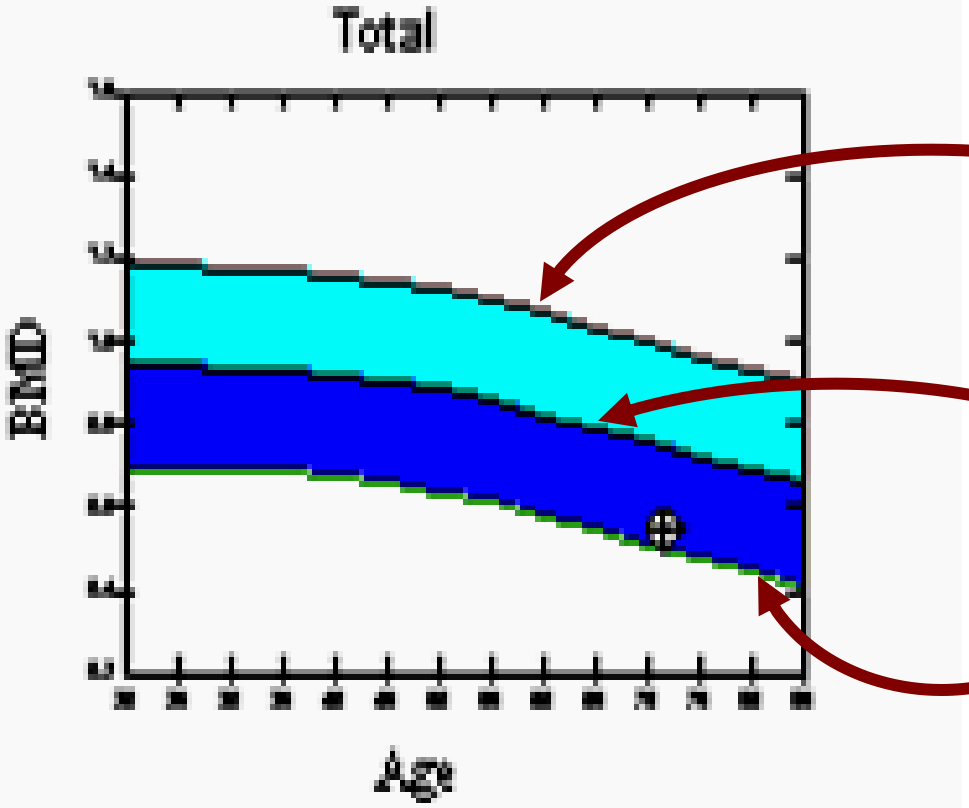
- Check patient positioning
- Check scan analysis
- Identify artifacts
- The disclaimer **“Image not for diagnosis”** is not a mandate to ignore the image

Review the Image



- Is positioning correct?
- Compare with prior study
- Are the proper regions identified?
- Are there other problems?
- Compression fractures?
- Degenerative changes?
- Get x-rays if not sure
- If possible, delete artifacts

Hologic Graph



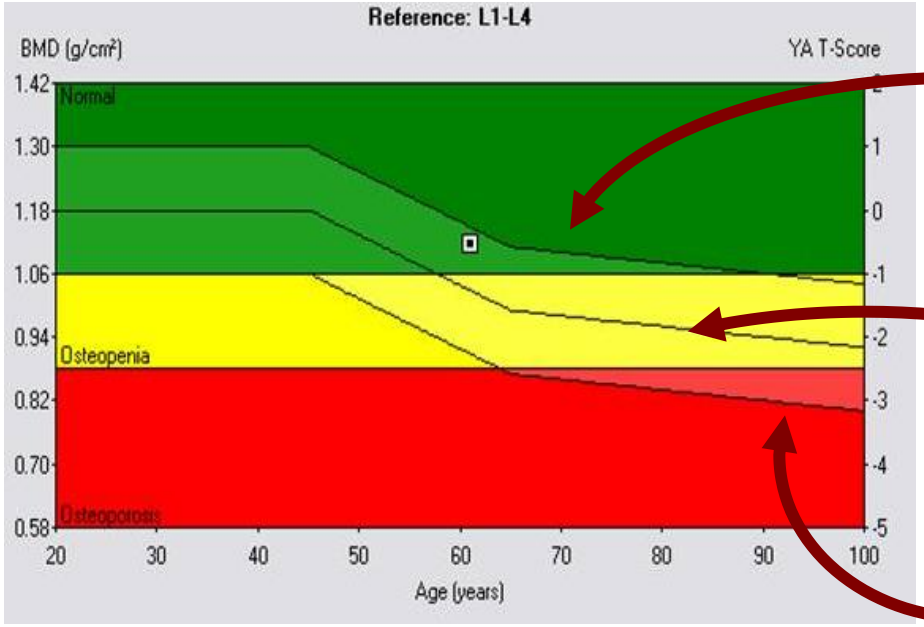
Lightly shaded area is above average for age; (top line = +2.0 SD)

Middle line is average for age

Darkly shaded area is below average for age; (bottom line = −2.0 SD)

The patient result is shown as a cross (or a half circle if result is off the scale)

GE-Healthcare Lunar Graph Default



Top line = +1.0 SD

Middle line is average for age

Darkly shaded area is below average for age; (bottom line = −1.0 SD)

The patient result is shown as a white box

Numerical Results

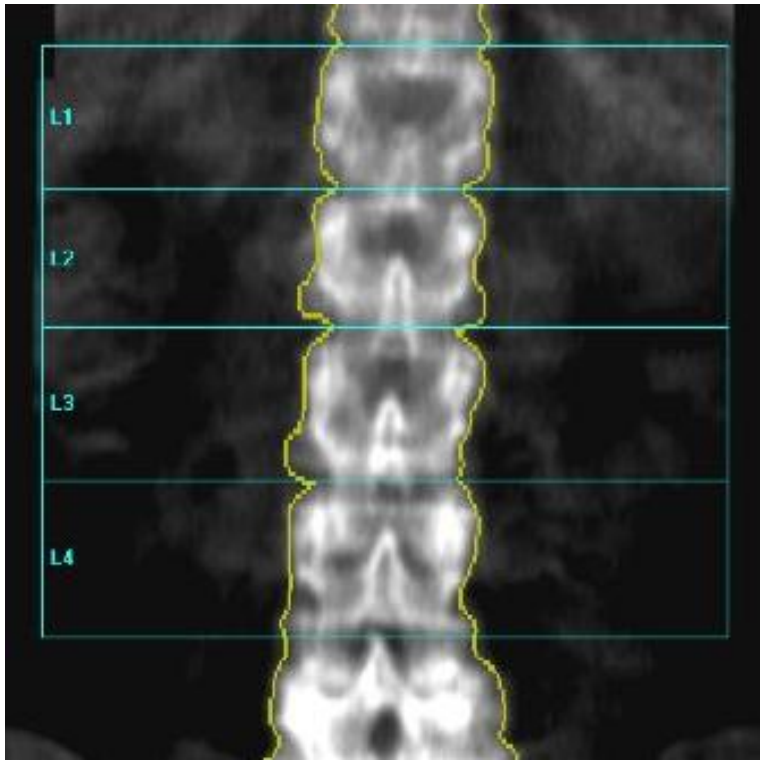
- Region of interest
- BMD in g/cm^2
  - Used for monitoring
- T-score
  - Used for diagnosis
- Additional data:
  - %, Z-score, BMC, area, etc
- Usually configurable

Numerical Results: Spine Look for Progression

- BMD should increase from L1 to L4
- Sometimes L4 ≤ L3
- BMC and area should also increase L1 to L4

Region	Est.Area (cm^2)	Est.BMC (grams)	BMD (gms/cm^2)
L1	11.81	6.95	0.589
L2	13.10	8.62	0.658
L3	14.10	9.81	0.695
L4	16.30	11.82	0.725
TOTAL	55.31	37.21	0.673

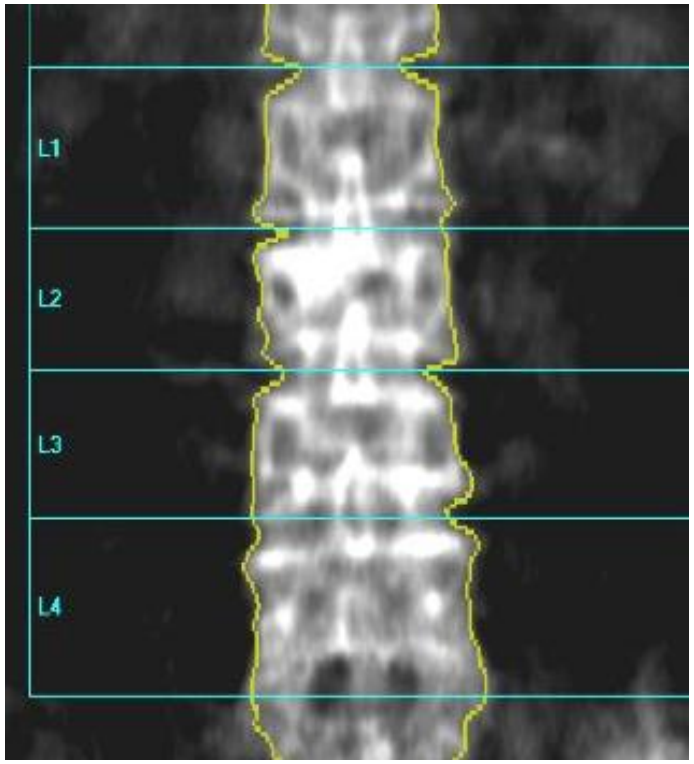
Agreement of Individual Vertebrae



Normal Progression and
T-Score Variation

Region	BMD (g/cm^2)	T-score
L1	0.832	-2.5
L2	0.919	-2.3
L3	0.984	-1.8
L4	0.998	-1.7

Discrepancy of Individual Vertebrae



Region	BMD (g/cm^2)	T-score
L1	0.755	-3.1
L2	0.972	-1.9
L3	0.970	-1.9
L4	0.768	-3.6

L1, L4 BMD reported
(excluding L2 and L3)

ISCD Official Position

L1-L4 Is Preferred for Diagnostic Purposes

Criteria for Exclusion of Vertebrae from Analysis

- Anatomically abnormal vertebrae may be excluded from analysis if:
  - They are clearly abnormal and non-assessable within the resolution of the system; or
  - There is more than a 1.0 T-score difference between the vertebra in question and adjacent vertebrae
- When vertebrae are excluded, the BMD of the remaining vertebrae is used to derive the T-score

Hans D, et. al. J Clin Densitom 2006, 9;15-21.

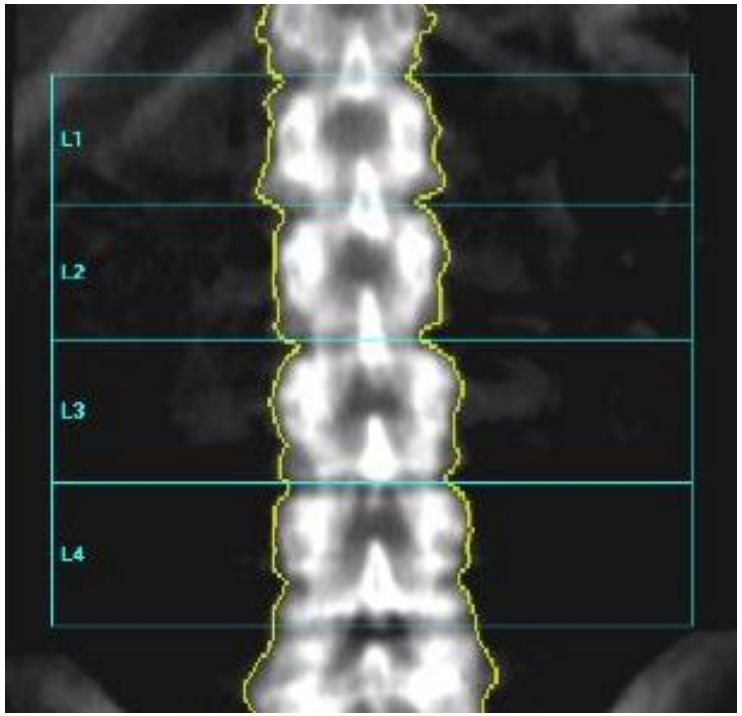
Follow-Up Scans

- Consistent patient positioning
- Consistent scan analysis
- Scan area should be similar

Scan date	Region	BMD (g/cm^2)	BMC (g)	Area (cm^2)
11/16/01	L1-L4	0.924	49.26	53.31
02/07/03	L1-L4	0.997	53.66	53.81
11/16/01	Neck - L	0.835	3.79	4.53
02/07/03	Neck - L	0.880	3.99	4.53

Good Follow-Up Scan

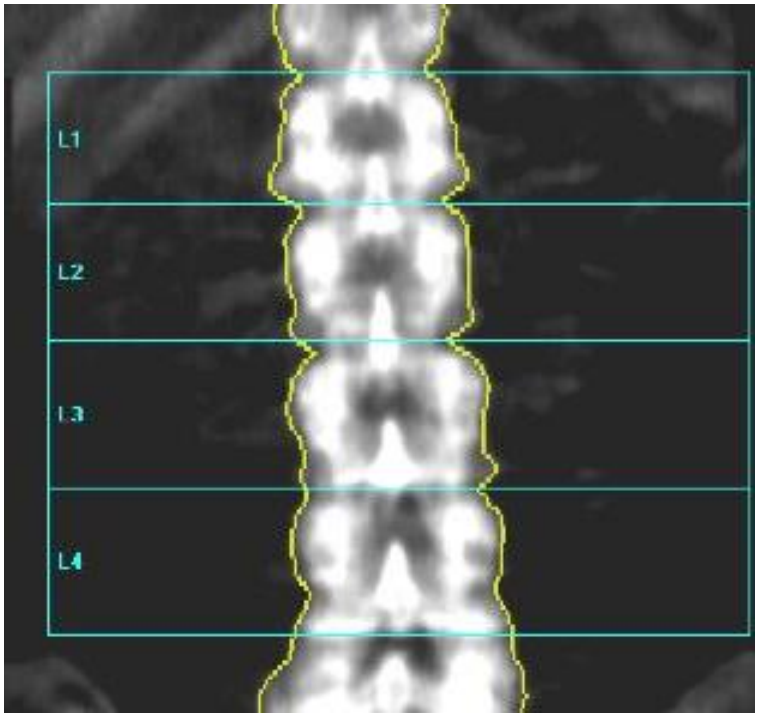
Baseline



L1: 1.312
L2: 1.324
L3: 1.448
L4: 1.411

L1-L4
BMD = 1.389
T-score = 1.7

Follow-up

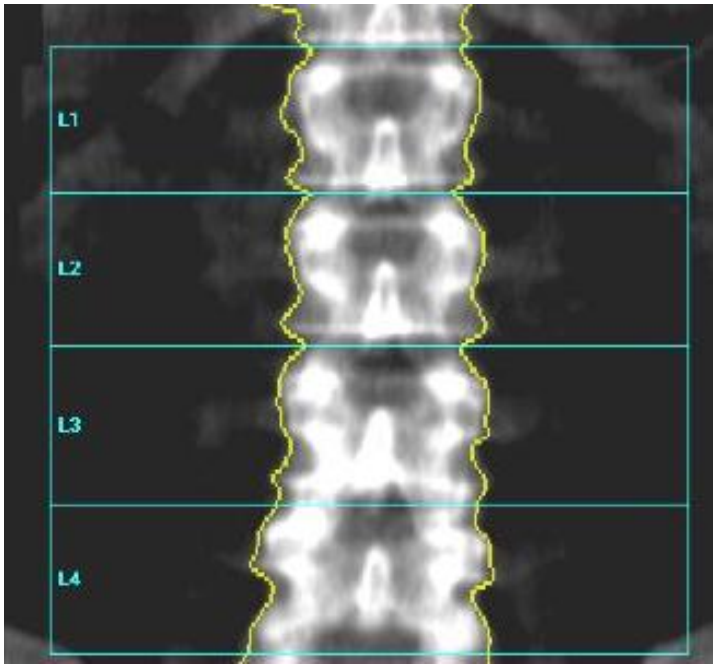


L1: 1.302
L2: 1.337
L3: 1.435
L4: 1.399

L1-L4
BMD = 1.372
T-score = 1.6

Poor Follow-Up Scan

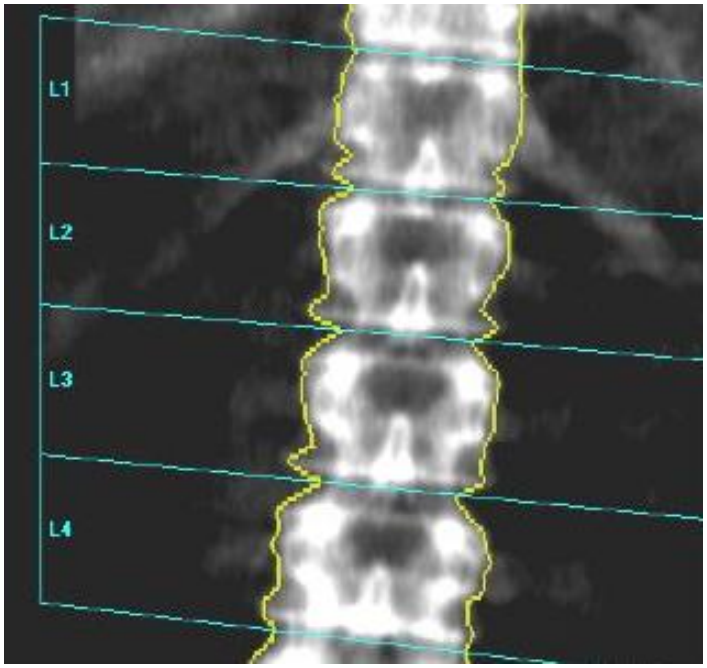
Baseline



L1: 0.992
L2: 1.103
L3: 1.237
L4: 1.254

L1-L4
BMD = 1.157
T-score = −0.5

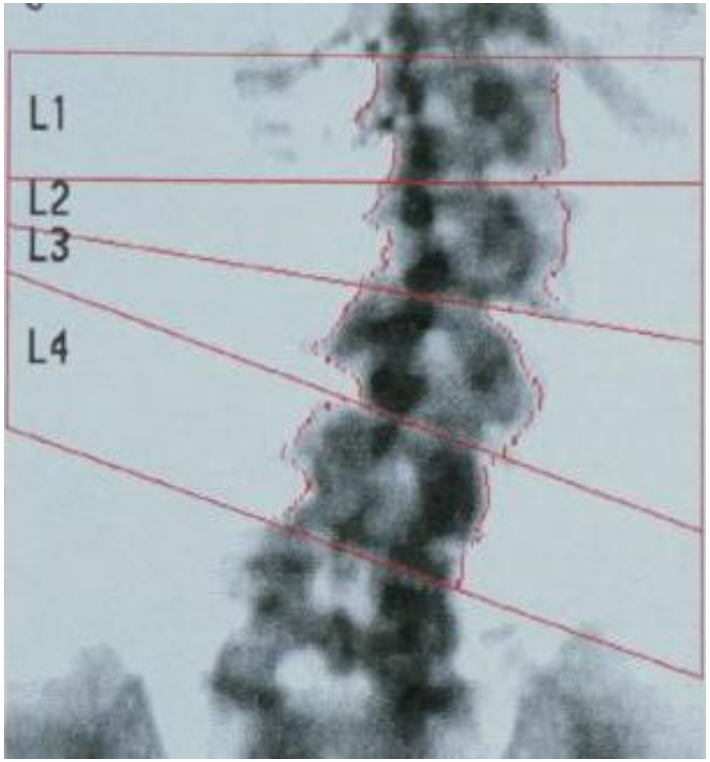
Follow-up



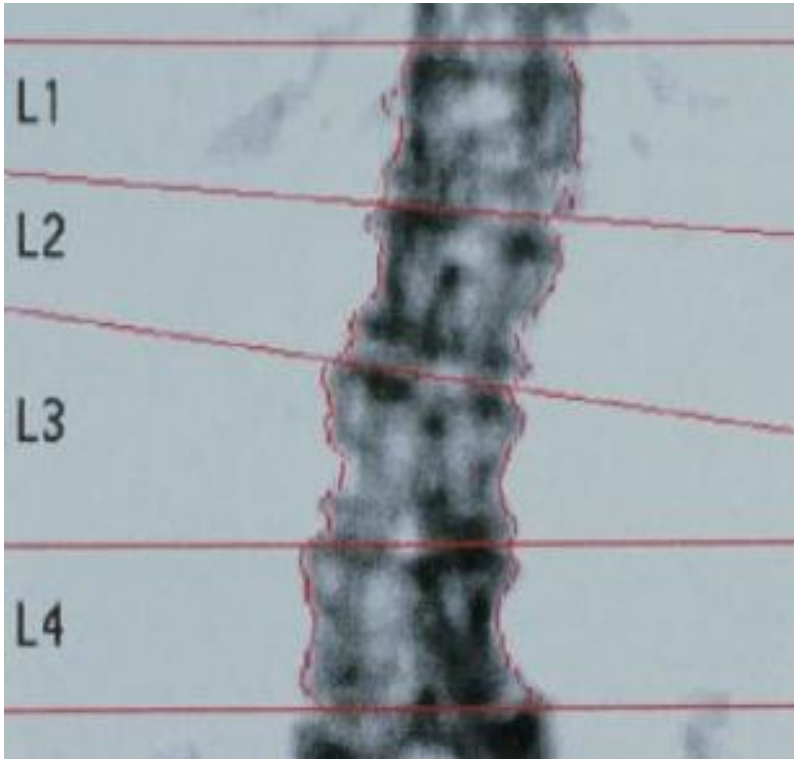
L1: 1.003
L2: 0.930
L3: 1.057
L4: 1.150

"L1-L4"
BMD = 1.043
T-score = −1.5

Spine Artifact: Degenerative Disease



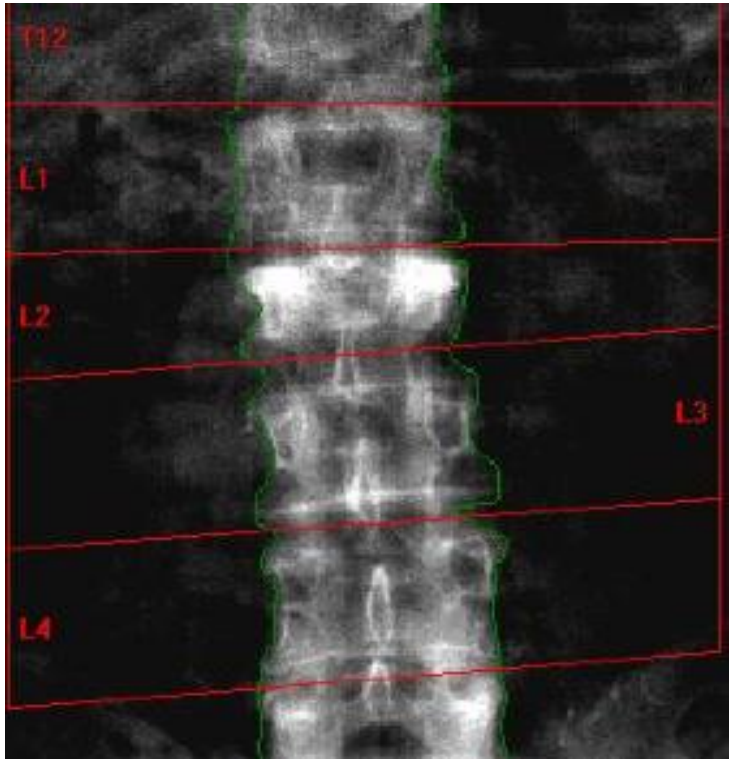
Case 1



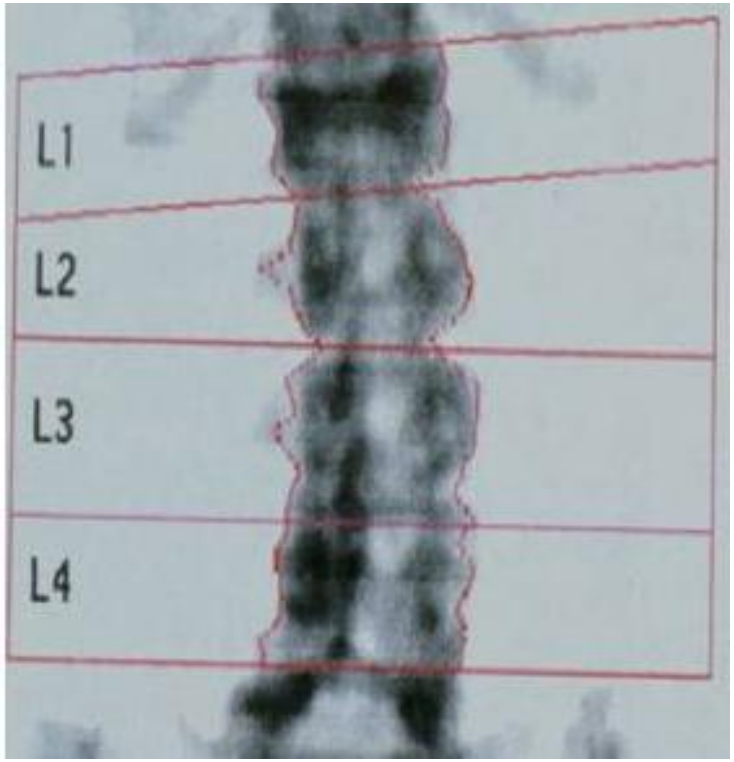
Case 2

Spine Artifact

Compression fractures



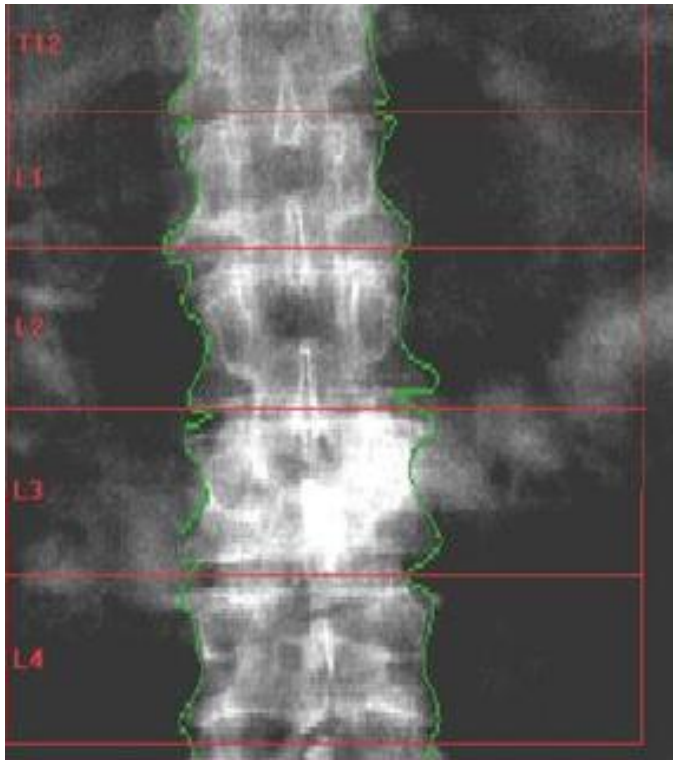
Case 1



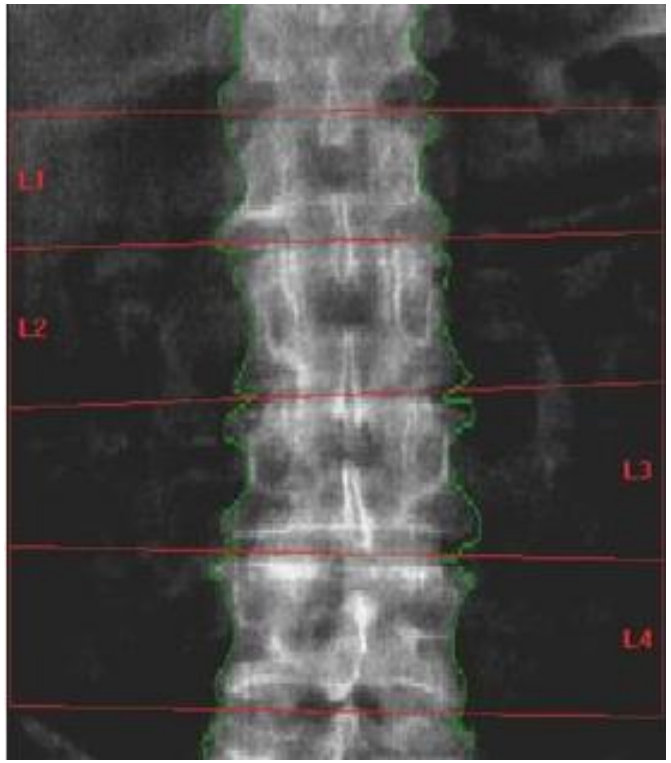
Case 2

Spine Artifact

GI contrast material



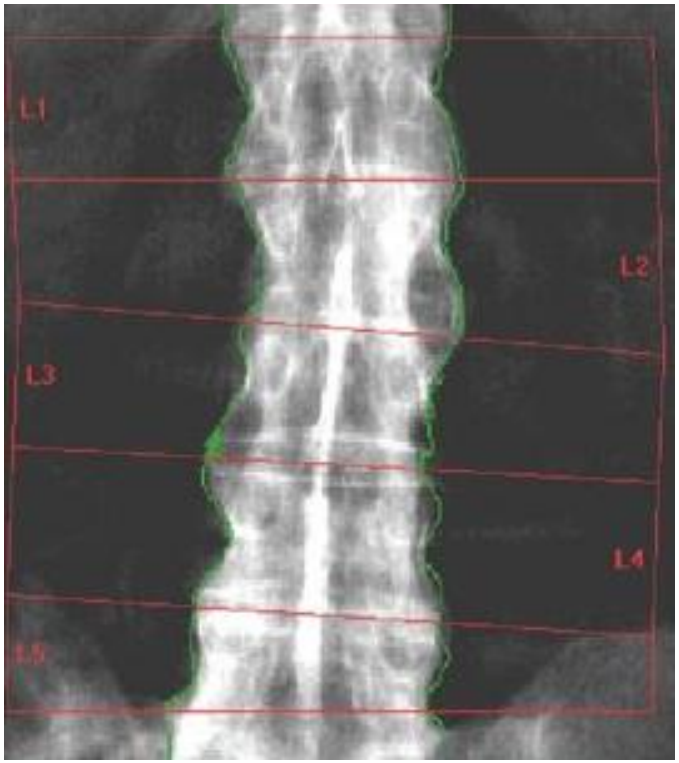
Initial scan
L1-L4 BMD = 1.268 g/cm^2



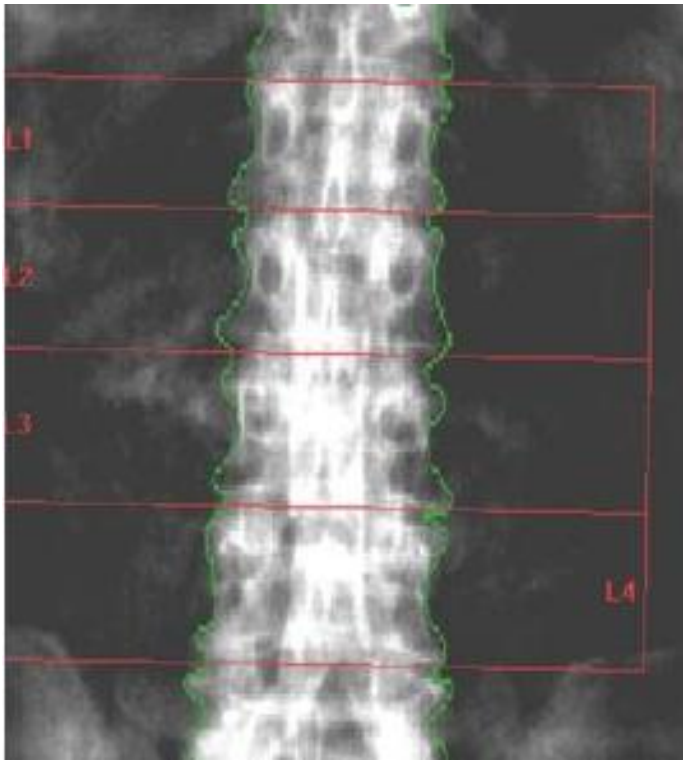
2 weeks Later
L1-L4 BMD = .929 g/cm^2

Spine Artifacts

Ankylosing spondylitis/calcified aorta



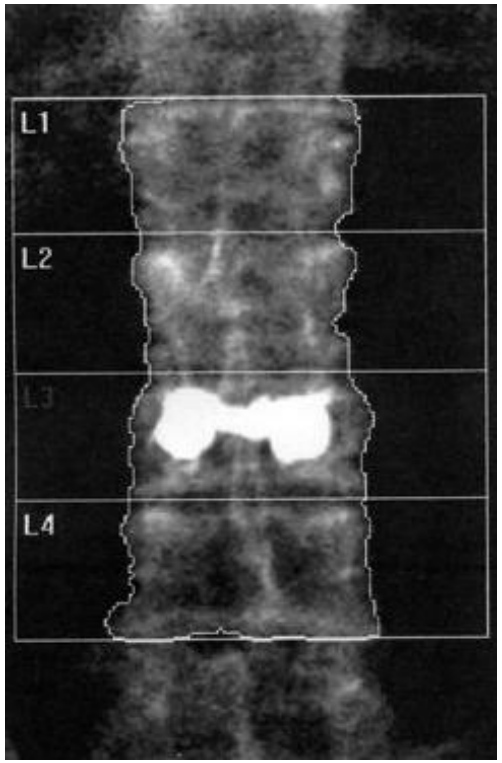
Case 1



Case 2

Spine Artifact

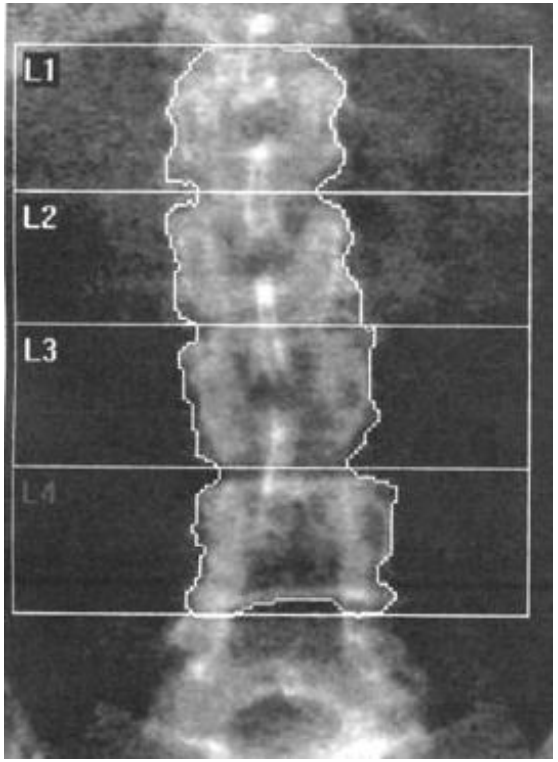
Vertebral augmentation, L3



Region	T-score
L1	0.3
L2	0.6
L3	14.7
L4	-2.6
L1, 2, 4	-0.7

Spine Artifact

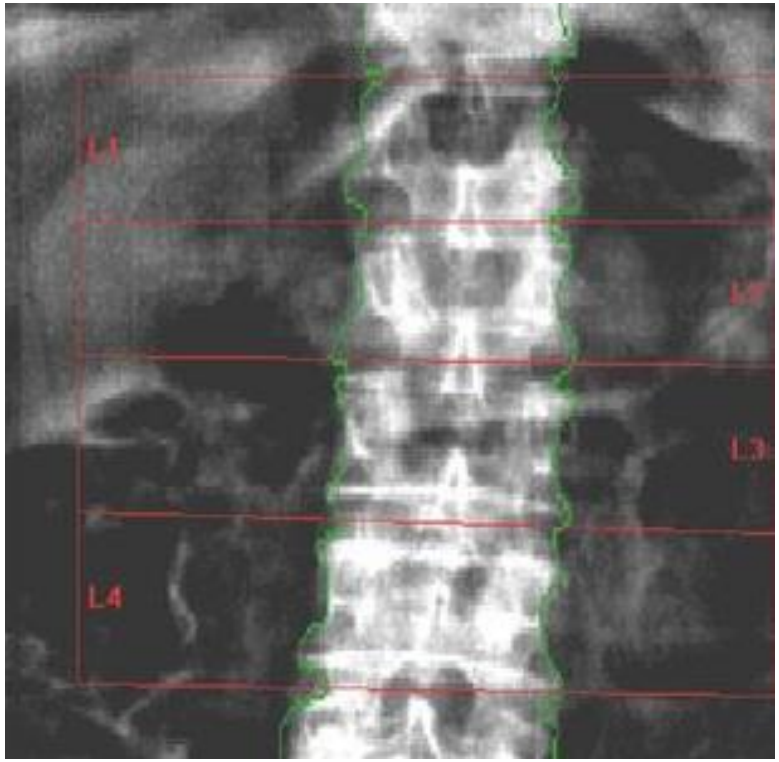
Laminectomy L4



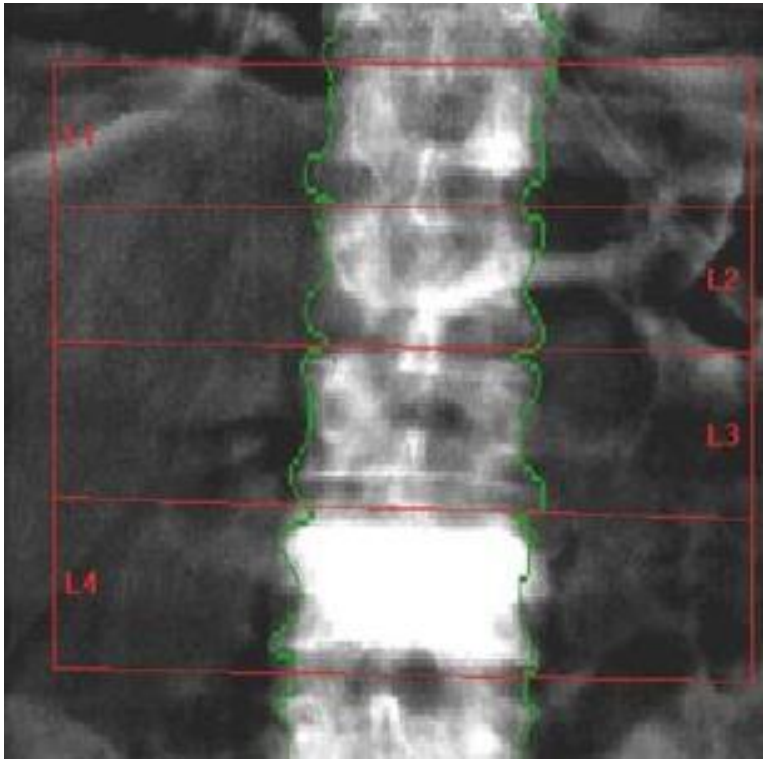
Region	T-score
L1	-1.6
L2	-1.6
L3	-2.0
L4	-3.1
L1-L3	-1.8

Spine Artifact

Prostate cancer



Baseline



2 years Later