Assessing fracture risk – the challenges of DXA and other techniques

Angelo A. Licata, MD, PhD, FACE, FACP
Vice-president, Ohio River Region Chapter AACE
Consultant, Director, Calcium Unit, Endocrine Metabolism Institute Cleveland Clinic
Consultant, NASA Glenn, Human Factors Research Group
Cleveland, Ohio

Conflict of interest: none

Objectives

• Recognize problems in the clinical use of DXA
• Appreciate the benefits and pitfalls of FRAX
• Understand the use of vertebral morphometry
DXA –
greatest medical advance in evaluating bone disease and fracture risk

Low bone mass – best predictor of increased risk of fracture

[when used correctly]

Why the consultation for abnormal report

• Patient being treated but DXA scan doesn’t change
• Patient being treated and the DXA scan decreases
• Never concerned about an increase
• What do we think?
  • Using the therapy or using it incorrectly
  • Careful questioning, bone turnover markers
  • BMD may not change or we can’t identify it with the technology
  • Micro-architectural elements [quality] transparent to DXA
    • Crystal size, collagen, turnover, micro-cracks, 3D structure
  • Our concern
    • Firstly – Is the decrease a real skeletal change or technical issue
    • Secondly – If real, why is it so and what to do.

What’s the concept behind bone densitometry?

Extrapolation of the Beer-Lambert Law or Beer’s Law
Beer's Law [Beer-Lambert Law]

- Any component’s concentration is measurable from its absorption of energy passing through it (e.g., light, x-ray, sound waves, etc.).

\[ C = \frac{A}{d} \]

- Bone is complex
- DXA = 2 energy levels
  - X-ray

\[ \text{BMD} = \frac{\text{bone mineral content}}{\text{area of bone}} \]

**T-Score: What it is . . .**

- T-score is derived, based on a reference database of the DXA manufacturer’s choosing
  \[ \text{T-score} = \frac{\text{BMD}_{\text{patient}} - \text{BMD}_{\text{Young Normal Reference}}}{\text{SD}_{\text{Young Normal Reference}}} \]
- It uses reference databases of untreated subjects
- It can change as database updated.
- Therefore
  - Reports using changes in t-scores can be misleading.
  - The t-score alone may not indicate high fracture risk in some cases.
  - It is population-based, so an individual patient may suffer a fracture at any given T-Score
DXA and the T-score ≤ -2.5

- The original application
  - assess risk for fragility fracture
  - caucasian women
  - postmenopausal
  - age 60-65 years
  - high prevalence osteoporosis
  - a surrogate for destruction and bone fragility

When all conditions exist, it implied primary osteoporosis.

Also calculates BMC.
Reproducibility good

Changes seen in calculations

Subtle difference in rotation
How does this play out in practice?

The changes noted on the previous slide are the type reported to patients and are the reason for referrals. How can we assess the validity?

Put another way, what changes are biological / real skeletal changes and what are technical / non skeletal?

Statistical approach advocated – LSC [least significant change]

Least significant change (LSC)

the minimal % or g/cm² change which indicates a real biological effect.

calculated by the BMD center
LSC = (C.V.) $2\sqrt{2}$
   = (C.V.) $2 \times 1.414$
   = (C.V.) $2.8 \approx 3\times$ (C.V.)

Least significant change (LSC)

<table>
<thead>
<tr>
<th>Precision (%)</th>
<th>LSC (%)</th>
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<tbody>
<tr>
<td>1.0</td>
<td>2.8</td>
</tr>
<tr>
<td>2.0</td>
<td>5.6</td>
</tr>
<tr>
<td>5.0</td>
<td>14.0</td>
</tr>
<tr>
<td>10.0</td>
<td>28.0</td>
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</tbody>
</table>

Often use point estimate g/cm² [BMC] (e.g., 0.03 g/cm²)
Confidence intervals not reported in my experience
Calculation from a center maybe the average of several technologists

If there is no calculated LSC.... what then??
Worst case scenario for precision guidelines by ISCD

- Lumbar Spine: 1.9% (LSC=5.3%)
- Total Hip: 1.8% (LSC=5.0%)
- Femoral Neck: 2.5% (LSC=6.9%)


Case - Hip issues

- A 70 y old women with history of vertebral fracture
- Using bisphosphonate for several years
- Bone mass stable for years,
- Then— hip bmd decreases > 7%.
**Case – spine issues**

- A 60 y old woman used ibandronate for several years.
- Bone markers [urine Ntx] were 60% lower on therapy
- Repeat bone testing showed 27-30% decrease in spine over 2-4 years.
- She was switched to teriparatide.
Machines and DXA results
### Case study

44 y woman
- Mild hypercalcemia - FHH
- Hx non Hodgkin lymphoma age 20
- Decreasing bone density
- Low normal bone turnover markers

<table>
<thead>
<tr>
<th>Year</th>
<th>Spine BMD</th>
<th>% Change</th>
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<tbody>
<tr>
<td>2014</td>
<td>0.75</td>
<td>-15.0</td>
</tr>
<tr>
<td>2012</td>
<td>0.81</td>
<td>-8.3</td>
</tr>
<tr>
<td>2007</td>
<td>0.89</td>
<td>-1.5</td>
</tr>
<tr>
<td>2005</td>
<td>0.92</td>
<td>-1.2</td>
</tr>
<tr>
<td>2003</td>
<td>0.88</td>
<td>--------</td>
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</tbody>
</table>

<table>
<thead>
<tr>
<th>Year</th>
<th>Total hip BMD</th>
<th>% Change</th>
</tr>
</thead>
<tbody>
<tr>
<td>2014</td>
<td>0.56</td>
<td>-18.4</td>
</tr>
<tr>
<td>2012</td>
<td>0.59</td>
<td>-12.9</td>
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<tr>
<td>2007</td>
<td>0.66</td>
<td>-3.0</td>
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<tr>
<td>2005</td>
<td>0.70</td>
<td>2.8</td>
</tr>
<tr>
<td>2003</td>
<td>0.68</td>
<td>--------</td>
</tr>
</tbody>
</table>

### Why DXA systems and data are not always comparable

- Manufacturers use different:
  - methods to produce energy
  - methods to detect x-rays
  - calibration methods
  - edge detection software
  - regions of interest possible
  - young normal databases
Adjustments to data from different manufacturers

Two similar [same mfg.] DXA systems

- Can cause differences in follow up testing
- "the assumption of equivalence between similar DXA systems is not justified"
- The LSC for each is different, a blended [or general LSC] is needed and it shows loss of sensitivity

FRAX®

WHO fracture risk assessment tool
Case Study

- A 35-year-old woman develops back pain after jogging.
- Her family doctor sends her for a DXA test.
- The result shows a spinal T-score of -2.5.
- She is otherwise healthy, athletic, normal growth and development, normal menses.
- The family doctor tells her she has osteoporosis [meaning ??low density or high risk for fracture??].
- The patient is very frightened.

Widespread application of DXA technology beyond the group for which it was originally developed [e.g., men, children, young patients, etc.] and mounting clinical experience caused a conundrum – discordance between BMD, T-scores and fracture risk.

This problem led to the question “What is BMD measuring and telling us?”

Fracture Risk by Age Range

(Hui et al, J Clin Invest; 1988, 5, 140-06)
Some confounding clinical observations
Osteopetrosis
Diabetes mellitus 2
Fluoride usage
Glucocorticoid usage
Clinical drug trials
- FxR[%] ≠ BMD changes
- FxR[%] before BMD changes

Osteoporosis
Compromises Bone Strength
Increases Risk of Fracture
Osteoporosis Compromises Bone Strength Increases Risk of Fracture

Bone Strength = Bone Density + Bone Quality + Loading

Adapted from NIH Consensus Development Panel on Osteoporosis. JAMA 2001

Bone Density + Loading

Bone Quality

Osteoporosis
Compromises Bone Strength
Increases Risk of Fracture

Bone Strength = Bone Density + Loading

BMD can’t measure this...

DXA
qCT

Use clinical risk factors

1. Multiple fractures
2. Turnover
3. Damage Accumulation
4. Mineralization
5. Collagen quality
6. Geometry, size

Clinical Risk Factors

- low body mass index
- previous fragility fracture
- parental history of hip fracture
- glucocorticoid treatment
- current smoking
- alcohol intake (3 or more units per day)
- rheumatoid arthritis
- other secondary causes of osteoporosis
Intent of FRAX

• FRAX® was primarily designed for the use of primary-care physicians, who have relatively little expert knowledge in the management of patients with osteoporosis.

• Offers practitioners a quantitative way of using clinical risk factors and avoids the subjectivity of estimating impact of clinical risk factors, projection over 10 yr. horizon.

• It’s a guideline, still need for clinical judgment, will change with population-data updates in local country.

• When to treat or not – use intervention thresholds – vary with local factors [data bases, economics, etc.]
  - NOF: 3% risk hip, 20% other fractures
  - UK: 7% other [Joint Bone Spine 76 (2009) 1-3]
  - China: 1.3% hip, 4% other [Endocrine (2014) 45:195–197]

FRAX usage “the pros and cons [limitations]”

• A few pros
  - When uncertain to RX
  - Use without BMD
  - Men > 50 and PM women
  - Low bone mass
  - T score [-1 to -2.5]
  - No Fr history
  - Available femoral BMD

• A few cons
  - Untreated patients
  - Availability data
  - Femoral neck BMD
  - Interpretations risk factors [dichotomous input]
  - Number and severity fractures
  - Secondary causes
  - Little effect except RA
  - Quantization effect
  - Excludes risk factors
  - Activity, Vit D, prior Rx
  - guideline
Vertebral morphometry and risk

BMD / T-scores

- A number [BMD/T-score] alone does not diagnose osteoporosis in every patient.
- The physician does the diagnosing based on input of clinical data 
  [e.g., clinical hx fracture with normal BMD]
- Prior fractures major risk for diagnosis regardless the DXA
  - “fractures beget fractures”
  - Implication weakened structure/quality

Vertebral fractures

- Clinical fractures 
  pain, spasm, etc.
  Varying degrees radiological compression
- Morphometric fractures [silent]
  height loss 
  anatomical malalignment 
  slow, insidious [years]
Vertebral fractures

- Clinical fractures
  - acute, sudden
  - pain, spasm, etc.
  - varying degrees radiological compression anterior to posterior height vertebral body
    - differs by 20% or more

Grading fractures vertebral

Semi-quantitative analysis of fracture severity

Clinical history
- Sick
- Pain, anorexic
- Abnormal labs
Silent fractures

height loss

Assessment Fx

- Suspicion
- Clinical history
  - stadiometer
- Routine X-ray
- DXA vfa [vertebral fracture assessment]

ISCD task force 2012

- Patients with prevalent vertebral fractures are at increased risk for future osteoporotic fractures of the spine, wrist and hip.
- 2/3rds of patients with vertebral fractures are asymptomatic, so patients often do not present with complaints of back pain.
- Up to 40% of patients who have osteoporotic vertebral fractures have BMD values that are better than -2.5, the WHO established definition for osteoporosis in post-menopausal women measured by central DXA.
- Prior vertebral fractures are a better predictor of future fracture than low BMD alone.
Some reasons to suspect vertebral fractures

- Age (women greater than or equal to 65 yrs and men greater than or equal to 70 yrs)
- Known height loss of greater than or equal to 1.5"
- History of vertebral fracture after age 45
- BMD evidence of osteoporosis at the hip or spine
- Corticosteroid use (greater than or equal to 5 mg/day for greater than or equal to 3 months)

VFA and DXA

- Improved imaging clarity and shorter acquisition times
- More evaluable vertebrae
What about the real thing?

When no technical issue found

- A real change in density
- Very unusual for chronic use anti-resorptives [especially bisphosphonates]
- Compliance and persistence issues
- Secondary diseases
  - Endocrine, drugs, malignancy, etc.

Summary

1. Hip ROI is the common site for unexpected changes, technical issues in positioning are common [spinal issues].
2. Updated equipment can invalidate past results even if a new machine from the same manufacturer.
3. The same machine in the same center with the same technologist is the ideal situation.
4. The LSC is important to understand and demand. The center calculates this for the machine and the technologist(s).
5. Must be vigilant ............
Take home message

I have not impugned or vilified DXA technology.

It works well, failure to heed clinical detail and poor reporting are the problems at many DXA centers.

Always look at images of the scans when in doubt about reported results.

Understand and use concept of LSC