Accuracy of DEXA scanning & other methods for determining BMD.

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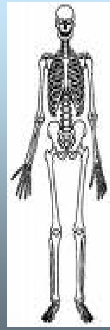
BMD- Measurement Site



- In general, densitometry techniques can be performed in either the axial or the appendicular skeleton, depending on the modality employed.
- Peripheral measurements, performed in the appendicular skeleton, help to predict the risk of fracture, however, they are less sensitive for the monitoring of therapy than are measurements in the axial skeleton because changes due to age, therapeutic intervention, and estrogen deficiencies occur less rapidly in appendicular bone than they do in the axial skeleton.
- For single energy measurements it is often necessary to surround the anatomical site by a constant thickness of tissue equivalent material to correct for overlying soft tissue – this restricts measurement to peripheral sites for these modalities.

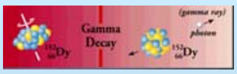
Bone Measurement Techniques

Dual-energy X-ray Absorptiometry (DEXA), DPA →	Spine, hip, forearm, calcaneus, whole body
Quantitative computed Tomography (qCT) →	Spine, hip, forearm
qUS, SXA, SPA →	Heel, patella, tibia forearm
p-QCT, RA →	Forearm, tibia

Single Photon Absorptiometry (SPA)

- The SPA technique uses a single gamma ray source (^{125}I) and a scintillation detector to measure photons transmitted through a particular anatomical site in the appendicular skeleton.
- The gamma source and detector were coupled and scanned in a rectilinear fashion across the region of interest.
- To correct for overlying soft tissue the anatomical site has to be surrounded by tissue equivalent material. Water is normally used because its attenuation closely matches that of soft tissue.
- This technique was applied to peripheral skeletal sites, most commonly the non-dominant forearm, wrist or heel.
- For application to sites in the axial skeleton, dual absorptiometry (DPA) was developed.

DPA

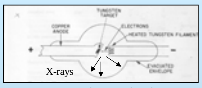


- DPA allows for simultaneous measurement of the transmission of gamma radiation of two different energies which compensates for the variation in overlying tissue and removes the need for the tissue equivalent material.
- ^{153}Gd is a common radionuclide used which provided dual energy peaks at 44 & 100keV photons which were counted separately by scintillation detectors.
- Factors which affect the accuracy of photon absoprtiometry include:
  - Inhomogeneity of soft tissue
  - Uncertainty in values of density and attenuation coefficients for both bone mineral and soft tissue components.

DPA

- The accuracy error of photon absorptiometry has been estimated at 4-8% [Blake et al, 1999].
- Limitations of SPA & DPA include:
  - Radionuclide decays and has to be replaced regularly
  - Long scanning times due to low photon flux (~40 mins)
  - Poor spatial resolution.
- The introduction of SXA & DXA systems which employ the use of an X-ray tube as a source of radiation overcame these limitations.

SXA



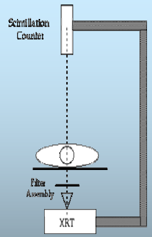
- A collimated photon beam is directed from an x-ray source through the measurement site.
- The photon attenuation of the beam by bone is then measured and converted to bone mineral content.
- The bone mineral content is computed from the increased absorption of the beam as it passes from a constant thickness of soft tissue or water bath into the bone.
- SXA is commonly used because it is relatively quick & simple to perform and results in a low radiation dose.
- SXA scan time approx 4 minutes and delivered a radiation exposure of 1.68 mrem (16.8µSv) [Kelly et al, 1993].
- However, the necessity of surrounding the body part with a soft tissue equivalent material restricts the SXA measurement to sites on the forearm or other parts of the appendicular skeleton. [Mirsky et al, 1998].

SXA- Performance

- Studies suggest SXA measurements correspond well with the status of the peripheral long bones but poorly with that of the axial skeleton [Schlenker et al, 1976]
- Blake estimates the accuracy of SXA as similar to PA methods [Blake, 1999].
- In a 1993 study Kelly et al, evaluated the performance of a SXA device with respect to precision *in vivo* and *in vitro*, scan time, image quality, and correlation with an existing dual energy X-ray absorptiometry (DXA) device.
  - SXA precision *in vivo*, expressed as a coefficient of variation (CV), was 0.66% for bone mineral content (BMC) and 1.05% for bone mineral density (BMD).
  - Precision *in vitro*, based on 78 BMC measurements of a forearm phantom over 195 days, was 0.53%.
  - Correlation with DXA at the 8 mm distal forearm site was high (r=0.97 for BMC and r=0.96 for BMD).
  - SXA image quality and spatial resolution were superior to SPA and comparable to DXA [Kelly et al, 1993]

DEXA

- Most widely used modality for the clincial measurement of bone mineral content [Compston et al, 1995]
- DEXA was introduced in 1987 and its measurement principle is based on the method of X-ray Spectrophotometry.
- Digital imaging to locate the skeletal regions of interest followed by estimation of X-ray attenuation in these regions
- Comparison of attenuation at high and low energy regions of the X-ray spectra yields an estimate of the BMD (g/cm²).
- DEXA provides bone mineral density measurements both axially and peripherally, as well as total body scans, but is most commonly applied to scanning of the lumbar spine (L1-L4) and the proximal femur.



Region	Est.Area (cm^2)	Est.BMC (grams)	BMD (gms/cm^2)
L1	10.12	5.02	0.497
L2	12.12	7.16	0.591
L3	13.08	8.08	0.673
L4	15.93	11.81	0.741
TOTAL	51.25	32.79	0.640

DEXA Performance

Factors affecting the accuracy of DEXA measurements:

- Variations in soft tissue composition within the X-ray beam
- Correct patient positioning and scan analysis
- Artefacts due to metal or clothing
- Scanner calibration
- Beam hardening
- Intereference from Isotopes (Nuc Med facility in close proximity)

Factors affecting the precision of DEXA measurements:

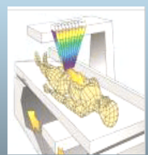
- Random errors due to photon & electronic noise
- Drifts in scanner calibration
- Changes in soft tissue composition (patient weight gain or loss)
- Consistent patient positioning and scan analysis.

DEXA Performance

- Literature suggests that DEXA can be used to detect small changes in bone mineral content at multiple anatomical sites, with little exposure to radiation, short examinations time, high resolution images [Mazess et al, 1993], and excellent precision (0.5 -> 2%) and accuracy (3->5%) [Sorenson et al, 1998]
- Other studies report accuracy as 5% and precision as 2-6% [e-readiography.net]
- Compared with DPA, DEXA requires less time per examination, is more reproducible, and involves less exposure to radiation [Mirsky et al, 1998]
- Compared with qCT, DEXA has superior precision is less expensive, and is associated with lower absorbed doses of radiation [Mirsky et al, 1998].

DEXA Performance

- Main disadvantage of DEXA is that it does not enable the examiner to differentiate between cortical and trabeculear bone.
- Some literature suggest that DEXA is of limited use in people with a spinal deformity or those who have had previous spinal surgery.



- The presence of vertebral compression fractures or osteoarthritis may interfere with the accuracy of the test; in such instances, CT scans may be more useful.

Quantitative Ultrasound (qUS)

- The use of US for the measurement of bone density has received widespread attention because:
  - Does not involve the use of radiation
  - Inexpensive (lower cost than DEXA)
  - Relatively simple to implement and process
  - Portable

- US can provide information about the density and elasticity of bone by measuring the velocity of sound through bone, and about the structure of bone by measuring the attenuation of the signal.

qUS- Principles

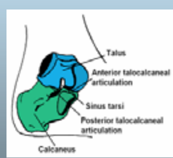
- Bone tissue can be characterized in terms of speed of sound and broadband ultrasound attenuation (BUA).
- Speed of sound and attenuation of a sound wave are affected by the density, compressibility, viscosity, elasticity, and structure of the material it is travelling through.
- This technology assumes that bones with different biomechanical properties properties have different ultrasound-determined values for attenuation and velocity.
- The propagation of the US wave through bone is affected by bone mass, bone architecture, and the directionality of loading.

qUS- Principles

- Pulse-echo (reflection) technique: uses a single transducer to transmit and receive the signal. The generated US pulse travels through the sample and is reflected at an interface to be detected by the same transducer.
- Transmission technique: uses two transducers, positioned either side of the heel, one to transmit and a second to receive. (preferred method with dealing with bone due to the bones highly attenuating nature).
- Transducers can be either fixed or mobile
  - Fixed transducers are not in direct contact with the heel and a set heel width is assumed when calculating the speed of sound and broadband ultrasound attenuation.
  - Mobile transducers can be brought into direct contact with the heel and the correct width can be measured.

qUS- Measurement Site

- Difficult to use US to measure common fracture sites (hip & vertebrae) because the depth of soft tissue surrounding these bones attenuates too much of the US signal so a reading cannot be obtained.
- Most popular US measurement site is the calcaneus
  - There is very little soft tissue which makes it easy to measure bone
  - It has a relatively flat surface which ensures good contact between the heel and the transducers
  - It is similar in composition to the main fracture sites (approx 90% trabecular bone)
  - It is easily accessible and requires very little patient preparation. [Evans, 2006]



qUS- Applications

- Newer US imaging devices offer a parametric image of broadband US attenuation (BUA) at the calcaneus.
- For a given material the attenuation of the US wave will be constant, known as its BUA index.
- This is a measure of the increase in attenuation of the ultrasound wave as a function of increasing frequency.
- An US wave covering a range of frequencies is passed through a known thickness of sample.

qUS- Applications

- The amplitude spectrum of the received signal is then compared to the spectrum of a reference material.
- The difference between the two spectra is plotted against frequency and the slope is the BUA index (dB/MHz).
- If it is then divided by the thickness of the measured sample, it gives a volumetric parameter in (dB/MHz)/cm.
- The precision of this technique was found to be 1.4 to 3.3 percent [Roux, 1996], the authors also noted that parametric imaging enhanced the reproducibility of US measurements of the calcaneus.

qUS - Performance

- Factors which affect accuracy & precision in qUS:
  - Operator dependant: Incorrect placement of the measurement region
  - Device dependant: Diffraction affects both attenuation & velocity measurements.
  - Patient dependant: Variability of bone width, soft tissue thickness or composition, marrow composition and temperature. [Evans, 2006].
- In some studies the values obtained with use of qUS have been shown to correlate well with those obtained with the use of standard bone densitometery techniques such as DEXA [Mirsky, 1998].
- At the calcaneus qUS and DEXA measurements have to have a correlation of approx. 0.8 to 0.85 [Gluer, 1997].

qUS - Performance

- However other studies found that the precision of QUS is generally poor and changes in qUS of the heel may not reflect changes in BMD at the spine or hip.
- Studies suggest that qUS is a useful tool in determining fracture risk [Hernandez, 2004].
- There is some evidence that qUS of the heel can predict fracture risk of hip and spine independently of BMD measurements.
- There is also some evidence that qUS in addition to BMD evaluation by DEXA may give a better estimate of fracture risk than DEXA scanning alone.

qUS - Performance

- But qUS has limited usefulness (compared to DEXA) for monitoring and comparing the effect of medications used to treat osteoporosis.
- Some studies suggest that qUS may reliably screen out patients unlikely to have a BMD in the osteporotic range, however subjects classified as osteporotic using this method require further investigation such as DEXA to confirm the diagnosis [Taal et al, 1999].
- qUS is generally used as an initial screening test. If results from an ultrasound test indicate that bone density is low, DEXA is recommended to confirm the results.

qCT

- PA, SXA and DEXA techniques are projection techniques and as a result can only measure BMD as an area density (2D), and they include mineral from both cortical and trabecular bone in the beam path.
- qCT provides a cross-sectional or 3-dimensional image from which the bone is measured directly, independent of the surrounding soft tissue
- A form of qCT called peripheral qCT (pQCT) measures the density of bones in peripheral limbs, wrist etc.

QCT isolates metabolically active trabecular bone

qCT

- Advantages of qCT include
  - Can measure trabecular and cortical bone separately, which offers an advantage in terms of the choice of treatment because cortical and trabecular bone do not change in parallel.
  - it is the only modality which allows direct measurement of a volume of bone, which can be expressed directly as density.
  - Can be performed on a standard hospital CT.
- Disadvantages are the relatively high radiation dose involved (~29μSv) [Kalender, 1992] and the high cost of scans, limited access to scanners due to their high clinical demand.

Clinical indications for QCT, defined by the National Osteoporosis Foundation

- To assess bone density of peri-menopausal women for initiation of estrogen replacement therapy.
- To establish a diagnosis of osteoporosis or assess its severity in the context of general clinical care.
- To monitor bone density in patients receiving glucocorticoid therapy.
- To diagnose low bone density in patients with metabolic disorders such as mild primary hyper-parathyroidism

qCT - Principles

- qCT involves the use of a mineral calibration phantom and a CT scanner.
- The phantom usually consists of hydroxyapatite in plastic and is scanned simultaneously with the vertebrae.
- A lateral CT scan localizes the mid-plane of two, three or four lumbar vertebral bodies.
- Quantitative readings are then obtained from a region of trabecular bone in the anterior portion of the vertebrae.

qCT - Principles

- The CT determinations of vertebral bone density are compared with known readings of solutions in the phantom.
- The measurements of the vertebrae are then averaged, and a commercially available software package is used to convert Hounsfield units into Bone mineral equivalents.

A series of axial scans are taken with the patient lying on a calibration phantom

qCT - Principles

- qCT is available in both single energy and dual energy modalities.
- The single energy technique offers better reproducibility and it is more commonly recommended [Mirsky, 1999].
- However, standard single energy CT analysis of the lumbar spine fails to account for increases in bone marrow fat concentration that occur with increasing age.
- As a result, measurements in elderly, osteoporotic patients may be falsely decreased by 20-25% [Cann, 1980].
- The accuracy is reportedly reduced with the use of Dual Energy CT but the dose of radiation is higher [Cann, 1980].
- Peripheral qCT systems with a small circular gantry are now available.
- Principle advantage of this technique is the reduced radiation exposure (typically $0.4\mu Sv$ to the skin) [Hosie et al, 1986].

qCT Accuracy

- Soft tissue inhomegenity affects the accuracy of qCT.
- The content of yellow marrow in the vertebrae may have a significant effect on the accuracy of BMD measurements.
- Machine related artefacts such as beam hardening, detected scatter and system drift can introduce errors.
- Accuracy and precision of qCT are reported as 5-8%.

Radiographic Absorptiometry (RA)

Radiographic absorpitometry (RA) is a technique for bone mass measurement from radiographs of peripheral sites, most commonly the hand or heel.

Its advantages include that it is less expensive and more widely available than other bone densitometry techniques, there is no need for specialised equipment, and it has been shown to be both precise and accurate, for obtaining bone-mineral content measurements of the phlanges of the hand [Yang, 1994].

The major disadvantage of RA is that, because measurements are sensitive to changes in overlying soft tissues, the technique is limited to the appendicular skeleteon [Mirsky, 1999].

Radiographic Absorptiometry (RA)

- The principle was first described in 1939, and RA became relatively widely used as a research technique in the 1960s, although interest in RA subsequently dwindled as more precise non-radiographic densitometry techniques became available.

- In traditional RA measurements, an aluminium wedge is included in the radiograph in order to correct for variables, such as voltage setting, exposure time, and film variables.
- However, it has recently gained renewed interest as a simpler, readily available screening tool.

Radiographic Absorptiometry (RA)

- Initially, two radiographs of the hand and an aluminium reference wedge are taken at different energies.
- The radiograph was then sent to a central reading facility where the image was captured electronically and was analysed to determine the mean density of the middle phlanges of the second, third and fourth fingers is calculated and the results are reported in aluminium equivalents.

- Also, standardized hand radiographs are taken with an aluminium step-wedge placed on the film and the imaged is analyzed with an optical densitometer. The BMD is determined by comparison with the defined density of the aluminium step-wedge.

Radiographic Absorptiometry (RA)

- This is a low-cost and potentially widely available technique but is it restricted to the appendicular bones such as the metacarpals and phalanges, which are surrounded by a relatively small amount of soft tissue.
- Recently, computerized image processing has been applied to radiography, with the result that current RA techniques applicable to a routine clinical setting are seemingly as precise and accurate as dual-energy or single-energy x ray absorptiometry (DXA or SXA) [Yates et al, 1995].
- In addition, recent studies demonstrate that the strength of association between low bone mass measured by RA and fracture risk is comparable to that for other forms of bone mass measurement [Yates et al, 1995].

RA Performance

- Cosman [1991] reported correlations between RA and the standard BMC techniques as *r*=0.58–0.9.
- Cosman also reported that RA measurements were found to predict low bone mass of the lumbar spine and femoral neck with 90% and 82% sensitivity respectively.
- Yang et al (1994) in a study of cadavera, found that the correlation between RA determination of BMC in the hand and DEXA determination of BMC in the forearm was good, at *r*=0.887, and that the short term precision error was small, CoV at 1% for BMC measurements.
- Problems include non-uniformity of film sensitivity and processing [Njeh, 2000].

Summary

- DPA – low radiation exposure and accuracy error of the order of 3-10% for DPA of the spine, but long scan times, poor resolution & precision errors range from 1.2-2% for the hip.
- SPA/SXA accuracy error ranges from 2-5% for SXA of the heel & forearm, but precision error is 1-2%. Not accurate for measuring BMD of the spine or Hip.
- RA is a low cost and widely available tool but is not commonly used.

[http://www.ncbi.nlm.nih.gov/books/bv.fcgi?rid=hstat]

Summary

- DEXA is still considered the gold standard, with established clinical efficacy. Low radiation dose and very good precision & accuracy. Multiple measurements sites possible.
- qUS a portable, low cost application that results in no radiation exposure to the patient, it is useful as a fracture risk assessment tool & to screen for osteoporosis and potentially has further applications
- qCT provides a £D image, allows separate analysis of trabecular and cortical bone, has good accuracy but is less precise than DEXA, is expensive and results in a larger radiation exposure to the patient.

[http://www.ncbi.nlm.nih.gov/books/bv.fcgi?rid=hstat]

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