A review of emerging trends in dual-energy X-ray absorptiometry (DXA)

Kevin E. Wilson

New developments in dual-energy X-ray absorptiometry (DXA) technology are leading to major improvements in diagnosing osteoporosis, more accurately determining future fracture risk and, most recently, even diagnosing cardiovascular disease.

New fan-beam DXA systems can detect vertebral fractures with fast, low-dose lateral images of the vertebra from T4 to L4 in as little as 10 seconds. Vertebral fractures are the most common fracture in osteoporosis and an indication for treatment irrespective of Bone Mineral Density [1-3]. However, without a diagnostic test such as that available on fan-beam DXA systems, as many as 75% of vertebral fractures would never come to clinical attention [4]. Some DXA systems can measure bone structure and strength using conventional DXA scans. Three-dimensional DXA scans take advantage of the rotating C-arms found on some of the newer DXA systems.

Recently, a DXA manufacturer received FDA clearance to assess an important risk factor for heart attacks and stroke - Abdominal Aortic Calcifications (AAC) - using the same scan.

Kevin E. Wilson

New directions in DXA imaging

Osteoporosis overview

Osteoporosis is a serious, yet not fully appreciated disease. Osteoporosis is a “silent” disease. In the U.S.A., four times as many men and nearly three times as many women have osteoporosis than report having the condition. One of the most dangerous myths about osteoporosis is that only women need to worry about bone health. Four out of every 10 Caucasian women aged 50 and older in the United States will experience a hip, spine or wrist fracture during the remainder of their life. Thirteen percent of Caucasian men in the U.S.A. will suffer a similar fate [5].

All fractures are associated with significant morbidity and mortality, but hip fractures are particularly traumatic. Twenty percent of women who suffer a hip fracture die within the first year. Because of the ageing population, it is estimated that the number of hip fractures could double or even triple in the U.S.A. by 2020 [6].

Measuring Bone Mineral Density (BMD)

Frailty fracture and BMD at the spine or hip measured with DXA are the two primary methods for diagnosing osteoporosis. While non-DXA measurements or risk factors can be used to better refine a patient’s future fracture risk, BMD with DXA is the only recognised diagnostic test for osteoporosis other than radiographic evidence of a fracture [2, 8]. In DXA systems, two energies of X-rays are used to calculate a 2D measurement of areal BMD. The indications and reimbursement for BMD vary from country to country. The International Society of Clinical Densitometry (ISCD) [2] has identified those patients most likely to benefit from BMD screenings as:

- Women aged 65 and older
- Postmenopausal women under the age of 65 with risk factors
- Men aged 70 and older
- Adults with a fragility fracture
- Adults with a disease associated with low bone mass or bone loss
- Adults taking medications associated with low bone mass or bone loss.

Additionally, BMD testing is indicated to monitor patient treatments, or if a patient is being considered for pharmacologic therapy. The International Osteoporosis Foundation [8] prefers a case finding strategy where clinical risk factors in addition to age, such as paternal history of hip fracture, smoking, corticosteroids use, etc., are used to select those who should be tested.

Vertebral Fracture Assessment (VFA)

Vertebral fractures, which are associated with increased disability and morbidity, are the most common osteoporotic fracture. However, only about one quarter of vertebral fractures come to clinical attention [4]. Nevertheless, women with vertebral fractures have been shown to have a five-fold increase in their risk for a subsequent vertebral fracture and a two-fold increase in the likelihood of a hip fracture. One out of every five women who have an incident vertebral fracture will suffer a subsequent fracture within the following twelve months [10]. The importance of low-trauma vertebral fractures is such that both the International Osteoporosis Foundation and the National Osteoporosis Foundation in the United States agree that its presence is an indication for the need for osteoporosis treatment irrespective of BMD.

Modern fan-beam DXA devices can perform vertebral fracture assessment of the T4 to L4 vertebrae in as little as 10 seconds. This is done without film and with 1/50th of the radiation dose of a conventional X-ray. For those DXA devices with a rotating C-arm, the lateral exam can be carried out without moving the patient from the supine position. By combining VFA with BMD, the two strongest risk factors for future fracture can be obtained on the same device with little additional exam time.

The American Medical Association recently established a Current Procedural Terminology (CPT) code for DXA bone densitometers that provides imaging of the spine for vertebral fractures and the lateral scan for BMD assessment. These codes also include reimbursement for BMD with VFA.

Incidence of vertebral fractures in U.S. females vs. other diseases [7]

Incidence of osteoporotic fractures in U.S. females vs. other diseases [7]

Impact of a hip fracture on U.S. female population [9]

VFA has the potential to improve the diagnostic accuracy in identifying women who are eligible for treatment. In fact, several studies have shown that for women over the age of 65, approximately 20 to 25% have vertebral fractures that would not qualify for treatment based on BMD alone [11, 12]. These are women who are at a very high risk of fracture and should be treated, but they would have been missed if VFA testing had not been done.

Hip Structural Analysis (HSA)

HSA is a proprietary program for computing the structural properties of various cross sections of the proximal femur, using 2D DXA scans.

Developed by Prof. Thomas Beck of Johns Hopkins University, HSA algorithms are able to calculate bone strength in the two dimensions projected by the DXA scan [13]. HSA is the leading bone structure analysis method for DXA scans used in research and pharmaceutical studies and has been included in over 30 peer-reviewed articles. Its commercial availability is expected after it has received FDA approval.
3D bone imaging
The natural extension of HSA is to consider the femur as the three-dimensional object that it is, and calculate its strength in 3D. The next generation of DXA imaging for the diagnosis of osteoporosis will use the rotating C-arm feature found on some DXA devices to take multiple projections of the femur. These multiple projections will be combined to form a tomographic 3D representation of the hip. This low-dose tomographic assessment is expected to become the ultimate clinical tool for diagnosis of osteoporosis. Not only will it give a more accurate picture of bone density, but also the geometry and underlying strength of a bone.

DXA as a predictor of heart disease and stroke
The FDA recently cleared one manufacturer’s DXA system for the visualisation of abdominal aortic calcification [14], which is strongly associated with cardiovascular disease [15-17]. This new indication targets the number one cause of morbidity and mortality in older women and men, i.e. heart disease and stroke.

The risk of heart disease and stroke increases with age. They are the leading causes of death of women in America and most developed countries, with nearly 35% of all female deaths in the U.S.A. occurring from cardiovascular disease.

Abdominal Aortic Calcification (AAC) is a particularly valuable measurement since it contributes independently of traditional clinical risk factors such as cholesterol, blood pressure, diabetes and age to the prediction of heart attack risk.

As shown in the graph below, a woman suffering from moderate to severe AAC is at 2.4 times increased risk of cardiovascular heart disease, even after adjusting for age, cigarettes, diabetes mellitus, systolic pressure, left ventricular hypertrophy, Body Mass Index (BMI) and cholesterol. Detection of moderate/severe AAC is thus equivalent to the risk incurred if that patient had an additional 960 mg/dL of total cholesterol [15].

Cardiovascular Heart Disease Multivariate Adjusted Relative Risk [15]

<table>
<thead>
<tr>
<th>AAC Score</th>
<th>Relative Risk</th>
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<tbody>
<tr>
<td>Moderate/Severe</td>
<td>2.41</td>
</tr>
<tr>
<td>Diabetes Present</td>
<td>1.00</td>
</tr>
<tr>
<td>Cholesterol 40 mg/dL</td>
<td>1.00</td>
</tr>
<tr>
<td>Left Ventricular Hypertrophy Present</td>
<td>1.00</td>
</tr>
<tr>
<td>Systolic Pressure 100 mm Hg</td>
<td>1.00</td>
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AAC also has a strong and graded association with coronary calcium score as measured by electron beam CT. There was a 10-fold increase and 20-fold increase in coronary calcium score in the presence of severe AAC in men and women, respectively [18].

Evaluating DXA devices
DXA technology systems are available from several manufacturers, each with different features and capabilities. Pencil-beam DXA devices are rapidly disappearing from the marketplace, as they are typically not capable of advanced measurements such as VFA and AAC detection. Fan-beam DXA devices dominate the current market, and fan-beam DXA devices with rotating C-arms are needed for 3D measurements as well as for sites that require high throughput VFA and AAC measurements.

As long as methods of evaluating DXA devices are not yet fully developed, traditional phantom measurements for evaluating radiological devices are still relevant. These include line pair phantoms for measuring the resolution and contrast/detail phantoms (e.g. the CDRAD Contrast Detail Digital and Conventional Radiography Phantom available from Cardinal Health). Resolution, while not critical for BMD measurements, is important for VFA, AAC detection and measurements of bone structure and strength.

In addition to image quality, long-term stability of the BMD measurements is required to detect very small changes. The ISCD recommends that a Quality Control phantom (different from a calibration phantom) be scanned at least weekly to monitor stability of the BMD measurement of the device [2].

Conclusion
DXA systems have advanced beyond BMD measurements. The new DXA devices are literally changing the way physicians and scientists look at osteoporosis and how hospital administrators think about the utility of DXA devices. VFA assessment allows for early detection of fractures, and fracture risks. HSA and 3D imaging promise to provide information on bone strength and structure. Abdominal Aortic Calcification detection and body composition measurements are extending DXA’s utility outside of the osteoporosis field and addressing the important preventive health fields of cardiovascular disease and physical fitness.

References

The Author
Kevin E. Wilson, PhD, is the Scientific Director for Hologic, Inc., Bedford (MA, U.S.A.). He was instrumental in bringing to market the first ultrasound device approved by the FDA for estimating BMD, the first DXA device approved for Vertebral Fracture Assessment, and the first DXA device approved for the detection of abdominal aortic calcifications. kwilson@hologic.com