REVIEW ARTICLE

Advances in imaging approaches to fracture risk evaluation

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Fragility fractures are a growing problem worldwide, and current methods for diagnosing osteoporosis do not always identify individuals who require treatment to prevent a fracture and may misidentify those not a risk. Traditionally, fracture risk is assessed using dual-energy X-ray absorptiometry, which provides measurements of areal bone mineral density at sites prone to fracture. Recent advances in imaging show promise in adding new information that could improve the prediction of fracture risk in the clinic. As reviewed herein, advances in quantitative computed tomography (QCT) predict hip and vertebral body strength; high-resolution HR-peripheral QCT (HR-pQCT) and micromagnetic resonance imaging assess the microarchitecture of trabecular bone; quantitative ultrasound measures the modulus or tissue stiffness of cortical bone; and quantitative ultrashort echo-time MRI methods quantify the concentrations of bound water and pore water in cortical bone, which reflect a variety of mechanical properties of bone. Each of these technologies provides unique characteristics of bone and may improve fracture risk diagnoses and reduce prevalence of fractures by helping to guide treatment decisions. (Translational Research 2016;■:1–14)

Abbreviations: BMD = bone mineral density; BUA = broadband ultrasound attenuation; DXA = dual-energy x-ray absorptiometry; FRAX = fracture risk algorithm; HR-pQCT = high-resolution peripheral quantitative computed tomography; MRI = magnetic resonance imaging; MRS = magnetic resonance spectroscopy; NMR = nuclear magnetic resonance; QUI = quantitative ultrasound index; QUS = quantitative ultrasound; SI = stiffness index; SoS = speed of sound; UTE = ultrashort echo time

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Submitted for publication August 15, 2016; revision submitted September 19, 2016; accepted for publication September 27, 2016.

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1931-5244/$ - see front matter

http://dx.doi.org/10.1016/j.trsl.2016.09.006

INTRODUCTION

Bone fractures are a widespread problem that affects over 75 million people in the world, with more than 2.3 million osteoporotic fractures per year globally.[1,2] Over a lifetime, the risk of a fracture is around 40% for women in developed countries.[3] The costs associated with bone fractures were estimated to be $19 billion in 2005 in the United States alone and are projected to increase by 50% by the year 2025.[4] In the EU, costs in 2010 were estimated to be €37 billion and are expected to increase by 25% in 2025.[1] An increase in fracture risk occurs with aging for both women and men.[2,4] Fractures are a large problem

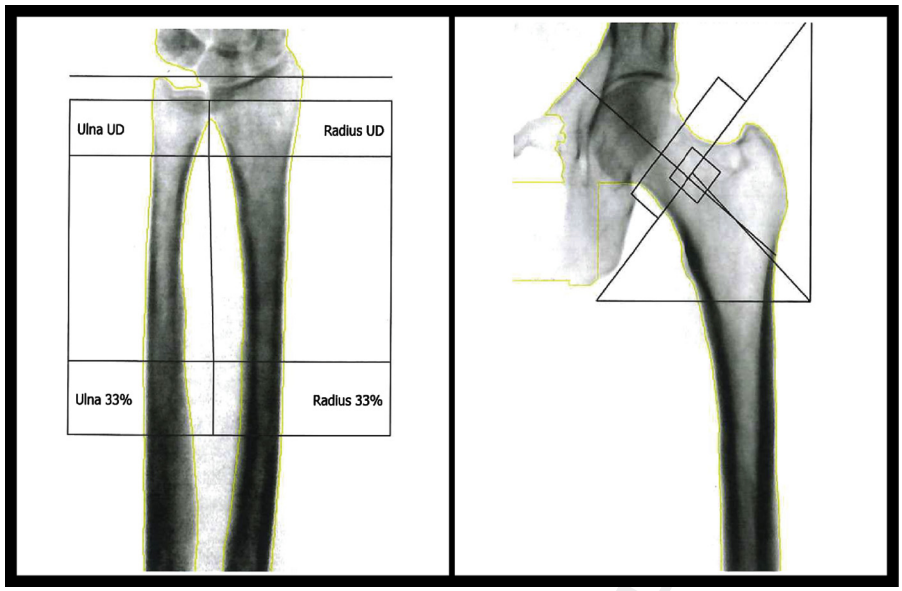

Fig 1. Representative DXA scans acquired in the forearm (left) and the hip (right). DXA, dual-energy X-ray absorptiometry.

with certain diseases and conditions, such as postmenopausal women and diabetes. Diabetes, in particular, has a rapidly increasing prevalence,[5] leading to even higher costs and an increasing need for comprehensive clinical procedures to accurately measure and diagnose fracture risk.

The most common imaging parameter used to diagnose high fracture risk is low bone mineral density (BMD) assessed by dual-energy X-ray absorptiometry (DXA) of the hip, spine, and distal radius. Examples of DXA images acquired in the radius and the hip are shown in Fig 1. DXA measures the transmission of X-ray beams through tissue at 2 different mean photon energies. The difference in dependence of X-ray attenuation on photon energy between bone mineral and soft tissues then allows for an estimate of BMD.[6] Because DXA uses 2D projection images, the resulting BMD values are areal estimates, computed in units of mineral mass per image pixel area. In clinical practice, however, DXA BMD is typically evaluated as a T-score (tabulated over a standard region of interest), defined as an individual's BMD relative to the standard deviation of BMD values of a young healthy population of the same ethnicity and sex.[7] The World Health Organization has defined osteoporosis as having a T-score lower than −2.5 or having a previous fragility fracture, and osteopenia is defined as having a T-score between −1 and −2.5.

DXA is a fast, inexpensive, and well-studied method that has very low radiation dose (5–20 μSv), but it also has many limitations. Areal BMD varies significantly based on anatomical structure, so the results are biased by bone size and orientation. Degenerative disc disease or aortic calcifications can lead to an increased apparent BMD and falsely lower apparent fracture risk,[8,9] whereas other imaging artifacts arising from excess soft tissue in obese patients or prosthetic implants in the background can also alter DXA results. In addition, DXA does not fully explain the increase in fracture risk with age[10] or diabetes.[11] Moreover, in a study of nearly 150,000 post-menopausal women (50–104 years), 82% of those that reported a fracture within 1 year had a baseline T-score greater than −2.5 (DXA at peripheral sites, namely heel, finger, or forearm).[12]

To overcome some of the limitations of DXA, it is now standard of care to consider additional risk factors in the diagnosis and treatment of osteoporosis. This is often done using algorithms that incorporate known risk factors, such as The World Health Organization's Fracture Risk Algorithm (FRAX) tool.[13] This online tool calculates the 10-year probability of a major osteoporotic fracture and of a hip fracture based on relevant risk factors (eg, age, sex, history of fracture, smoking status, alcohol consumption, and various diseases associated with high fracture) with or without hip BMD. The FRAX model is widely used in the clinic and is continuing to be expanded to include more countries. However, FRAX does not include all ethnicities or diseases, for instance type-2 diabetes, and is only designed to help guide clinical decisions. Other algorithms, such as Garvan and QFracture, have also been introduced as