MEDPACE

Q&A WITH NELSON B. WATTS

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How did you become interested in DXA imaging?

I had a long interest in osteoporosis, metabolic bone diseases and calcium abnormalities. Before bone densitometry, we could try to guess from x-rays who had osteoporosis, but an overpenetrated film would be misleading and you had to lose 30% or so of your bone mass for a standard x-ray to show "osteoprorosis." To be certain about the diagnosis, we had to wait for a fracture to occur. Bone densitometry provides a clinical tool to allow identification of patients at high risk of fracture BEFORE the first fracture occurs. It also provides assessment of severity for patients who have had fractures and is a tool for monitoring treatment.

What information does a bone density test provide and what other measurements are calculated that can be beneficial?

Regional DXA (dual-energy x-ray absorptiometry) allows measurement at the hip, spine and forearm — key sites for osteoporosis-related fractures. Although the main output is bone mineral density (bone mineral content [BMC] in grams divided by the projected area in square cm^2), Z-scores (comparing the person with norms for age, race and sex) answers the question of how this person compares with what is expected, and T-scores (comparing with young normal values) answers the question of how this person compares with what is desirable.

Tell us a little bit about the role DXA scans play in combatting osteoporosis.

I prefer to talk about "bone mineral density (BMD) measurements" rather than "DXA scans." The image is important to determine the correct regions of interest and to see if there are artifacts or local structural changes that might influence the result, but the important output is the quantification of how much material is packed into the bone space. Up to a point, the more material (or density), the stronger the bone. The term "scan" is often confused with a nuclear medicine bone scan, which is clearly not the same thing as a BMD test.

What is total body composition (TBC)?

Using dual-energy allows the quantification of the non-bone soft tissue (fat and lean). Information can be obtained about specific skeletal areas, but not as precise as regional measurements (spine, hip, and forearm) which are used for the diagnosis and management of patients. Regional BMD measurements are a common and well-accepted clinical tool. Whole-body measurements are used mainly for research (for example: obesity, cachexia/sarcopenia, and metabolic disorders) or as an option at fitness centers so changes in fat and lean mass with exercise can be tracked. By measuring the three body compartments (fat, muscle, and bone) across the entire body or body regions, we can track changes that may show potential clinical benefit such as decrease in fat mass, while maintaining muscle and bone mass.

Concerning new pharmaceuticals, what do you see as the role of DXA in clinical trials?

Reducing fracture risk is the main benefit of drugs to treat osteoporosis. Unfortunately, change in BMD does not correlate strongly with fracture risk reduction. FDA and others have been looking at surrogate markers with hopes of a pathway for drug approval that would not require a fracture end-point trial, but so far, that seems unlikely. Having said that, BMD change in Phase 2 trials is typically used to select the dose of drug used in Phase 3, and many smaller trials are conducted where BMD is the primary outcome. It's important to remember differences in BMD gains between agents does not necessarily mean that fracture reduction would be different.

What are the benefits that you see in using central assessment vs local assessment of DXA imaging in clinical trials?

Regional DXA is used for trials where bone is the main outcome of interest – BMD gains with drugs to treat osteoporosis, BMD losses with drugs that have adverse skeletal effects. Body composition is helpful for drugs or diseases that affect body composition, increasing or decreasing fat and/or lean mass. Central assessment has a potential benefit for clinical trials because they minimize variability. Besides using the same reader, it also standardizes the analysis software that is then used across all centers as well as the corresponding lookup tables of T-score and Z-score.

Looking at your publication history and the work you've done, what do you feel the future holds for DXA scanning?

DXA hasn't changed much in the 30 or so years that the technique has been available. For some time now, both dual and single-energy images have been used for vertebral fracture assessment. Newer equipment has the option of a long hip scan to look for early signs of atypical femur fracture. In response to the increasing prevalence of obesity, table weight limits have increased from around 300 pounds in the early days to 450 pounds or more today. Trabecular Bone Score (TBS) uses DXA-derived data to provide an index of microarchitecture; that information, in turn, can be useful for patients whose DXA results are at the margin of "OK" or "not OK" to better classify fracture risk. While the same standard lumbar spine acquisition can be used, this does at minimum require calibration with a TBS specific phantom for the measurements to be obtained. Overall, though, I don't see much change in the basic procedure – it's held up remarkably well.

ABOUT THE AUTHOR

Nelson B. Watts, MD, FACP, MACE, CCD, currently serves as Director of Osteoporosis and Bone Health Services for Mercy Health, an integrated health system in Cincinnati, Ohio. He has a long career in osteoporosis research at Emory University and the University of Cincinnati. He has served as President of the American College of Endocrinology, President of the International Society of Clinical Densitometry, Chair of the FDA's Advisory Committee for Endocrine and Metabolic Drugs and on the ABIM subspecialty board in Endocrinology and Metabolism. He is active in numerous professional organizations and serves on several editorial boards. He has published numerous, books, book chapters, abstracts and articles in such journals as the New England Journal of Medicine and the Journal of the American Medical Association.

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