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EDITORIAL

# Bone Mass Measurement: Which Site to Measure?

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Many unresolved issues exist regarding the early diagnosis, prevention, and treatment of osteoporosis. The development of noninvasive methods for determination of bone mass now enables physicians to estimate the bone mineral content at almost any skeletal site. Single-photon absorptiometry of the midshaft radius is the oldest and most precise method available, but this measurement is of a site not prone to osteoporotic fractures. Single-photon absorptiometry of the distal radius and dual-photon absorptiometry of the hip or spine are less precise methods, but measure sites where the most common (spine) and most serious (hip) fractures occur. Given the ill-defined constraints imposed by radiation exposure, time and cost, it would be desirable to identify a single measurement site that would enable a physician to diagnose osteopenia and monitor therapy throughout the skeleton, much in the way that the brachial artery is used in blood pressure determinations. Riis and Christiansen [1] compare spinal and radial bone mass measurements in this regard.

The main conclusion of Riis and Christiansen is that single-photon absorptiometry of the forearm is superior to dual-photon absorptiometry of the spine when either bone loss due to estrogen deficiency or estrogen replacement therapy is the focus of study, regardless of whether groups or individuals are the unit of analysis. It is critical to recognize that this conclusion is composed of four elements, each of which can be supported with varying degrees of success. These elements are: (1) that bone loss due to estrogen deficiency proceeds at approximately equal (or proportional) rates at all skeletal sites, such that strong correlations between rates of bone loss at varying sites would be observed in groups; (2) that rapid bone loss in an individual at any skeletal site would be detectable by measurements of the forearm; (3) and (4) that the effects of estrogen therapy would demonstrate the same characteristics for groups (as point 1) and individuals (as point 2) as outlined for estrogen-related bone loss.

Underlying several of the aforementioned elements is the assumption that bone mass and changes in bone mass in the radius are representative of these skeletal characteristics at other bony sites, such as the spine and hip. Although the authors refer to correlations (e.g., between changes in the proximal and distal radius) of 0.6 as "high," the implication of correlations of this magnitude is that a measurement at one site can account for approximately 36 percent of the variability ($r^2$) at another. Two related questions arise then: (1) Is the relatively small magnitude of the $r^2$ merely a result of measurement error, or (2) Do different skeletal sites behave differently with respect to rates of bone loss? It is probable that both measurement error and biologic variability contribute to the relatively small portion of the accounted-for variance. The authors cite work that emphasizes differences in the patterns of bone loss in trabecular and cortical bone [2], but fail to recognize the implications of these data. Thus, although for research protocols, where group characteristics are the outcomes of interest, single-photon absorptiometry probably offers some superior features (e.g., smaller variance-to-change ratios), this has little relevance when an individual patient is being considered. Moreover, although the authors and others have shown clearly that virtually all skeletal sites are sensitive to estrogen deficiency and its therapeutic replacement, no such data exist for other potential therapies, for example, fluoride or calcitonin.

Many of the conclusions offered by Riis and Christiansen are, however, correct. Single-photon absorptiometry of the forearm has in general been found to have better

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long-term in vivo reproducibility than dual-photon absorptiometry of the spine. The reasons for these differences in precision are probably those listed in the aforementioned discussion. However, as the authors recognize, the long-term in vivo precision for dual-photon absorptiometry that they observed is much worse than that found by others [3]. For example, the long-term (five measurements over 16 months) in vivo reproducibility for dual-photon absorptiometry of the spine at our center was 1.42 percent, a figure much lower than that found by Riis and Christiansen. Thus, although the direction of the differences in precision certainly favors single-photon absorptiometry, the magnitude of this difference is probably much smaller than indicated. Finally in this regard, recently available equipment for the measurement of spinal bone mass, using radiographic technology, appears to be of even better precision.

The authors also show that both forearm and spine measurements demonstrate the efficacy of estrogen therapy in the prevention of bone loss. This conclusion is absolutely correct, but merely reinforces many previous publications that have shown reduced bone loss in the radius [4] and in the spine, reduced incidence of vertebral deformities [5], and, most recently, reduced incidence of hip fractures [6] in those receiving therapeutic estrogens. These facts are of little relevance in assessment of the technology for several reasons. Estrogen's beneficial effects on bone are accepted and future studies are unlikely to be necessary except to examine estrogen effects in conjunction with other therapies. It is unlikely in this case that peer review will accept the Riis-Christiansen data as adequate to eliminate the need for dual-photon absorptiometry in the evaluation of other therapies.

In order to show that a single measurement would be superior to (or even an adequate substitute for) measurements at other sites, several criteria would need to be fulfilled. First, the site measured would need to adequately reflect the processes occurring at other skeletal sites *in individuals*; both this study and others show this to be untrue. Although on average there was no bone loss at any skeletal site in the estrogen group, the magnitude of the correlations between sites (even between both forearm sites) indicated that between 65 percent and 85 percent of the variance in bone loss could not be accounted for by measurements of other sites. Second, absolute bone mass, the factor most likely to relate to fracture risk, would need to be highly correlated between sites; these correlations are generally better than those between rates of loss. Although not mentioned in the Riis-Christiansen article, others have reported correlations with single-photon absorptiometry of the radius on the order of 0.4 to 0.6 with the spine, 0.7 to 0.9 with the hip, and 0.6 to 0.8 with the total skeleton [7]. Thus, although the information ($r^2$ = 16 to 80 percent) contained in these data generally exceeds that for bone loss, it is less than perfect, suggesting that measurements at the site of primary interest are probably necessary. Finally, attention must be given to the interventions under consideration. Although the authors make it clear that this study applies to estrogen therapy, which is expected to have systemic effects, other interventions may not be expected to behave this same way. For example, exercise programs may only affect sites stressed by muscular contractions, calcitonin may only be effective at sites with high turnover, and the effects of sodium fluoride are probably much different in the spine than in the long bones.

Several other issues are only hinted at by the authors, but require further consideration. For example, can single- or dual-photon absorptiometry be used to follow the effects of therapy in individuals? Although Riis and Christiansen show that the variance of change in bone mass is much smaller for single-photon absorptiometry than for dual-photon absorptiometry, this does not necessarily imply that single-photon absorptiometry is adequate to follow the effects of therapy in individuals. As has been pointed out by Heaney [8], even when the precision is quite good (as with single-photon absorptiometry), the confidence intervals around the changes in bone mass are broad. The evaluation of estrogen therapy involves the monitoring of potential ill effects and the alterations in mineral metabolism. It is plausible, but untested, that serum concentration of osteocalcin or bone-specific alkaline phosphatase may provide efficient estimates of changes in skeletal metabolism. Establishing the effectiveness of estrogen therapy in the short term (one year or less) for an individual may be beyond the precision of either single- or dual-photon absorptiometry, and thus the "superiority" of single-photon absorptiometry in this application is moot.

Within the narrow application of estrogen therapy to changes in bone mass in groups, single-photon absorptiometry is, as Riis and Christiansen demonstrate, more efficient. But its use for individuals, for other therapies, and for monitoring therapy is less certain.

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