

## The Utility of Single-Photon Absorptiometry and Dual-Energy X-ray Absorptiometry

Two decades ago researchers at the University of Wisconsin showed that  $^{125}\text{I}$  photon absorptiometry could be used to measure bone mineral in the forearm easily and accurately with little radiation exposure (1). Surrounding the arm with water or other soft tissue-equivalent material of constant thickness provided uniform extra-skeletal attenuation; the incremental attenuation by bones was linearly related to their dry weight and ash weight. Marrow fat, because it is not water-equivalent, caused the instrument to underestimate bone mineral, but empirical study showed that these errors were less than 10% (2). To compensate for differences in bone size, the measurements of bone mineral were divided by the bone width to give a ratio ( $\text{g}/\text{cm}^2$ ) known in this field as "bone density." Correction for bone width narrows the normal range in population surveys and "density" is therefore used for diagnosis instead of bone mineral. Subsequent commercial development automated the data analysis and substituted digital computer techniques to improve precision, but did not alter the basic conceptual design.

These  $^{125}\text{I}$ -based instruments (now known as single-photon absorptiometers or SPA) have been widely used for many years and their medical utility is well established. Prospective follow-up studies in Sweden, Indiana, and Hawaii (3-5) have shown that SPA measurements can identify elderly women at particular risk of fractures, and this has been confirmed by a U.S. multi-center trial involving follow-up of approximately 9,000 elderly women (6). The Swedish study (3) showed that the technique has equal predictive power in women aged 50-59 (younger than those in the other studies). The predictive power extends to hip fractures (6) and to men (7). The U.S. multi-center trial showed that SPA forearm measurement are as good as SPA heel or dual-energy x-ray absorptiometry (DEXA) spine or hip measurements for predicting future total fractures in elderly women (8).

The information content of bone density measurements can be expressed quantitatively by comparing the results to those obtained in healthy young adults, or age-matched adults, of the same sex. The former comparison defines whether a person has osteopenia. The latter defines a person's future fracture risk, relative to a cohort of the same age and sex. An American woman aged 65 or older has a 30%-40% increase in fracture risk if her forearm bone density is one standard deviation below the age- and sex-adjusted mean, a 60%-80% increase in risk if her test results are two standard deviations below the mean, etc. (8). Quantitative estimates of future fracture risk in men and younger women must be extrapolated from the studies in Sweden, which show a steep increase in fracture risk for every decrement in bone density. This relationship is steep and linear without any fracture threshold in Swedish men and women aged 50-70. It was difficult to establish such a relationship in Swedes older than 70.

Though arm, heel, spine, and hip measurements are equally good at predicting *total* fractures, measurements in a specific bone are probably the best predictor of future fractures in that same bone, because a bone's strength is highly correlated with its own mineral density, but less well correlated with the density of bones elsewhere in the body. This plausible argument has been confirmed by recent unpublished results from the U.S. multi-center trial: for the prediction of hip fractures in elderly women, hip densitometry is slightly but significantly superior to forearm, spine, or heel densitometry (8). The best predictor of future vertebral fractures has not yet been determined by prospective studies, but spine measurements are the winner in cross-sectional comparisons of vertebral crush fracture victims versus age- and sex-matched controls. The measurements that are optimum in patients with hyperparathyroidism differ from those listed above. In that disease, cortical bone is lost earlier than trabecular bone, and forearm diaphyseal osteopenia is initially worse than spinal osteopenia. This pattern is the reverse of that found in all other common forms of osteopenia (11,12).

In a recent issue of the *Journal*, Larcos and Wahner (9) showed that SPA and DEXA measurements of forearm bone mineral are tightly correlated ( $r = 0.99$ ) over the clinically-important range of measurements. Bone "density" (area-corrected mineral) measurements are not quite so highly correlated ( $r = 0.95$ ). These results must be confirmed in a larger group of people, but suggest that measurements of the forearm with DEXA or SPA provide equivalent diagnostic information.

In addition to early diagnoses of osteopenia, bone density measurements can also monitor bone loss and treatment. Because most osteopenic diseases evolve slowly, measurements must be exceptionally reproducible to be clinically useful. Forearm bone mineral loss in early postmenopausal women averages only 2%-3% per year. To decide whether

Received Sept. 20, 1991; revision accepted Sept. 25, 1991.

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treatment is arresting such loss, based on measurements 12 mo apart, each measurement must have an uncertainty (measurement reproducibility) of less than 1%. Most quantitative measurements used in clinical medicine have a reproducibility of 3%–5%: for radioimmunoassays these variations are often 7%–15%.

The reproducibility of SPA and DEXA measurements is limited by anatomy. Bone width and thickness vary every few millimeters proximal or distal along the forearm, and with them bone mass. SPA and DEXA can compensate for variations in bone width, but not for variations in bone thickness. The reproducibility of forearm SPA and DEXA measurements therefore depends upon the ability to reproduce exactly the location of the measurement. It is necessary to control also the pronation/supination of the forearm, since rotation of the bones alters their thickness in the path of the measuring photon beam. The DEXA instrument evaluated by Larcos and Wahner measures the entire forearm and generates a digital radiogram of it. This image can be used to define reproducibly a region of interest to be used for the bone density measurement. SPA measurements do not generate an image. They are positioned over a skin mark whose position has been previously defined by surface measurements with a ruler. Alternatively, the region of interest for SPA measurements can be defined by the distance separating the radius and ulna. Either alternative seems less reproducible, *a priori*, than positioning based on a digital radiograph. However, Larcos and Wahner found no difference in the short-term (same-day) reproducibility of the two methods (1.5%–1.7% for DEXA versus 1%–2% for SPA in an earlier study from their unit). This disappointing result suggests that DEXA offers no advantages over SPA for forearm bone densitometry (except lower operating costs). Furthermore, serial DEXA forearm measurements are not reproducible enough to evaluate therapy in individual patients with post-menopausal osteoporosis. Further work is needed to confirm this result, including a study with serial measurements of the same patients by SPA and DEXA in parallel. This is particularly important because other investigators have claimed that measurements of forearm bone mineral density with the same DEXA instrument have 0.6%–1.0% reproducibility, which is good enough for serial evaluations of individual patients (10).

Early diagnosis and precise monitoring of osteopenia are medically useful only if treatments exist to arrest or reverse bone loss. Bone loss caused by deficiency of androgens, estrogens, vitamin D metabolites, or excess of parathyroid hormone, glucocorticoids, or thyroid hormones, can all be treated successfully. Post-menopausal bone loss can be arrested by treatment with estrogens and progestins, or salmon calcitonin given by nasal spray. Thus, millions of women and men have bone diseases whose presymptomatic diagnoses can be greatly facilitated by DEXA or SPA measurements. It is not yet clear that these measurements can also be used successfully to follow the treatment of individual patients.

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