

# Role of Bone Quality in Osteoporosis Gets Clearer

BY KERRI WACHTER  
Senior Writer

NEW ORLEANS — Of all the factors that contribute to bone strength, the rate of turnover may be most clinically relevant, David Dempster, Ph.D., said at the annual meeting of the International Society for Clinical Densitometry.

At the same time, several recent advances may soon transform the way bone is assessed.

Bone turnover affects each and every one of the other variables that factor into bone strength, including structural factors and material properties, said Dr. Dempster, professor of clinical pathology at Columbia University, New York.

High bone turnover increases remodeling space, accelerates bone loss, disrupts the trabecular microarchitecture, increases mechanical stress concentration, decreases mineralization density, and increases cortical porosity—each of which can undermine the strength of the bone, Dr. Dempster explained.

When osteoclast activity exceeds osteoblast activity, there's a deficit on the surface of the trabeculae and within the cortex. "This may not amount to much in terms of bone mass ... but I think that a small amount of missing bone may be important."

As bone mass declines, there is an exponential increase in fracture risk. "Simply by preventing a small amount of bone loss, you will prevent that patient from going up a steep slope in terms of fracture risk," Dr. Dempster said.

Another consequence of high

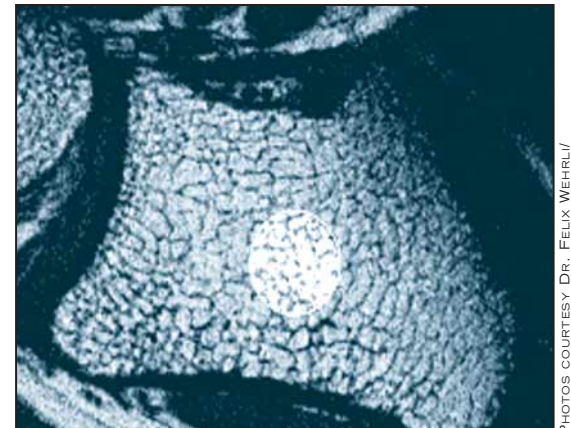
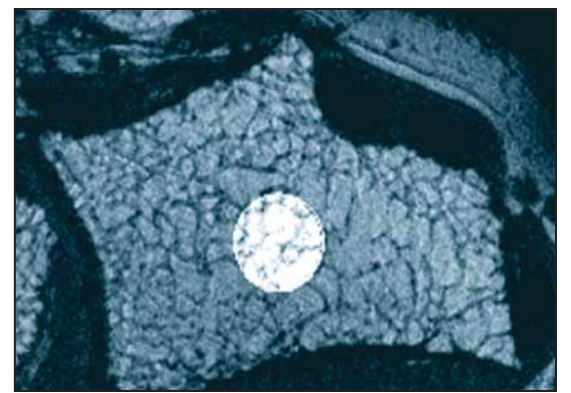
turnover is the increase in the destruction of the trabecular microarchitecture. As bone turnover increases, there is a preferential loss of the horizontal trabeculae known as cross-ties, Dr. Dempster said.

"I'm talking about high turnover in a catabolic sense ... where resorption exceeds formation." This type of turnover occurs shortly after menopause or shortly after the introduction of glucocorticoids, said Dr. Dempster, who is also the director of the Regional Bone Center at the Helen Hayes Hospital in West Haverstraw, N.Y.

After menopause, a confluence of three phenomena can occur: a greater number of osteoclasts gather on the bone surface, osteoclasts become more efficient at breaking bone down, and the plates may become thinner. The result is that instead of sweeping across the trabecular surface—as with normal bone turnover—the osteoclasts tend to penetrate through the trabecular plate, leaving osteoblasts without a template for creating new bone. Supportive horizontal trabecular rods eventually become disconnected.

Mechanical stress concentration is another important element of bone strength. Osteoclast resorption cavities are the mechanical stress points. Without these cavities, intact trabeculae bend in response to stress but do not break. When resorption cavities are present, the same force will cause the trabeculae to break.

With high bone turnover, mineral density declines. While measuring bone mineral density (BMD) captures large-scale in-



The BMD scores for patient A (top) and patient B (bottom) are identical. But three-dimensional composites of the area from which structural biomarkers are derived (left) and axial MRI slices of the distal radius (right) reveal that patient A requires aggressive treatment, while patient B does not.

formation on mineralization density, it doesn't provide information on the local distribution of minerals. Nor do conventional BMD measures provide information on the collagen-to-mineral ratio. Too much mineral makes bones brittle; too much collagen makes them weak.

So far, markers of bone turnover have been shown to be useful in the research setting, but they aren't ready for clinical use. Still, once they are ready, "I think that a BMD test coupled with a good measure of bone turnover in an individual patient would give you much more informa-

tion than you currently have," Dr. Dempster said.

Improvements to turnover measurement are imminent, as more of these tests are incorporated into auto-analyzer formats. In addition, progress is being made in defining what the normal premenopausal range is for these markers.

"We [also] have some very good research going on looking at how we can assess microarchitecture noninvasively," he said. Quantitative CT is starting to be used to assess bone strength in hip structural analysis. This technique not only mea-

sures BMD but it also assesses the structural geometry of cross-sections at specific locations of the hip. The evaluation of bone microarchitecture has benefited from the use of new techniques such as peripheral quantitative CT and high-resolution micro MRI.

In the past, bone microarchitecture has been hampered by the need to extract bone samples from volunteers and look at these samples under a powerful microscope. These new technologies give researchers an easier way to study a larger pool of volunteers. ■

## Study Shows BMD Screening Reduces Incidence of Hip Fractures

BY KATE JOHNSON  
Montreal Bureau

Bone density screening was associated with fewer hip fractures compared with usual medical care in a study of more than 3,000 adults aged 65 and older.

"Although some groups recommend screening, no study had proved that screening prevents fractures. Our study provides new evidence for the effectiveness of osteoporosis screening," lead researcher Lisa M. Kern, M.D., of Cornell University, New York, said in a statement.

"We believe that our study is the first to measure and find a direct link between screening for osteoporosis and fewer incident hip fractures," the researchers said. But because the study was not randomized, "the observed relationship between screening and hip fracture could be diminished by a small unmeasured con-

founder," they noted (*Ann. Intern. Med.* 2005;142:173-81).

The study included 3,107 participants in the larger Cardiovascular Health Study (CHS). Participants were assigned to a study arm based on the state where they resided.

In one arm, 1,422 participants from California and Pennsylvania were offered osteoporosis screening using dual-energy x-ray absorptiometry (DXA) at the hip. Both the participants and their primary care providers were given a graph showing the results of their bone scan in relation to the normal range of bone mineral density (BMD). The graph did not label the participants as normal, osteopenic or osteoporotic and did not recommend any particular intervention.

In the other arm, 1,685 participants in Maryland and North Carolina received usual medical care.

The participants were followed for 6

years from the time of their BMD scan, or if they did not receive a scan, from the date of their annual appointment as a CHS participant. They were observed until one of the following events occurred: a hip fracture, death, loss to follow-up, or end of the surveillance period.

Compared with usual care, osteoporosis screening was associated with a statistically significant reduction in the risk of hip fracture. The incidence of fractures per 1,000 person-years was 4.8 in the screened group (total 33) and 8.2 in the usual care group (total 69), linking screening to a 36% reduction in hip fractures.

The largest benefit for screening was in participants aged 85 years and older. "If this result is replicated in other studies, it suggests that guidelines should not set an upper age limit for osteoporosis screening among ambulatory adults," the researchers wrote.

While acknowledging that the mechanism of the association between screening and a reduction in fractures is unclear, the authors offered several possible explanations. They found limited evidence that screening may have led to interventions for low bone density. A total of 33% of participants who were offered screening had a BMD below the age-matched mean, and these participants were more likely to start using calcium or bisphosphonates in the year after screening, compared with participants whose bone densities were above average. In addition, more screened than nonscreened participants began using multivitamins.

In addition, a smaller percentage of the screened group had falls in the year after screening, compared with the nonscreened group (16% vs. 20%, respectively), although no information on fall prevention was collected. ■