Advanced Hip Assessment

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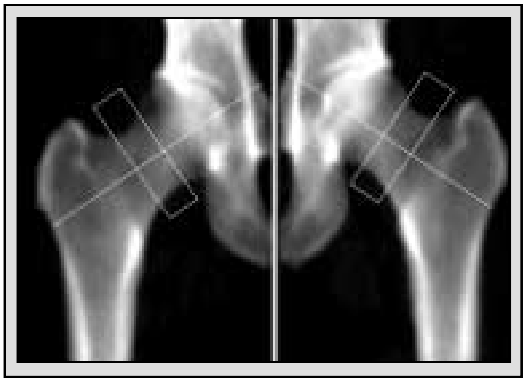


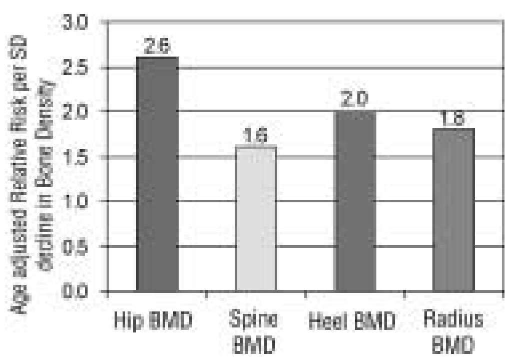
Hip fractures represent the most serious consequence of osteoporosis. In the United States, one out of every six Caucasian women will suffer a hip fracture during her lifetime; 20-25% of these women will die as a result. Among the survivors of hip fracture, half of the patients are unable to resume normal activity for at least a year after their injury, often requiring long-term health care.

For the assessment of hip fracture risk, a femoral bone density measurement is the preferred clinical measurement.

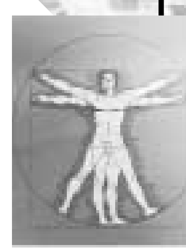
Yet since the introduction of central bone density systems in the 1980s, little progress has been made in the analysis of the proximal femur scan. The femoral neck region, first introduced in the days of dual photon absorptiometry (DPA) systems, remains the default region almost 20 years later. The total hip, trochanteric, shaft, and Ward's area are also essentially unchanged.

Femoral bone densitometry has been the center of several important advances since the 1980s:

- *Multiple prospective studies have shown that hip density measurements are the best predictor of hip fracture in elderly Caucasian women*
- *Several new drugs have been cleared by the FDA that increase femoral bone density and reduce hip fractures*
- *Researchers have published articles examining the utility of measuring both hips, the relative importance of the different femoral regions, and the use of new femoral BMD measurements*
- *Geometric measurements derived from proximal femur DXA scans have been reported, including hip axis length*
- *Advances in x-ray tubes and detectors have had a significant impact on measurement speed and precision*



SCIENCE — in bone densitometry



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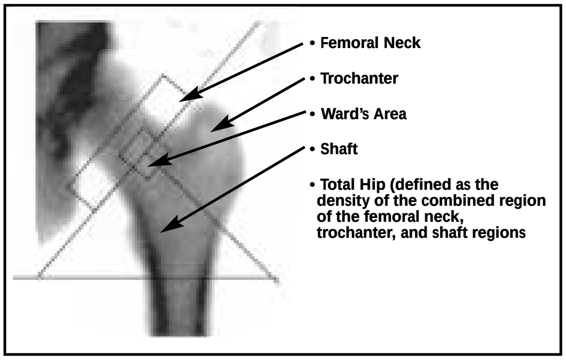
Advanced Hip Assessment

A new software package called Advanced Hip Assessment, developed for GE Lunar densitometers, provides the first major advance in femoral densitometry analysis since the introduction of DXA in 1987.

Advanced Hip Assessment includes all the standard femoral regions of interest that have previously been available:

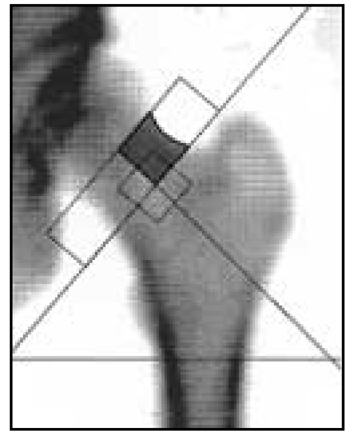


Advanced Hip Assessment goes beyond the standard femoral DXA analysis to include:

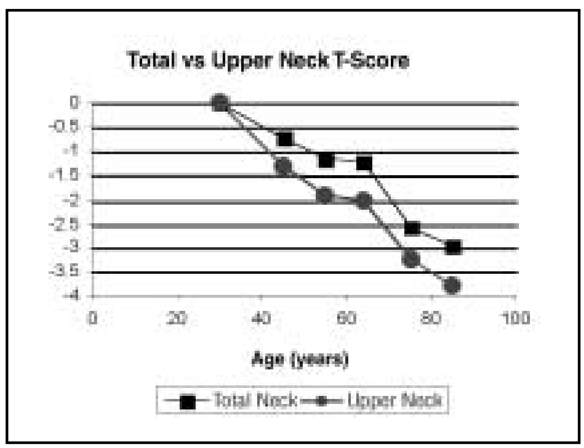
- **Measurement of the new regions of interest, including upper femoral neck.**
- **Automated determination of hip axis length**
- **Sequential measurement of both hips**
- **Improved precision**

Enhanced Measurement Regions

The standard femoral measurement regions have remained largely unchanged since the introduction of bone densitometry. They were based on attempts to localize the bone density at the fracture prone areas of the femur, such as the cervical neck, the trochanter, and the shaft region. At the time that these regions were derived, prospective studies comparing hip density to fracture risk had not been performed. These regions were developed based on clinical experience, comparison to experiments in excised bones, and intuition. The structure of the proximal femur is particularly suited to a regional analysis. The primary tensile trabeculae, which run the length of the upper femoral neck, are thought to be important to bone strength. To aid in the research in this area, an upper femoral neck region is now available using the enhanced resolution and edge detection capabilities of the Advanced Hip Assessment system.



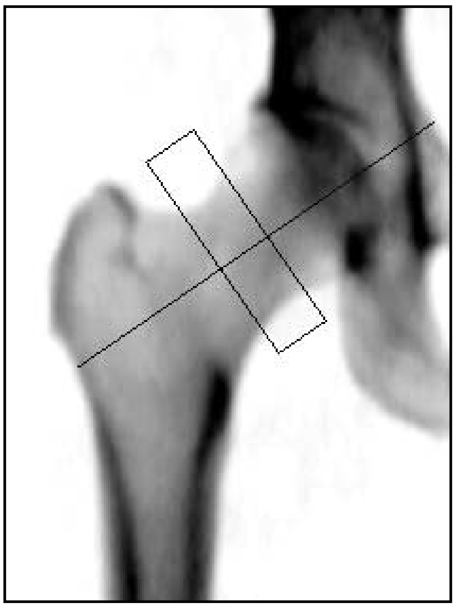
The upper portion of the femoral neck has been reported to be a sensitive predictor of neck fractures, even in patients where the lower femoral neck is not different from controls. Studies have demonstrated that the femoral fractures usually are initiated in the upper neck region. The thickness and porosity of the bone in the upper neck region is believed to be critical to maintaining femoral strength. The upper neck demonstrates a more rapid age related decline than the standard femoral neck region, suggesting it may provide some advantage for the early detection of osteoporosis.



Geometric Measurements

The single best predictor of hip fracture is femoral bone density. But bone density is not the sole factor influencing whether or not a fracture will occur. According to engineering principles, strength depends on (1) the mechanical properties of the materials, (2) the object's geometry and shape, and (3) the loading conditions, in terms of magnitude, rate, and direction, of force applied to the object. If the geometry of the hip is related to fracture risk, geometric measurements might be used together with densitometric measurements for a better assessment of hip fracture risk than might be obtained from just a density measurement alone.

Based on this premise, several researchers have derived geometric measurements from DXA images of the hip. These include the hip axis



length, the femoral neck length (the segment of the hip axis length which extends only to the femoral head), femoral neck width, and the neck/shaft angle. Of these, the hip axis length (HAL) has been the most thoroughly studied and shown the most promising results for assessing hip fracture risk.

HAL has been demonstrated in several prospective studies to predict fractures.

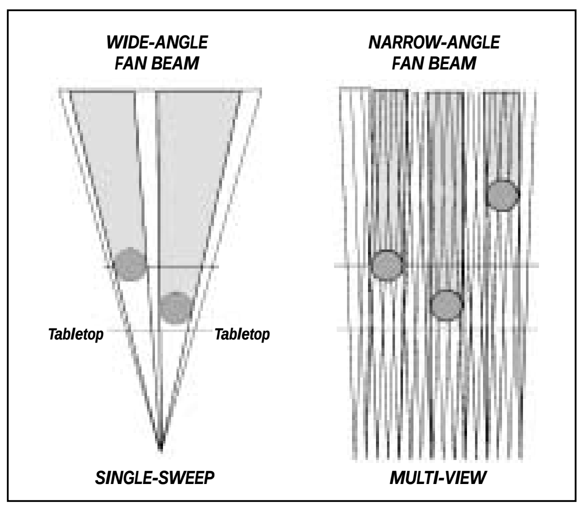
Each centimeter (10%) increase in HAL increases hip fracture risk by 50-80%, depending on the study[1-21]. For short-term prediction of hip fracture (within 2 years), HAL was shown to predict hip fractures independent of BMD. The use of HAL for predicting long-term fracture risk (more than 2 years) remains to be determined.

As one might expect, HAL is related to height, with taller patients typically having longer HAL values. HAL is also weakly correlated with body weight. Thus HAL is best used when corrected for both height and weight.

Most of the previous studies with HAL were performed on pencil beam systems that are not susceptible to magnification error. Use of wide-angle fan beams will cause geometric distortions and variations in HAL.

Wide-angle fan beam systems are subject to inaccuracies associated with magnification.

When measured on these fanbeam systems, HAL must be carefully corrected for varying height of the femur off the table. When using narrow fanbeam systems with multi-view image reconstruction (such as the GE Lunar Prodigy), HAL can be measured accurately without any adverse influence of elevation off the table. Precision error of HAL on the Prodigy was 0.7%.



Additional measures of femoral geometry, such as femoral neck length, neck width, or neck shaft angle, have been reported in a few studies. Many of these studies were based on radiographs, and few provided positive evidence for these measurements for predicting hip fracture from DXA images.

Of the various geometric measurements that have been studied, HAL represents the best candidate for clinical use. While HAL cannot be viewed as a stand-alone clinical predictor, it can potentially provide utility in conjunction with BMD to identify high-risk patients. Based on the available data, elderly Caucasian women with height and weight adjusted HAL of above 12 cm would be 80% higher risk than those with an average HAL (10.5 cm). The use of HAL in younger women (under 65), men, and non-Caucasians has not yet been studied. The ultimate clinical utility of a HAL measurement remains to be determined. By including the measurement in the Advanced Hip Assessment package, the clinical utility of the measurement can be more easily investigated.

Dual Femur

Left and right femur measurements are highly correlated. This has been shown in several studies comparing the measurements. For clinical use, the relevant question is how often will a difference between the left and right femur change either the diagnosis or management of an individual patient.

Studies have confirmed an average BMD difference between left and right femora is negligible. However, the standard error between the two measurements is 0.05 g/cm^2 at the total hip and femoral neck. In other words, if only one hip is measured, the other hip will differ by an average of +0.05 g/cm^2. For patients with T-scores approaching the NOF or WHO guidelines for osteoporosis, the potential for misclassification becomes significant. For example, if the left hip is measured and found to have a femoral neck T-score of –1.8, there is a 34% chance that the opposite femoral neck will be –2.0 or less, and an 8% chance that it will be –2.5 or less.

In situations where the T-score at one hip is within 0.5 standard deviations of the level considered to be at risk, the use of the second hip measurement can be important. Dual Femur provides this information with little additional scan time and preparation.

"Measurement of both hips greatly reduces precision error and facilitates the evaluation of skeletal response at the femur."

Improved Precision

When DXA was introduced in 1987, significant advances in precision were seen compared to isotope based DPA systems. These advances were due primarily to increased radiation flux and improved analysis software. Increased radiation flux reduces precision error by increasing the size of the signal at the radiation detector. By increasing the signal, and maintaining an equivalent noise level in the detector system, the signal to noise ratio increases and precision error goes down. Enhanced analysis software reduces precision error by reproducibly detecting bone edges and minimizing variations as bone density and positioning change from scan to scan.

In the Advanced Hip Assessment System, additional enhancements in photon flux, coupled with the improved detector efficiency of Prodigy, have improved precision even more. The greater dynamic range of the digital detector system can handle a much larger range of tissue density and is comparatively insensitive

T-score	0.0	-0.5	-1.0	-1.5	-1.6	-1.7	-1.8	-1.9	-2.0	-2.1	-2.2	-2.3	-2.4
% missed at -2.0	0.0%	0.1%	2.3%	15.9%	21.2%	27.4%	34.5%	42.1%					
% missed at -2.5	0.0%	0.0%	0.1%	2.3%	3.6%	5.5%	8.1%	11.5%	15.9%	21.2%	27.4%	34.5%	42.1%

to air in the scan field. Use of tissue equivalent materials (rice bags) to pad around the hip of thin patients is no longer necessary. The result is a dramatic improvement in precision for both the single and Dual Femur measurement as shown below.

	Single Femur		Dual Femur	
	SD (g/cm²)	%CV	SD (g/cm²)	%CV
Neck	0.013	1.27%	0.008	0.77%
Wards	0.011	1.29%	0.009	1.01%
Trochanter	0.013	1.50%	0.009	1.03%
Total Femur	0.010	0.94%	0.006	0.60%
Upper Neck	0.014	1.56%	0.011	1.17%

Precision determined in 20 volunteers with a mean age of 40 years. Each subject was measured 5 times. Precision is expressed as the root mean square standard deviation (SD) and coefficient of variation (%CV).

With the advances in precision obtained in the Advanced Hip Assessment system, it is now feasible to use the femur for monitoring therapeutic response. The combination of improved precision with the Dual Femur measurement provides a further improvement in precision and reduction in the least significant change.

The Dual Femur BMD (average of L/R) provides an additional 30-40% improvement in precision compared to a single femur measurement.

Data from clinical studies confirm that the use of Advanced Hip Assessment with the Dual Femur option is almost as sensitive as a spine BMD measurement for assessing response to anti-resorptive therapy. The table below shows the average time needed to detect a change in BMD for a treatment increasing BMD 5% per year at the spine and 3% per year at the femur using the spine measurement, and single hip measurement, and Dual Femur with Advanced Hip Assessment.

With the improved precision offered by Advanced Hip Assessment, combined with a Dual Femur measurement, sensitivity to femoral change approaches that of the spine. In elderly patients, where spinal degenerations can mask the true bone density, the femoral measurement can provide a significant advantage for assessing both the bone density changes and reductions in fracture risk associated with therapy.

	Expected Change per Year	Percision Error	Least Significant Change (95% Confidence)	Minimum Time needed to detect Significant Change
Spine	**5%**	**1.0%**	**2.8%**	**7 Months**
Single Femur (Neck Region)	**3%**	**1.3%**	**3.6%**	**15 Months**
Dual Femur (average of Neck Regions)	**3%**	**0.8%**	**2.2%**	**9 Months**

Conclusions

Advanced Hip Assessment combines several advances in DXA measurement of the proximal femur into a single software package. It maintains the conventional femoral regions of interest, but with a precision previously obtained only at the spine. This feature alone represents a significant advance in femoral densitometry.

For those interested in more advanced applications, the software incorporates several unique features, including upper neck region of interest, automated hip axis length measurement, and sequential Dual Femur measurement. ***Upper neck BMD and hip axis length are new additions to the conventional femoral measurements, and both have been reported to be associated with hip fractures.*** *Dual Femur enables a rapid assessment of both hips, which is of importance in those with T-scores approaching, yet not yet reaching, diagnostic or therapeutic thresholds.*

Dual Femur reduces precision error compared to a single femur measurement, yielding precision errors less than observed at the spine. *With this decrease in precision error, monitoring of bone changes is now possible at the femur with utility comparable to the spine.*

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