Omnisense or DXA

An In-Depth Comparison

Introduction

The following document summarizes a series of clinical studies conducted to compare Sunlight Omnisense™ technology and Dual X-ray Absorptiometry (DXA) technology. These studies consistently show that Omnisense provides an accurate aid to physicians in the diagnosis of osteoporosis and can serve as a viable alternative to radiation-based technologies.

It is important to note that a comparison between a *Quantitative Ultrasound* (QUS) device – Omnisense - and a *Dual X-ray Absorptiometry* (DXA) device is complex. The Omnisense and DXA devices are based on two distinctly different technologies and measure two different parameters; *Speed of Sound* (SOS) and *Bone Mineral Density* (BMD).

However, since the diagnosis of Osteoporosis concerns ***assessment of fracture risk*** – and not assessment of bone mass – there is, indeed, a basis for comparison. In order to compare the two technologies, one must evaluate each device's ability to assess fracture risk, along with their relative advantages and disadvantages.

This document presents data that show Omnisense measurements to be a valid estimate of osteoporotic fracture risk. Hence, Omnisense SOS measurements have profound clinical value that, in many cases, may even be considered superior to that of DXA.

Sunlight

During the last two decades, DXA has been used extensively, and has been accepted as a standard for assessment of fracture risk. However, it is neither a perfect technology nor is it without controversy. The following are a few of the many limitations of the technology and the problems associated with its diagnostic capabilities:

- ***BMD discriminatory ability for fractures is not very high:***
  Research has shown that there is a large overlap between Bone Mineral Density (BMD) measurements of non-fractured subjects and measurements of fractured subjects. This implies that low-trauma fractures can occur at *low, normal* or even *high* BMD. This research further suggests that factors other than BMD may be significant in the occurrence of fracture.[1]

- ***Accuracy errors, especially in the case of Lumbar Spine BMD:***
  After the age of 60, false high values of spine BMD are encountered. This may occur due to various other diseases, such as vascular calcification, osteomalacia and osteoarthritis. These false high measurements may lead to a misdiagnosis (false negative), and consequently to an incorrect decision regarding treatment.

- ***BMD is not a valid measure of bone strength:***
  BMD is a crude expression of bone mineral concentration for a given area. It does not take into account such properties as bone size or architecture. BMD is also influenced by body mass and growth, while the measurement of true density should not be influenced by these factors [2,3].

- ***Problems of reproducibility (precision):***
  In order to monitor bone changes following treatment, as well as over time, it is essential that a diagnostic tool have the lowest precision error possible. Unfortunately, DXA technology is unable to ensure an adequate degree of precision. For example, a patient's position during a DXA hip measurement, may be at a slightly different angle –thus causing the marking of a different *Region of Interest* (ROI) between one exam and the next.

- ***Discrepancies between different devices of the same brand:***
  There is a significant degree of variability between one DXA device and another. This is so even when the devices are of the same type and by the same manufacturer[4]. Thus implying that when a patient undergoes follow up testing for monitoring purposes, the results, if not taken on the exact same device, must be referred to with caution. It has also been found that accuracy errors sometimes occur following a repair. These errors can be difficult to detect even when using the routine recommended operating procedures[5]. Moreover, in the case of a new model even of the same brand, there is normally no backward compatibility.

The Omnisense Solution

1. Omnisense SOS is more informative than DXA BMD

"Osteoporosis is a systemic skeletal disease, characterized by reduced bone mass and micro architectural deterioration of bone tissue. Consequently, the disease increases bone fragility and susceptibility to fracture, typically at the Hip, Spine, and Wrist[6]".

Traditional Dual X-ray Absorptiometry is limited to measuring one property only, *Bone Mineral Density* (BMD) also known as Bone Mass. Conversely, *Speed of Sound* (SOS) measurements give a much broader perspective. SOS measurements reflect several varied bone properties such as; density, elasticity, cortical thickness and micro-architecture, thus providing a more complete picture of the bone's fragility[7, 20].

2. Diagnostic ability

The Omnisense's ability for diagnosis and fracture prediction was tested and evaluated in *in-vivo* and *in vitro* studies.[8, 10, 11, 14, 15, 21] All studies concluded that Omnisense's measurements of the distal 1/3 radius are a reliable predictor of fractures. In addition, measurements at the radius by Omnisense could predict any type of osteoporotic fracture equal to or better than Dual X-ray Absorptiometry.
A summary of these studies is presented below.

- ***Omnisense can predict hip fractures***
  An *in vitro* study of the ability of ultrasound velocity measurements at the radius, phalanx and femur to predict the failure load of elderly cadaveric femura was performed in the Orthopedic Biometrics Laboratory, Beth Israel Deaconess Medical Center, Boston MA[8]. A high correlation was observed between femoral failure load and femur BMD measurements ($r=0.83$, $p<0.001$) as well as with SOS measured at the distal 1/3 radius using the Omnisense ($r=0.73$, $p=0.008$). Velocity at the radius, correlated significantly with trochanteric BMD ($r=0.59$, $p=0.03$). It was concluded that velocity measurements at the radius are potentially useful predictors of femoral failure loads.

- ***Fracture discrimination by Omnisense***
  Knapp, *et al.*, at the Osteoporosis Unit of the Guy's Hospital and the Twin and Genetic Epidemiology Unit of the St. Thomas Hospital in London, UK, report the results of vertebral and wrist fracture discrimination in two different studies[10, 11]. The Omnisense's ability to discriminate vertebral fractures was compared to that of conventional DXA of the hip and spine. The measurements at the radius were found to have similar differentiation power

to those of DXA of the spine. Results from the second study suggest that the Omnisense SOS measurements of the radius are equal to or superior than DXA in predicting wrist fracture patients from controls (odds ratio of 2.4; 95% C.I. 1.2-5.0, compared to odds ratio <2.0 of DXA of L1-4, neck of femur and total hip).

3. Omnisense displays better sensitivity than DXA

Due to the nature of the disease, no absolute test has been developed to determine the presence of osteoporosis in the case of a specific patient. The only indisputable clinical evidence for diagnosing osteoporosis is the presence of a low traumatic or a traumatic fracture.

The following classification study was based on the above concept: A group of individuals, diagnosed with osteoporosis as determined by the presence of an atraumatic fracture, was measured by both DXA and Omnisense. This approach was used as a definitive method to evaluate the sensitivity of each device. To make this determination, the researchers looked at the percentage of subjects who were **actually classified** as Osteoporotic, according to the WHO criteria (T-score < -2.5). A "normal" result (T-score>-1) would of course mean a misdiagnosis (false negative). (see 'red bars' Figure 1)

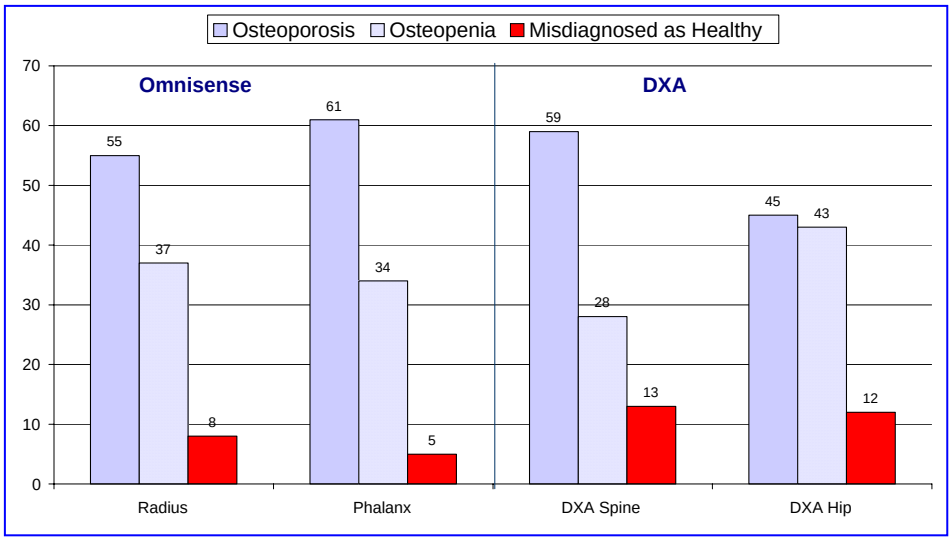

Figure 1: Study results for 150 fractured individuals, classified according to the WHO criteria

Omnisense classified a higher percentage of osteoporotic individuals as osteoporotic or osteopenic than DXA. Conversely, DXA had a higher rate of misdiagnosis.

- ***Omnisense's Reference Database demonstrates WHO criteria applicability***

  The following chart presents a comparison of Omnisense and other diagnostic devices' Reference Data curves, in terms of T-scores. Omnisense's Reference database demonstrates that "SOS curves of the RAD and PLX expressed as T-scores cross the T=-2.5 level close to age of 75. This T-score value is the WHO threshold for osteoporosis diagnosed by BMD measured at any site"[9].

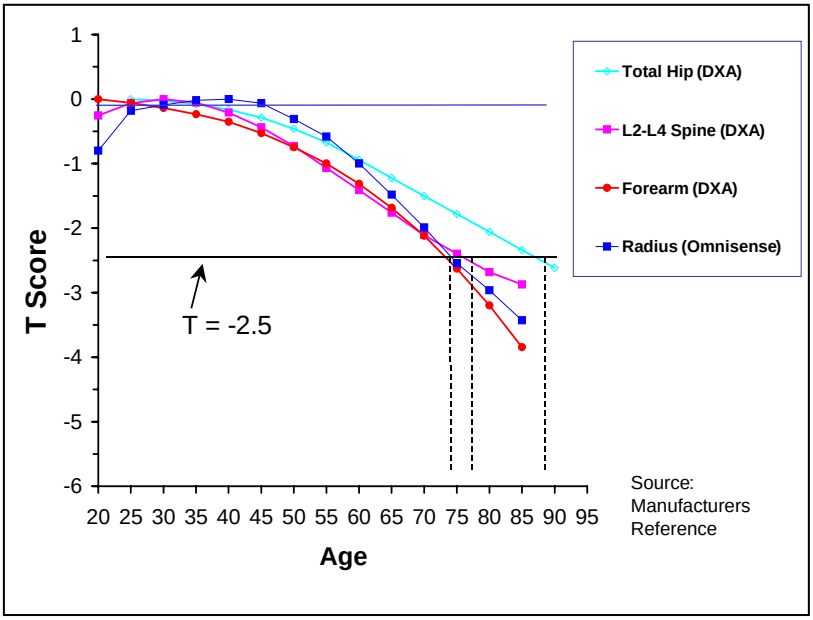

Figure 2 – Comparison between reference database of different devices (applicability of WHO criteria)

It should also be noted that, the DXA hip database indicates a consistently higher T-Score signifying a lower suggested prevalence of osteoporosis in each age group.

4. Omnisense detects and monitors bone changes

"The SOS measured by Omnisense has a precision error low enough in comparison with the expected annual change in a patients' measurement to make it suitable for monitoring bone changes which occur in the early years following menopause (i.e., age range approximately 50-65 years)"[12]

Several studies were undertaken to evaluate the Omnisense's ability to detect bone changes, both due to aging and as response to treatment. [13, 15, 16, 17, 19, 22]

- ***Precision***

  The precision of Omnisense measurements was studied by Barkmann, *et al*. and reported in a paper published in the Journal of Clinical Densitometry[15]. Inter-observer and intra-observer *in-vivo* precision errors, Coefficient of Variation (CV), were found to range from 0.2-0.3% and 0.3-0.7%, respectively, while measuring at different skeletal sites. Another study by Knapp, *et al*., presented at the ASBMR 20th Annual Meeting in 1998, reports *in vitro* CV of 0.03% and *in-vivo* root mean square of CV (RMSCV) of 0.54% for the radius[22].

- ***HRT Studies***

  The discriminatory ability, at the radius, by Omnisense, is also demonstrated while comparing a treated to an un-treated population. Hormone Replacement Therapy (HRT) is a well-recognized treatment for the prevention of osteoporosis. Knapp, *et al*. performed a study aimed at investigating the ability of Omnisense QUS measurements at the radius and the tibia to differentiate between subjects receiving HRT and age matched controls[16]. The study findings confirmed that, even with small study groups, the "QUS measurements demonstrate significant and relatively large differences (in units of T-scores) between the two subject groups. DXA measurements, of Total Hip, Neck of Femur and L1-L4 (spine) on the other hand, show less than half the difference between the groups, none of which achieve statistical significance". In other words DXA did not find any appreciable difference between the HRT treated group and the un-treated group.

  In a similar study[17], Omnisense demonstrated significant discriminatory ability and determined that more women in the non-treated group were osteoporotic than in the treated group. This further demonstrates the Omnisense's high sensitivity to bone change following treatment.

- ***Follow up studies***

  A longitudinal study[19] designed to measure bone response to treatment, was presented at the ASBMR 2000, Toronto. The interim results demonstrated a significant increase in SOS values at the radius and tibia as a result of Alendronate (Fosamax) treatment. They further determined that bone changes induced by treatment are detectable as early as 6 months after initiation of treatment at the radius and 9 months after initiation of treatment at the tibia.

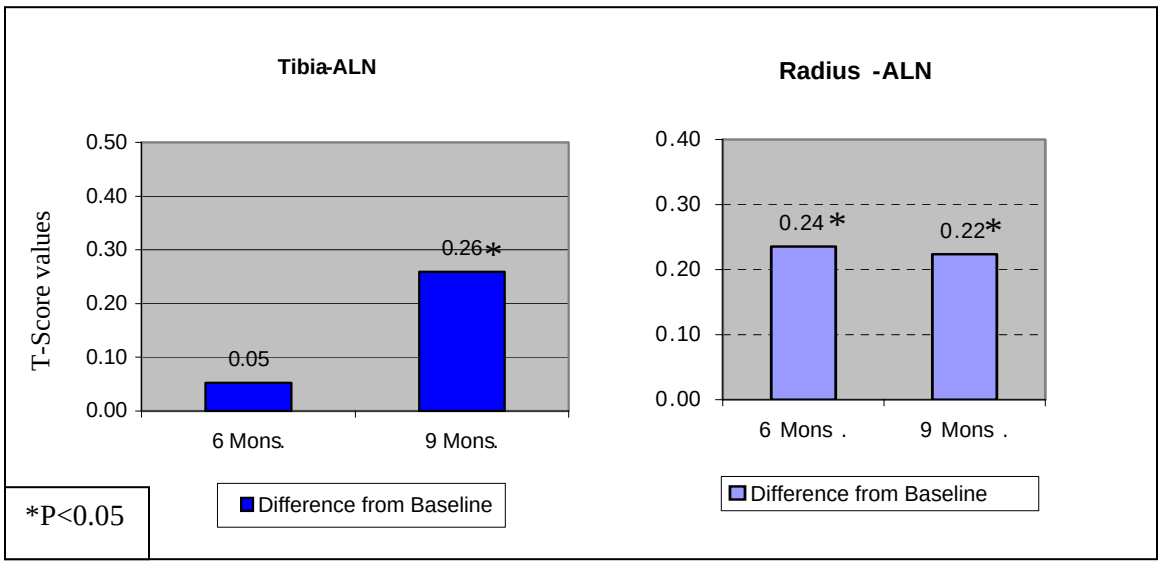

Figure 3 – Increase in SOS values at the Tibia and Radius

5. Secondary Osteoporosis

A study[18] was performed to evaluate the discrimination ability of Omnisense in patients with metabolic diseases. The study provides *in-vivo* evidence that hyperthyroidism affects cortical more than trabecular bone. DXA measurements detect lower BMD at the femoral neck but not at the lumbar spine. In contrast to DXA, SOS, measured by Omnisense, was sensitive to hyperthyroidism to the same degree at all measurement sites.

Conclusions

The above data from recent scientific publications and meetings substantiate Omnisense's diagnostic abilities and the clinical value of its quantitative ultrasound measurements. These studies confirm that Omnisense has proven itself to be an accurate aid to physicians in the diagnosis of osteoporosis and is a viable office-based alternative to radiation based DXA technologies.

Due to its:

- Accuracy in predicting osteoporotic fractures
- Capacity to monitor and detect bone changes
- Increased sensitivity over DXA
- Ability in fracture discrimination
- Applicability of WHO criteria
- Sensitivity to secondary osteoporosis

Sunlight Omnisense™'s QUS technology is fast becoming the accepted method of choice for the assessment and monitoring of bone changes due to aging and in response to treatment.

References:

1. S. Pors Nielsen; "The Fallacy of BMD: A Critical Review of the Diagnostic Use of Dual X-Ray Absorptiometry", *Clin Rheumatol* 2000 19:174-183
2. Ott S M et al, "Evaluation of vertebral volumetric vs. areal bone mineral density during growth." *Bone* 1997 Jun;20(6):553-6
3. Pors Nielsen et al, "Bone densitometry – two or three dimension?" In: *Current Research in Osteoporosis and Bone Mineral Measurement V*, Ring E F J, Elvins D M & Bhalla AK (eds) pp34-35. London: British Institute of Radiology.
4. Formica C A, "Standardization of BMD measurements." Editorial. *Osteoporos Int*. 1998; 8:1-3.
5. Blake G M et al., "An unexpected change in DXA calibration not detected by routine quality control checks." *Osteoporos Int* 1999; 9:115-120.
6. Kanis et al., "Guidelines for diagnosis and management of osteoporosis", *Osteoporos Int* 1997; 7:390-406.
7. Sievanen H, and the Bone research Group at the UKK Institute in Tampere, Finland "QUS Derived Speed of Sound and Cortical Bone Structure", (abstract) presented at the ASBMR 21st Annual Meeting in St. Louis, MI, USA, September 1999.
8. Bouxsein, ML et al., "Prediction of Femoral Failure Load from Femoral BMD and Ultrasonic Velocity at the Femur, Radius and Phalanx" (abstract), presented at the ASBMR 21st Annual Meeting in St. Louis, MI, USA, September 1999.
9. Weiss M, Ben Shlomo A, Hagag P, Rapoport M, "Reference Database for Bone Speed of Sound Measurement by a Novel Quantitative Multi-site Ultrasound Device", *Osteoporos Int* 2000 11:688-696.
10. Knapp et al. "Multiple Site Ultrasound Measurements Predict Vertebral Fractures in Postmenopausal Women" (abstract), presented at the ASBMR 21st Annual Meeting in St. Louis, MI, USA, September 1999.
11. Knapp et al. "Ultrasound Measurements at the Radius Predict Wrist Fractures in Postmenopausal Women" (abstract), presented at the Annual Meeting of the Bone and Tooth Society in Bristol, UK, June 1999.
12. Sunlight Omnisense™ FDA PMA (Pre-Market Application) approval, January 20, 2000.
13. Weiss M et al., "The importance of precision – new hopes for monitoring osteoporosis treatment by QUS" (abstract), presented at the ISCD meeting, Brazil 2000.
14. Weiss M, Ben Shlomo A, Hagag P, Ish-Shalom S. "Discrimination Of Proximal Hip Fracture Measurement At The Radius". *Osteoporos Int* 2000 11:411-416.
15. Barkmann R. et al., "A new method for Quantitative Ultrasound measurements at multiple skeletal sites – first results of precision and fracture discrimination.", *J. Clin Densitom* 2000 spring (1) 1-7.
16. Knapp, K et al. "Quantitative Ultrasound Measurements Detect Skeletal Changes in Cortical Bone Following HRT Use" (abstract), presented at the 11th International Workshop on Calcified Tissues, Eilat, Israel, February 1999.
17. Weiss M et al. "Effect of Estrogen Replacement Therapy on Speed of Sound at Multiple Skeletal Sites" *Maturitus* 2000 (35) 237-243.
18. Ben Shlomo A, Weiss M et al., "Thyroid Dysfunctional State Detected by QUS Measurement at Multiple Skeletal Sites" (abstract), presented at the ASBMR 2nd Joint Meeting, California, USA, December, 1998. Also In Press.
19. M. Weiss et al., "Early Affect of Alendronate or Raloxifene Treatment in Osteoporotic Women Monitored by Multi-Site QUS", (Abstract) presented at the ASBMR 22nd Annual Meting in Toronto, Canada, September 2000.
20. Njeh C.F. et al., "An in vitro investigation of the dependence on sample thickness of the speed of sound along the specimen" *Medical Engineering & Physics*, 1999 September, 21: 651-659.
21. Hans, D. et al., "Does Combining the Results from Multiple Bone Sites Measured by a New Quantitative Ultrasound Device Improve Discrimination of Hip Fracture?", *J Bone Min Res*, 1999, Vol. 14, No. 4 644-651

22. Knapp, K et al. “Preliminary Results Of The Sunlight Omnisense™ Bone Sonometer: In-Vivo And In-Vitro Precision And Correlation With Dxa.” (abstract), The ASBMR-IBMS 2nd Joint Meeting, California, USA, December 1998.

FOR MORE INFORMATION, PLEASE CONTACT US AT:
Wallach Surgical Devices, Inc.