OSCARE MEDICAL

Contents

Oscare Medical Oy

- Oscare Medical – Better Bone Health – Better Life
- Markets a low frequency ultrasound device for screening osteoporosis
- The technology is based on research carried out in university of Jyväskylä, Finland since 2002
- The company was founded in 2007 to make the innovation into a sellable product
- The technology is patented and was granted a CE-mark in fall 2013

Oscare Medical Oy

- Revenio health technology group publicly listed in NASDAQ OMX Helsinki owns the majority of Oscare shares
- Oscare has distributors in Finland, Poland and Latvia and is currently expanding to other European markets

OsCare Sono™ measurement

- Performed on the forearm radius bone
- Tells the speed of ultrasound in the bone, which correlates with[1, 2, 3]
  - Cortical thickness
  - Mineral density
  - Elasticity of the bone
- Provides valuable information on bone strength and fracture risk

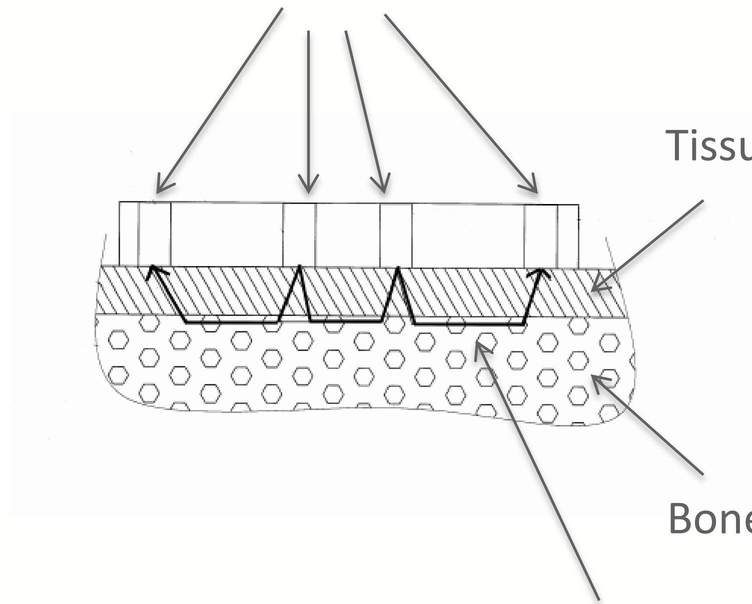
1 Kilappa et al. Low-frequency axial ultrasound velocity correlates with bone mineral density and cortical thickness in the radius and tibia in pre- and postmenopausal women. Osteoporos Int 22(4):1103-13, 2011

2 Muller et al. Prediction of bone mechanical properties using QUS and pQCT: Study of the human distal radius. Med Eng & Physics 30: 761–767, 2008

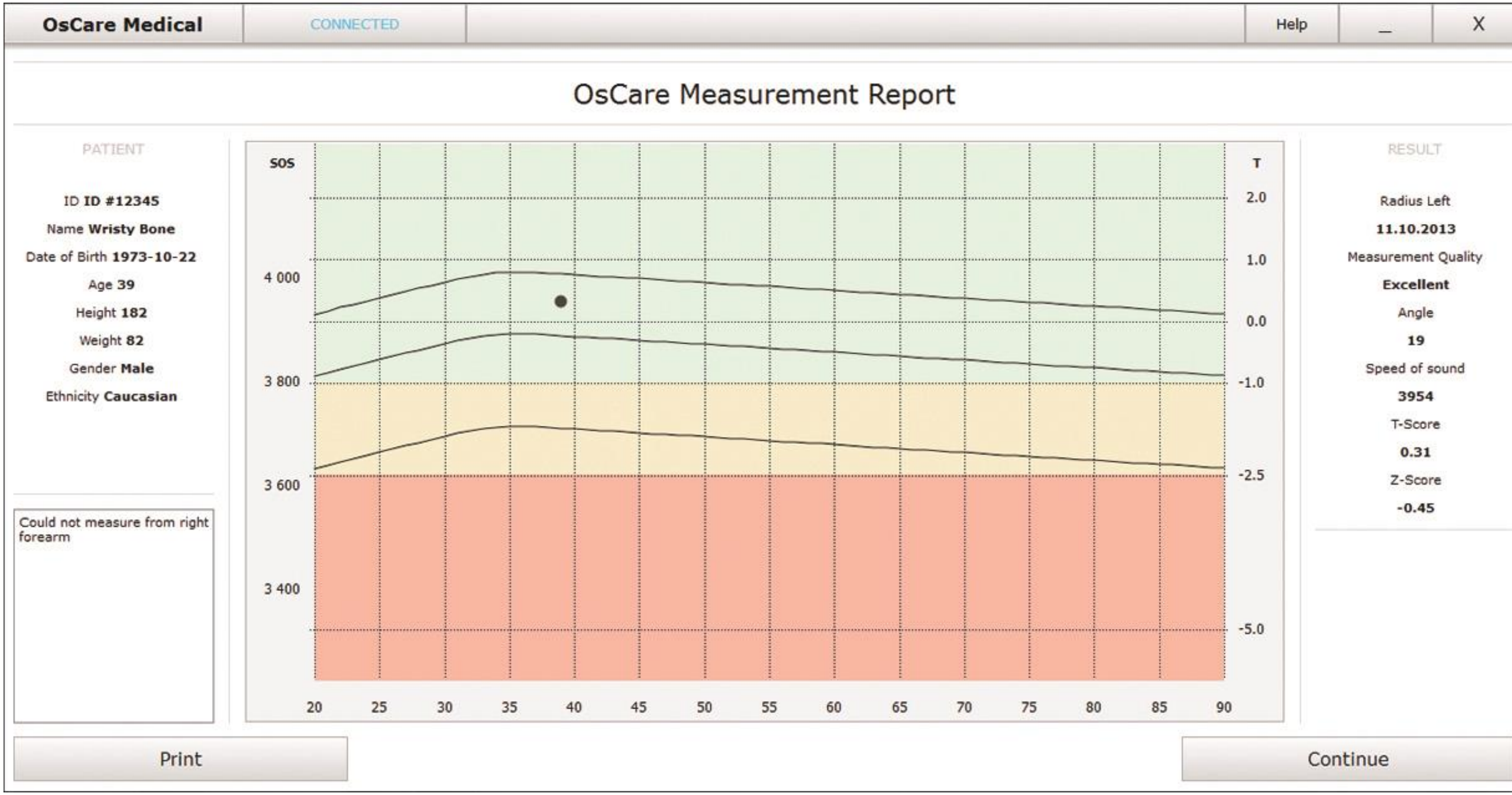
3 Raum et al. Bone microstructure and elastic tissue properties are reflected in QUS axial transmission measurements. Ultras Med Biol 31(9):1225-35, 2005

OsCare Sono^{TM} technology

- The device houses several ultrasonic heads enabling a bidirectional measurement. Based on this, an operational logic is used in order to eliminate the effect of soft tissue.
- The device uses low-frequency ultrasound (around 200 kHz) which travels deeper in the bone tissue than higher frequency, and thus produces better measuring resolution at different bone densities and better correlation with cortical thickness



OsCare measurement report



Interpretation of measurement results

- OsCare Sono^{TM} reports the speed of ultrasound and patient's T-score and Z-score
- T-score compares the patient's measurement result to the average result in apparently healthy young females, reported as the number of standard deviations below or above this average
  - If patient's T-score is more than -1 (green area in the report), the result is in the same range as the result in most healthy young females.
  - If patient's T-score is between -2.5 and -1 (yellow area in the report), the result is decreased compared to most healthy young females. The patient should be given advise on bone health and if other clinical risk factors of osteoporosis are present, specialist consultation can be considered.
  - If patient's T-score is less than -2.5 (red area in the report), relative risk of osteoporosis is considerably increased. The patient should be advised to see a specialist.

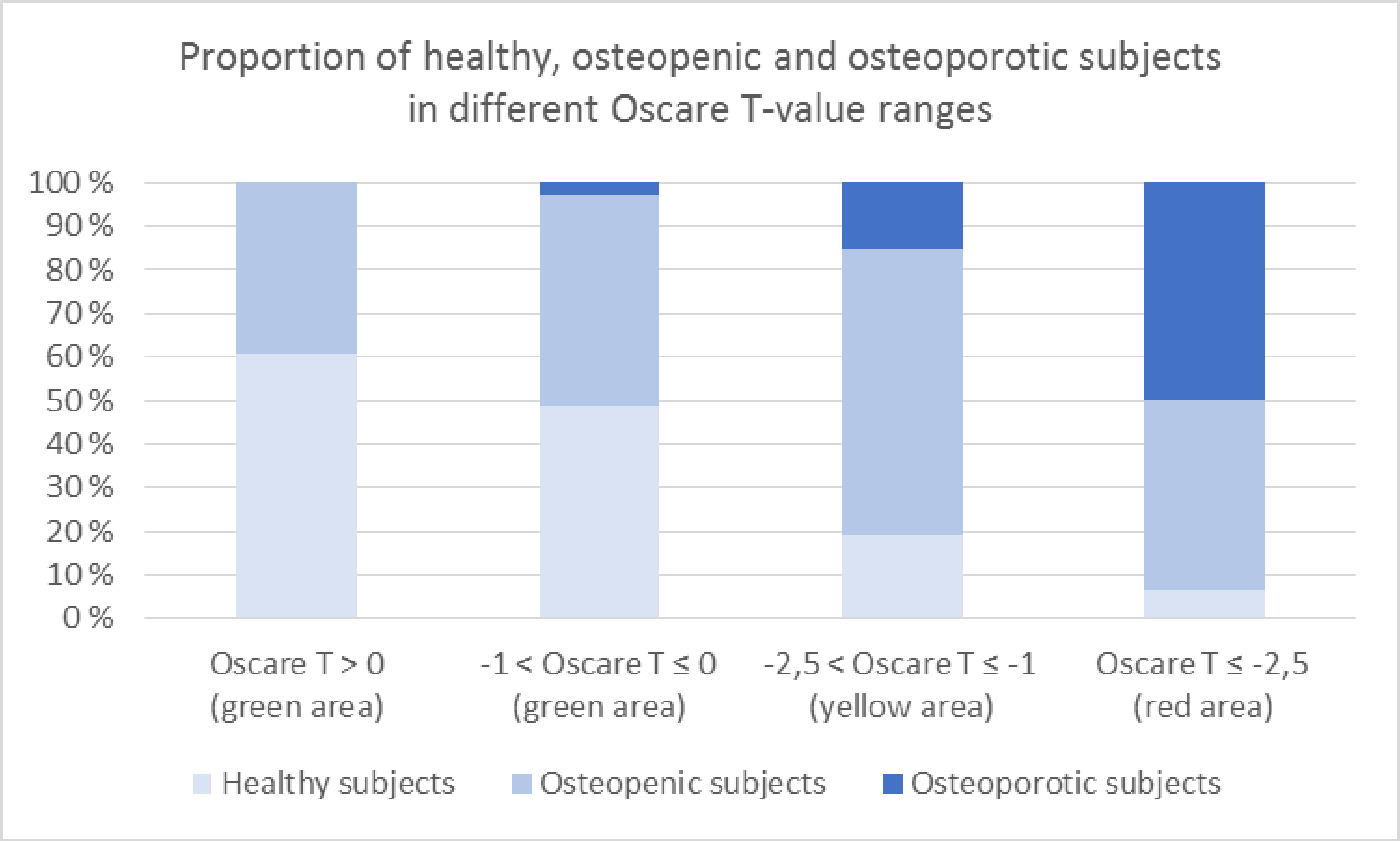
Interpretation of measurement results

- Z-score compares the measurement result to the average in individuals of the same gender and age
  - The upper most curve in the report shows the average result per age
  - The middle curve in the report shows the -1 standard deviation result per age
  - The bottom most curve in the report shows the -2,5 standard deviations result per age
- Z-score is useful for determining whether there are other contributing factors affecting the bone loss, in addition to ageing. These factors may include thyroid abnormalities, malnutrition, medication interactions and excessive use of tobacco.

Practical advise on measurement

- It is important to push with the sensor extra soft tissue (e.g. tendons, muscle, fat) away from between the measurement sensor and the bone
- The sensor needs to be pushed firmly on the bone (using a force of about 3 kg)
- The sensor should be positioned parallel to the bone
- Measurement angle should be between 10 and 20 degrees from a vertical plane, tilting the sensor towards the back of the patient’s hand
- Tiny movements back and forth improve the measurement quality. The sensor should be kept parallel to the bone and the measurement angle optimal.
- In about 5% of the people, the measurement is not possible because of too much soft tissue on top of the bone or soft tissue that cannot be pushed aside

Comparison to DXA



With decreasing Oscare T-value, the proportion of osteoporotic subjects increases and that of healthy subjects decreases. Data gathered in UKK Institute, Tampere is based on DXA (GE Lunar Prodigy Advance) and Oscare measurements of 244 home dwelling 70-80 year old women not known to have bone diseases. Subjects were classified as healthy, osteopenic or osteoporotic based on DXA measurement. Data courtesy of Dr. Harri Sievänen.

Clinical evidence – Fracture risk estimation

- *P. Moilanen, M. Määttä, V. Kilappa, L. Xu, P.H. Nicholson, M. Alén, J. Timonen, T. Jämsä, S. Cheng, " Discrimination of fractures by low-frequency axial transmission ultrasound in postmenopausal females," Osteoporos Int, 24(2):723-730, 2013.*
- The aim of the study was to evaluate the ability of low-frequency axial transmission ultrasound to discriminate fractures retrospectively in postmenopausal women. The study involved 95 female subjects aged 45-88 years, whose fracture information was gathered retrospectively. The fracture group was defined as subjects with one or more low or moderate energy fractures. The radius and tibial shaft were measured with a low-frequency ultrasonometer to assess the velocity of the first arriving signal. Site-matched pQCT (peripheral quantitative computed tomography) was used to measure volumetric cortical and subcortical bone mineral density and cortical thickness. DXA (dual x-ray absorptiometry) was used to measure areal BMD for the whole body, lumbar, spine and hip.
- The majority of the fractures were in the upper limb. Velocity of low frequency ultrasound in the radius discriminated fractures with an age and BMI adjusted odds ratio of 2.06 (95% CI 1.21-3.50, $p<0.01$), equally well as DXA and pQCT.

Clinical evidence – Correlation with bone mineral density and cortical thickness

- *V. Kilappa, P. Moilanen, L. Xu, P.H. Nicholson, J. Timonen, S. Cheng, "Low-frequency axial ultrasound velocity correlates with bone mineral density and cortical thickness in the radius and tibia in pre- and postmenopausal women," Osteoporos Int 22(4):1103-13, 2011.*
- Low frequency (LF) ultrasound provides enhanced sensitivity to thickness and endosteal properties of the cortical wall of radius and tibia compared to using higher frequencies (e.g. 1 MHz). The aim of this study was to evaluate the extent to which LF measurement reflects cortical thickness and bone mineral density. LF ultrasound velocity was compared to site matched pQCT (peripheral quantitative computed tomography) measurements. The study included 159 premenopausal and 95 postmenopausal females.
- Velocity (LF) correlated best with cortical bone mineral density in postmenopausal females in the radius ($R=0,85$, $p<0.001$), and significantly also with subcortical bone mineral density ($R=0.759$) and with cortical thickness ($R=0.761$), $p<0.001$. Similar trends but weaker correlations were found for tibia and for premenopausal women.

Other peer-reviewed publications

- *M. Määttä, P. Moilanen, P.H. Nicholson, S. Cheng, J. Timonen, T. Jämsä, ”Correlation of tibial low-frequency ultrasound velocity with femoral radiographic measurements and BMD in elderly women,” Ultrasound Med Biol 35(6):903-011, 2009.*
- *M. Muller, D. Mitton, P. Moilanen, V. Bousson, M. Talmant, and P. Laugier, "Prediction of bone mechanical properties using QUS and pQCT: Study of the human distal radius," Med Eng Phys, 30(6): 761-767, 2008.*
- *P. Moilanen, “Ultrasonic guided waves in bone,” IEEE Trans. Ultrason. Ferroelect. Freq. Contr., 55(6): 1277-1286, 2008.*
- *P. Moilanen, M. Talmant, V. Kilappa, P.H.F. Nicholson, S. Cheng, J. Timonen, P. Laugier, “Modeling the impact of soft tissue on axial transmission measurements of ultrasonic guided waves in long bones,” J. Acoust. Soc. Am., 124(4): 2364-2373, 2008.*
- *P. Moilanen, P. H. Nicholson, V. Kilappa, S. Cheng, and J. Timonen, "Assessment of the cortical bone thickness using ultrasonic guided waves: modelling and in vitro study," Ultrasound Med Biol, 33: 254-262, 2007.*
- *P. Moilanen, M. Talmant, V. Bousson, P. H. F. Nicholson, S. Cheng, J. Timonen, and P. Laugier, "Ultrasonically determined thickness of long cortical bones: Two-dimensional simulations of in vitro experiments," J Acoust Soc Am, 122: 1818-1826, 2007.*
- *P. Moilanen, M. Talmant, P. H. F. Nicholson, S. Cheng, J. Timonen, and P. Laugier, "Ultrasonically determined thickness of long cortical bones: Three-dimensional simulations of in vitro experiments," J Acoust Soc Am, 122, 2439-2445, 2007.*
- *P. Moilanen, P.H.F. Nicholson, V. Kilappa, S. Cheng, J. Timonen, “Measuring guided waves in long bones: modeling and experiments in free and immersed plates,” Ultrasound Med Biol, 32: 709-719, 2006.*
- *M. Muller, P. Moilanen, E. Bossy, V. Kilappa, P.H.F. Nicholson, J. Timonen, M. Talmant, S. Cheng, P. Laugier, “In vitro comparison of three different approaches using ultrasonic axial transmission for cortical bone assessment,” Ultrasound Med Biol, 31: 633-642, 2005.*
- *P. Moilanen, V. Kilappa, P.H.F. Nicholson, J. Timonen, S. Cheng, ”Thickness sensitivity of ultrasound velocity in long bone phantoms. Ultrasound Med Biol,” 30: 1517-1521, 2004.*
- *P. Moilanen, P.H.F. Nicholson, T. Kärkkäinen, Q. Wang, J. Timonen, S. Cheng, “Assessment of the tibia using ultrasonic guided waves in pubertal girls,” Osteoporos Int, 14: 1020-1027, 2003.*
- *P.H.F. Nicholson, P. Moilanen, T. Kärkkäinen, J. Timonen, S. Cheng, “Guided ultrasonic waves in long bones: modelling, experiment and in vivo application,” Physiol Meas, 23: 755-68, 2002.*

OSCARE MEDICAL
Äyritie 22
01510 Vantaa
Finland