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# ACOUSTICS 2012

## Improvement of the precision of Quantitative Ultrasound (QUS) measurements at the calcaneus by tilting of the beam incidence angle

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QUS measurements at the calcaneus can be used for the estimation of osteoporotic fracture risk, but its feasibility for therapy monitoring is still unclear. One reason might be the limited precision of commercial devices. Our intent was to investigate the impact of the beam incidence angle at the calcaneus on the precision of the speed of sound (SOS). We developed a device with an array (120 elements) as receiver ( $d=100\text{mm}$ ) and one single element emitter of the same size. Both are placed on opposite sides of the foot and mounted on a c-arm which can be rotated and tilted. SOS of 7 volunteers was measured three times with repositioning under different beam incidence angles. Best precision could be achieved from measurements under optimal angles and with individual definition of the ROI combined with a correction for variations in the temperature of the foot and the coupling medium. The precision error was five times lower than the error of a measurement at a fixed incidence angle and fixed ROI, a method which is used in most commercial devices. By using individually defined regions of interest and incidence angles the precision of calcaneus QUS measurements can be substantially improved.

## 1 Introduction

Osteoporosis is a bone disease, which affects mainly elderly women. 30-40 % of all women 50 years and older suffer from osteoporosis [1]. The WHO classifies this disease as one of the ten most significant [2]. Effective treatment to reduce the fracture risk exists. Besides the diagnosis of osteoporosis and estimation of fracture risk a sensitive therapy monitoring is needed.

The gold standard today is the DXA which exposes the patient to radiation and is therefore not permitted for every medical practice. Furthermore the DXA measures only the bone mineral density and does not consider other fracture relevant parameters like microstructure [3] or material properties [4]. Treatment monitoring using DXA has some drawbacks. The most sensitive measurement at the spine is affected by degenerative changes while the precision at the hip is too poor.

Quantitative ultrasound (QUS) at the calcaneus is proven to predict osteoporotic fracture risk [5]. However, contradictory studies about the ability of QUS devices for monitoring exist, which might be due to their low precision. Slight changes of the bone mass have to be detected, so the improvement of the precision and sensitivity is a crucial point.

We developed a new calcaneus QUS device aiming primarily at the improvement of the precision by taking into account known error sources [6]. Sources of errors include the temperature of the coupling medium as well as the foot temperature and errors during repositioning due to the anatomical shape of the bone measured.

## 2 Materials and Method

### 2.1 Devices

The developed device uses an ultrasound array with 120 cells as receiver and one single transducer as emitter. Both have a diameter of 100 mm and a center frequency of 500 kHz with small bandwidth. Receiver and transmitter are mounted in capsules. The cells of the array are squarish and have an edge length of 6 mm. The received signals of the cells are multiplexed and then amplified by a Voltage Gain Amplifier (VGA) with an integrated Low Noise Amplifier (LNA). The gain of the LNA is 19dB, the gain of the VGA can be adjusted by software from 7.5dB to 55.5dB. A 14 bit Analog-Digital-Converter (ADC) samples the signal with a sampling frequency of 40 MHz in a range of two volts. To obtain a complete image of the array, the emitter has to be excited for each array cell separately, i.e. 120 times. This process takes less than one second.

The emitter and the receiver are positioned on opposite sides of the foot with a pitch of 110 mm and mounted on a c-arm, which can be rotated around a vertical axis and tilted around a horizontal axis to adjust the ultrasound beam incidence angle (as shown in Figure 1).

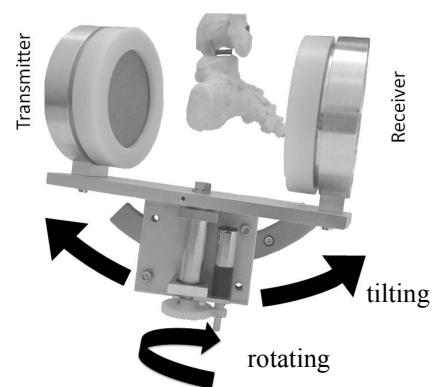


Figure 1: Setup of the measurement. The ultrasound beam can be adjusted by tilting and rotation (see arrows)

The coupling with the skin is realized with castor oil filled flexible membranes (as shown in Figure 2). The oil is tempered at 33°C. Its acoustic impedance matches to the impedance of soft tissue, so the reflection coefficient is minimized in contrast to coupling with water.



Figure 2: Coupling with oil filled membranes

The oil is stored and tempered in an aluminum box which has a volume of two liters. A membrane separates an air and an oil compartment. To inflate the membranes which couple to the foot, air is pumped into the air compartment of the box (as shown in Figure 3).

The air pressure in the air compartment and the oil pressure in the membranes can be measured. The whole device is surrounded by isolating walls as the air is tempered to 33°C, too. This prevents the oil and the foot from cooling during the measurement. The temperature of the oil at the beginning and the end of the measurement and the temperature of the foot during the measurement can be measured.

The repositioning of the foot is facilitated by footholds for the heel and the right edge of the foot. Only the right foot can be measured with this setup.

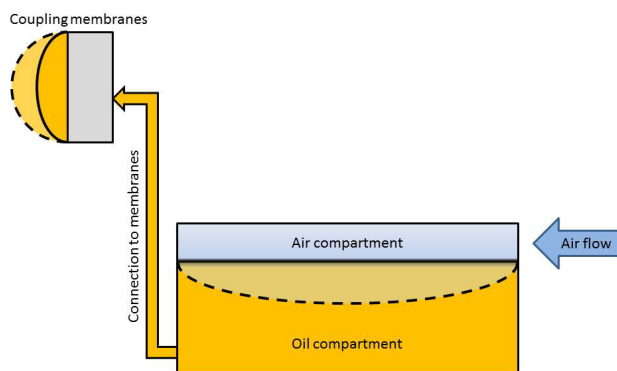


Figure 3: Oil management. The blue arrow indicates the air flowing into the air compartment and suppressing the oil out of the box into the membranes

## 2.2 Subjects

7 female volunteers aged from 24 to 45 participated in the study. No exclusion criteria were applied. Each measurement was repeated three times with repositioning.

## 2.3 Measurement procedure

The default scanning angles are for rotation -7° to 21° (step size 7°) and for tilting -7° to 10° (step size 4°). At first the foot is placed in the device to check whether the default scanning angles are sufficient for the volunteer. If the capsules would contact the foot, the default angles have to be adjusted. The membranes are not inflated in this step of preparing the measurement.

Before a measurement can be performed, the oil has to be homogenized. This is done by inflating and draining the membranes three times.

The temperature sensor is attached to the foot near the vein at the lateral side of the ankle before inserting the foot into the device. For temperature coupling a small amount of greasy skin care cream is applied between temperature sensor and skin. To isolate the sensor from the warm air inside of the device a small piece of neoprene is fixed on the sensor.

When inserting the foot into the device it has to be neatly aligned to the footholds. The coupling between the skin and the membranes is done with 70% Isopropanol-spray which is sprayed extensively on the membranes and the area between the ankle and the heel.

The first measurement is a preparing scan and used to adjust the gain of the ultrasound signals, to find a first SOS minimum in the default scanning angles and to allow the foot to acclimatize to the tempered air. For the following measurements the scanning angles are adjusted so the area around the SOS minimum can be scanned with smaller step sizes which are usually half the size of the default step sizes.

The SOS is averaged over 5 measurements at each pair of angles. The temperature of the foot during the measurement is stored, too.

Between the measurements the foot was repositioned.

## 2.4 Analysis

Two methods of defining the region of interest in the array were applied: averaging of the signals over a circular region of 24 mm diameter at a fixed position (commonly used method in commercial devices, e.g. the Achilles Insight, GE Lunar) and a method with a variable ROI of appr. 6mm \* 12 mm (two neighboured cells of the array), defined as the region with highest signal amplitudes. The ROI is identified by the highest amplitude of the first oscillation in the bone individually for each image. The Time of Flight (TOF) of the signal is determined by the first zero crossing with a negative slope. With Equation (1), which considers the thickness of the bone  $d = 30 \text{ mm}$ , the reference time of flight  $TOF_{ref}$  in oil and the reference SOS  $v_{ref}$  of the oil, the apparent SOS of the bone can be calculated. After plotting these SOS values for both ROIs individually against the angles, the lowest SOS values and the SOS values at the angles 0° and 0° were taken.

$$SOS = \frac{d}{\frac{d}{v_{ref}} + TOF_b - TOF_{ref}} \quad (1)$$

For each scan the temperature of the foot  $T_{foot}$  is defined as the temperature being recorded at those angles, in which the final SOS value was chosen. Additionally, a temperature difference  $\Delta T_{foot}$  was calculated as difference between  $T_{foot}$  and the foot temperature at the beginning of the concerning scan. Since oil temperature could not be measured inside of the membranes during the measurement,  $T_{oil}$  was defined as the temperature of the oil during the draining of the oil from the membranes. This temperature was measured in a connected tube.

For each method patient ID,  $T_{foot}$ ,  $\Delta T_{foot}$  and  $T_{oil}$  were included in a multivariate model for the estimation of SOS. Variables, which significantly contributed to the model, were used to correct SOS for the temperature impact. Precision errors were calculated as the root mean square error of the precision values over the three measurements of all subjects.

### 3 Results

The ranges of the SOS varied from 131 m/s to 102 m/s depending on the ROI and the angles. The widest range was at the fixed angles with a fixed ROI and temperature adjustment. The smallest range was at the variable angles with a variable ROI and no temperature adjustment. The highest SOS can be found at the fixed angles referring to table 1.

Table 1: Distribution of SOS

	Temperatur corrected		SOS / m/s	
			Fixed angles	Variable angles
ROI fixed	original	min	1494	1477
		max	1616	1595
		range	122	118
	corrected	min	1493	1470
		max	1624	1579
		range	131	109
ROI variable	original	min	1497	1493
		max	1620	1595
		range	123	102
	corrected	min	1482	1467
		max	1600	1574
		range	118	107

The best precision (0.9 m/s) was achieved at the variable angles with a variable ROI and temperature adjustment. The poorest precision (4.4 m/s) was at the fixed angles with a fixed ROI and without temperature adjustment corresponding to a measurement on a commercial device with fixed ROI. Data are depicted in table 2.

Table 2: Distribution of the SOS precision

	Temperature corrected	SD SOS / m/s	
		Fixed angles	Variable angles
ROI fixed	original	4.4	2.4
	corrected	3.8	2.2
ROI variable	original	3.6	2.3
	corrected	2.3	0.9

The oil temperature varied from 32.2 °C to 33.4 °C with a standard deviation of 0.1 °C over the three measurements of each volunteer. The temperature of the foot ranged from 28.9 °C to 32.3 °C with a standard deviation of 0.2 °C. Range in  $\Delta T_{\text{foot}}$  was -0.10 to 0.13 °C.

Only in the method using variable angles and a variable ROI  $T_{\text{foot}}$ ,  $\Delta T_{\text{foot}}$  and  $T_{\text{oil}}$  all contributed significantly to the model. In this method, temperature coefficients are  $-13.1 \frac{\text{m/s}}{^\circ\text{C}}$  for  $T_{\text{oil}}$ ,  $-8.5 \frac{\text{m/s}}{^\circ\text{C}}$  for  $T_{\text{foot}}$  and  $-14 \frac{\text{m/s}}{^\circ\text{C}}$  for  $\Delta T_{\text{foot}}$ .

The angles of the SOS minima varied from 1° to 25° for the rotation and from -7° to 7° for the tilting. The range of the rotation angles is 24°, the range of the tilting angles 14°. In Figure 4 the spreading of the SOS minima is shown.

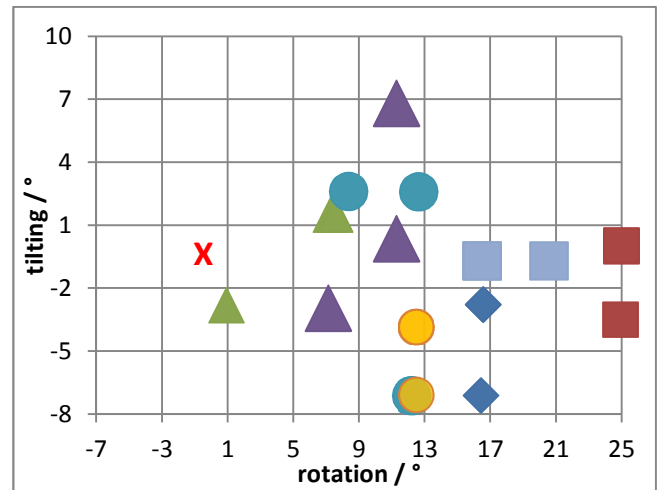


Figure 4: Spreading of the SOS minima; marks of the same color and size stand for one volunteer. The red cross marks the fixed angles.

### 4 Discussion

Because the cells of the array are relatively large the definition of the ROI is suboptimal. Sophisticated interpolation techniques might help to improve the definition of the best ROI, however, until now our method of averaging over two array cells performed best. Nevertheless, a substantial improvement in the precision could be achieved by finding the optimal ROI and the best angles. Using data from the OPUS-study we could estimate that 1% change in lumbar spine BMD measured by DXA corresponds to a change of 3 m/s in SOS of calcaneus QUS. Considering that a “good” short term precision error of the DXA measurements is about 1% we can conclude that our precision is roughly three times better. If these results can be reproduced in a larger subject group and if the low precision error can also be reproduced in long-term precision data the improved device might be used for sensitive monitoring purposes.

The rotation of the beam incidence angle is more crucial than the tilting if we consider the distribution of the SOS minima over the angles. The range for the rotation angle is 10° higher than the range of the tilting angle. Furthermore all the SOS minima are found in the positive rotation angles and are all different to the angle 0°. The tilting angle varies around the angle 0° in both directions within 7°.

Some SOS minima are not well defined because they are positioned at the boundaries of the range in the angles. This might be improved by increasing the tilting range; however, this will not be possible for the rotation angles because the capsule would collide with the foot. This would require a redesign of the device, e.g. including the use of smaller capsules.

The temperature of the foot which is used to correct the SOS values is just the temperature of the surface of the skin and might not represent the core temperature of the foot. Nevertheless, the temperature coefficients found in the model, are realistic as the temperature coefficient for fat is  $-7.1 \frac{\text{m/s}}{^\circ\text{C}}$  [7] and correlates well with the temperature coefficient of  $T_{\text{foot}}$  found in the model ( $-8.5 \frac{\text{m/s}}{^\circ\text{C}}$ ). SOS of castor oil declines at 3.6 m/s per 1°C increase in



temperature. According to equation 1 a variation of -3.6 m/s in  $v_{ref}$  would result in a variation of about -9 m/s in SOS, which is in the same order as the -13.1 m/s in our model.

We also included the change of the foot temperature into the model because the temperature of the foot is not constant. Former investigations showed a drift of foot temperature and SOS when cold feet were put into a warmer environment. Because our foot temperature measurement at the skin besides of the ankle is only an estimation of the tissue temperature within the ultrasound beam this measurement of temperature dynamics might add to the precision of SOS. If this also is the case in measurements at feet with a larger variety of foot temperature still has to be examined.

A limitation of the analysis is the use of a multivariate model with temperature coefficients defined from the results of just this model. Therefore, a validation of the analysis procedure has to be done using an independent study.

## 5 Outlook

A redesign of the device is on the way comprising a smaller array (diameter of 70 mm) with a higher resolution (256 cells, edge length 3.25mm) and an improved oil temperature management system.

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