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Estimation of femoral bone density from trabecular direct wave and cortical guided wave ultrasound velocities measured at the proximal femur in vivo

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Bone mineral density (BMD) of the proximal femur measured using bone densitometry is a predictor of hip fracture risk. We developed a Quantitative Ultrasound (QUS) scanner for measurements at this site with similar performance (FemUS). In this study, we tested if ultrasound velocities of direct waves through trabecular bone and of guided waves through cortical bone could be used to estimate BMD.

In two centres, Kiel and Odense, we measured time-of-flight (TOF) of waves through the trabecular greater trochanter and cortical intertrochanter as well as a wave through soft tissue only. TOF was adjusted for leg width using ultrasound echoes reflected from the skin of the leg to yield apparent speed of sound (SOS) of different wave components. Data were cross-calibrated between centres and pooled. Bivariate correlation and multivariate analyses were used to compare QUS results with hip BMD.

BMD correlated significantly both with trabecular and cortical SOS but not soft tissue SOS. The combination of trabecular, cortical and soft tissue SOS improved the correlation and all three variables contributed independently. In conclusion, multiwave ultrasound methods allow estimation of hip l BMD with a residual error of about 10%.

1 Introduction

Osteoporotic fractures of the hip are associated with considerable mortality and costs to the society [1]. Effective treatments reduce the number of fractures, provided that patients with a high fracture risk are identified and targeted for treatment. The best validated quantitative method for the estimation of osteoporotic fracture risk is DXA (dual x-ray absorptiometry) of spine and hip [2]. As a radiation free approach, ultrasound based procedures (Quantitative Ultrasound, QUS) have been developed [3]. QUS of the calcaneus has shown similar performance as central DXA regarding the prediction of osteoporotic fractures at any skeletal site [4].

However, the risk of hip fracture is best predicted by DXA measurements directly at the proximal femur [5]. In theory, QUS measurements at the femur could be used to combine the potential of QUS measurements with the predictive power of measurements at the hip. However, no *in vivo* QUS measurements at the main fracture sites, *i.e.* the spine and the proximal femur have previously been published.

In vitro measurements have recently been successfully performed by the groups in Kiel and Paris [6] demonstration proof-of-principle regarding QUS measurements at the femur. Correlation coefficients of R^2 = 0.8 - 0.9 were obtained in the correlation between femur SOS and hip BMD.

We developed an ultrasound device for direct *in vivo* QUS measurements at the proximal femur and tested the quality of correlations between QUS and hip BMD.

2 Materials and Methods

2.1 The FemUS device

Measurements were performed in two centers (Kiel, Germany, and Odense, Denmark) using the FemUS prototype. The device comprises two ultrasound transducers of 600 kHz frequency mounted opposite to each other on a C-arm in a distance of 50 cm. Both transducers are able to transmit and receive ultrasonic waves. The arm can be moved in two linear directions. Additionally, the scan area can be rotated around two axes. The principal arrangement is depicted in figure 1. All movements are driven by motors and controlled through a PC. For better ultrasound coupling the transducers are submitted in a temperature-controlled water bath. A recess in the water bath allows positioning of the patient's body, lying on a table, between the transducers. Inflatable, water filled membranes were used to establish water mediated contact between transducers and patients skin without the existence of air within this path. Small pulses were used to generate the acoustical waves and A/D converters were used to digitize signals received and store them on the PC. Figure 2 shows an image of the complete device as it was used for the *in vivo* measurements.

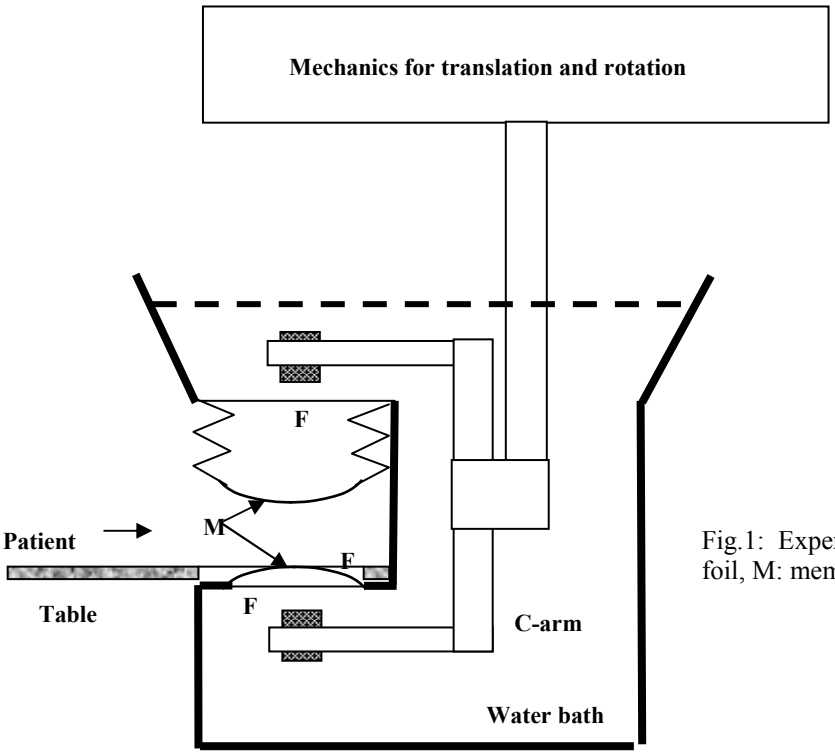

Fig.1: Experimental prototype of the FemUS device (F: foil, M: membrane)

Figure 2: FemUs device ready for patient measurements

2.2 Measurements

In Kiel, where the device was built, the method was set up, and in Odense the method was tested in a different environment. Participants were positioned on the table and the leg was rotated as during DXA measurements. The proximal femur region was scanned with ultrasonic beams perpendicular to the surface of the table.

Ultrasonic propagation is complex and very often, especially in irregular shaped objects, a multi-path transmission occurs leading to a superposition of single parts of the wave and a complex signal received. To address this problem, we developed methods to separate the single waves [7]. In our first calculations, we selected a region within the greater trochanter where a wave directly transmitted through the trabecular part of the bone could be identified. Within a region of two cm², nine signals were evaluated and the calculated variables were averaged (region "T" in figure 3). A guided wave could be identified at its low time of flight in all subjects in a region below the smaller trochanter at the medial cortical part of the femur shaft (region "C" in figure 3). Beside the femoral shaft, signals were also evaluated passing through soft tissue only (regions "S" in figure 3). In regions the "C" and "S", only SOS values were calculated.

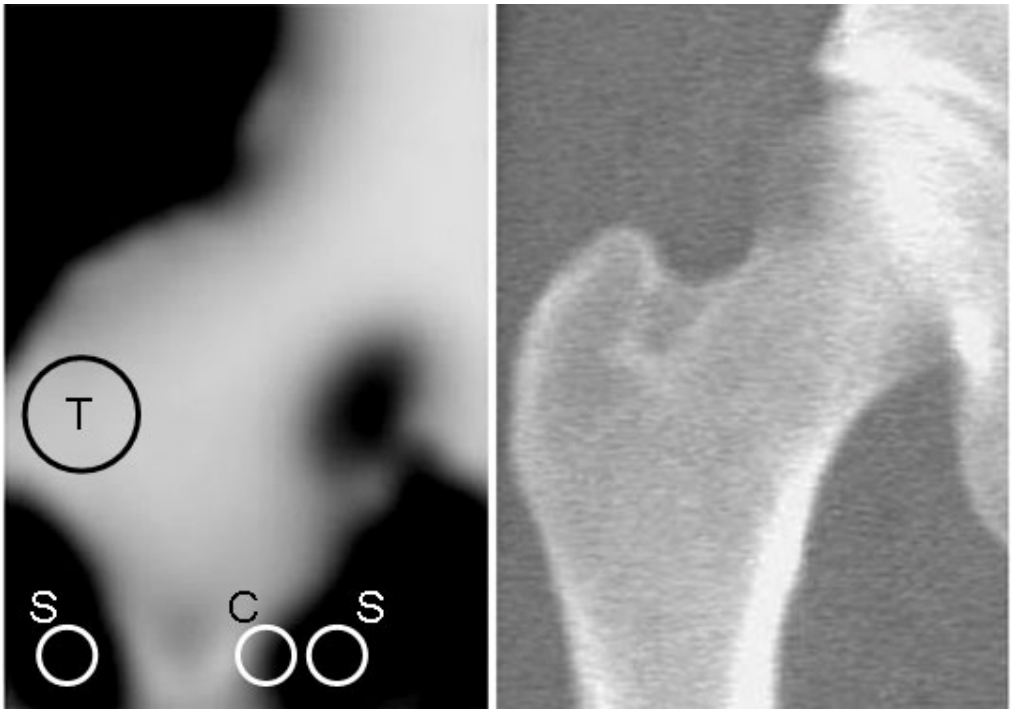

Fig. 3: Example of a QUS attenuation image (left) in comparison with a DXA image (right) with measured regions (T: trabecular region, C: cortical region, S: soft tissue regions)

SOS can be calculated as ratio between transducer separation and time-of-flight. Time of flight, however, depends on properties and dimensions of the different tissues penetrated, i.e. bone, soft tissue (in particular muscle and fat), and water. To overcome at least the impact of the varying ratio of thigh width and length of the water path, a special calculation method was applied corresponding to a virtually filling of the water pathways with fat. For this, the times of flight of the wave within the water pathways were measured using the echoes from the surface of the skin on both sides of the thigh. Thereafter, the times of flight were recalculated using SOS of body fat. This way, a new overall time of flight was calculated corresponding to a mixture of bone, muscle and fat, minimizing the impact of different sizes of the thigh. SOS was then recalculated as the ratio between transducer separation and the corrected time of flight. This procedure was applied to all SOS values, trochanteric (SOSt), cortical (SOSc), and in soft tissue (SOSst).

A total of 62 participants were measured using both the FemUS as described and DXA (Discovery, Hologic, Waltham, Ma) at the hip. DXA devices were cross calibrated using the European Spine Phantom (ESP). The studies were approved by the local ethical committees in Kiel and Odense. Participants gave their informed consent.

2.3 Statistical analyses

Spearman correlation coefficients (R) and residual errors (RMSE) were calculated for single correlations between all QUS variables and total hip BMD. Additionally, we determined the best model for the estimation of BMD combining SOSt, SOSc and SOSst.

3 Results

BMD correlated significantly both with trabecular and cortical SOS but not soft tissue SOS. The combination of trabecular, cortical and soft tissue SOS improved the correlation. All three variables contributed independently from each other. All correlations were significant at $p < 0.0001$. In table 1, results of the pooled data are presented. Similar and consistent results could be obtained using data from each centres separately. The best estimation of hip BMD had a residual error of about 10% equivalent to half of a population standard deviation.

	R^2	RMSE / % T-Score
SOS_t	0.58	69
SOS_c	0.56	71
Combination	0.72	57

Table 1: Correlation coefficients R^2 and residual errors (RMSE)

4 Discussion

Our study demonstrated that *in vivo* QUS measurements at the proximal femur are feasible and that SOS correlates with BMD as measured by DXA at this site.

Using our newly designed prototype for measurements of QUS transmission and reflection, we demonstrated that SOS through the greater trochanter (SOSt) and SOS through the intertrochanteric shaft (SOSc) both correlated with total hip BMD. Moreover, the combination of SOSt, SOSc and SOS_{st} through soft tissue performed even better. Further improvement of the method could enable the evaluation of larger areas *e.g.* total hip.

Some new and interesting features could be tested with this device. A "guided wave" through the proximal shaft could be evaluated to achieve information about the cortical bone. Until now, such waves have been evaluated in axial transmission measurements (especially at radius and tibia) and transverse measurements (at the finger phalanges) only. Our device measured the transverse wave through the cortical shell of the shaft directly below the smaller trochanter. Such waves were also detectable at the inferior part of the femoral neck; however, in some subjects the amplitude was too low for an evaluation. With higher signals and improved signal analysis it might also be possible to evaluate this skeletal site and obtain information on the femoral neck cortex.

Our method of evaluating reflections from the skin to reduce the impact of thigh thickness on SOS values was successful. This approach substantially improved the correlation of QUS measurements with BMD. Whether the evaluation of reflections from the bone surfaces can be used to improve the results further, still has to be evaluated.

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