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Characterization of a new ultrasound device designed for measuring cortical porosity at the human tibia: A phantom study

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ABSTRACT

Quantitative ultrasound (QUS) measurements of trabecular bone are a useful tool for the assessment of osteoporotic fracture risk. However, cortical bone properties (e.g. porosity) have an impact on bone strength as well and thus current research is focused on QUS assessment of cortical bone properties. Simulation studies of ultrasound propagation through cortical bone indicate that anisotropy, calculated from the ratio of the velocities in axial and tangential directions, is correlated with porosity. However, this relationship is affected by error sources, specifically bone surface curvature and variability of probe positioning. With the aim of *in vivo* estimation of cortical porosity a new ultrasound device was developed, which sequentially measures velocities in 3 different directions (axial = 0° and ±37.5°) using the axial transmission method. Measurements on planar porosity phantoms (0–25%) were performed to confirm the results of the afore mentioned simulation studies. Additionally, measurements on cylindrical phantoms without pores (min. radius = 34 mm for strongest curvature) were performed to estimate the influence of surface curvature on velocity measurements (the tibia bone surface is fairly flat but may show surface curvature in some patients). The velocities in the axial and ±37.5° directions were used to calculate an anisotropy index. The velocities measured on the porosity phantoms showed a decrease by −6.3 ± 0.2 m/s and −10.1 ± 0.2 m/s per percent increase in porosity in axial and ±37.5° directions, respectively. Surface curvature had an effect on the velocities measured in ±37.5° directions which could be minimized by a correction algorithm resulting in an error of 5 m/s. The anisotropy index could be used to estimate porosity with an accuracy error of 1.5%. These results indicate that an estimation of porosity using velocity measurements in different directions might be feasible, even in bones with curved surface. These results obtained on phantom material indicate that the approach tested may be suited for porosity measurements on human tibia bone.

1. Introduction

Quantitative Ultrasound (QUS) measurements can be used to estimate the osteoporotic fracture risk. Best results have been achieved using through transmission measurements at the calcaneus, a skeletal site consisting predominantly of trabecular bone. However, cortical bone also substantially contributes to the breaking strength of bones. One study e.g. indicates that the strength of the femur neck mostly depends on the strength of its cortical bone [1]. In long bones the fragility depends among other factors on cortical porosity [2–4]. Yeni et al. [5] reported a significant correlation of increasing porosity and decreasing tension and shear fracture toughness of human tibia shaft and the subtrochanteric region at the femur; McCalden et al. [6] reported a 76% decrease of cortical strength induced by changes in porosity at the human femur shaft. The relationship of cortical porosity with hip fracture status has been studied in detail by the team of Reeve and Loveridge [7,8]. These findings indicate that cortical bone properties, especially cortical porosity, have a substantial impact on the strength of bone and the ability to measure this property may improve fracture risk assessment.

The porosity of cortical bone varies from 3 to 27% [9] and increases with age [6,10] or disease [4]. X-ray imaging methods used to examine the *in vivo* bone status only have limited access to measuring cortical porosity. The Dual Energy X-Ray Absorptiometry (DXA), which is the preferred method to measure (areal) bone mineral density (aBMD) and osteoporotic fracture risk, mainly depends on bone mass and size but does not provide any

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information about structural parameters or material properties. High Resolution peripheral Quantitative Computer Tomography (HR-pQCT) is the X-Ray method with the highest resolution up to date but prone to motion artifacts and limited to peripheral measurement sites such as the distal radius or the distal tibia. The standard protocol of the Xtreme CT uses a reconstructed isotropic voxel size of 82 μm but the actual spatial resolution near the center of the field of view is lower with approximately 130 μm and decreasing with increasing distance to this center [11]. Therefore, structures smaller than 100 μm cannot be segmented in the image. The pore sizes in cortical bone vary between 7 and 400 μm [12] where in healthy bone the mean pore size is approximately 60 μm [13]. Thus it is possible to estimate the porosity of the larger pores with HR-pQCT which are likely to be of particular relevance for increased fracture risk, as indicated by a study from Wachter et al., who found a negative correlation of yield stress with the average pore diameter at the human femoral midshaft [14]. Due to radiation exposure limitations porosity measurements remain challenging at the proximal femur [15], the site of the most devastating type of osteoporotic fracture, and it is unclear to what extent HR-pQCT measurements of peripheral bone sites would improve hip fracture risk prediction based on standard methods.

QUS transmission measurements in cortical bone might offer an alternative approach for the measurement of bone properties. A number of new QUS approaches for measuring cortical bone properties have recently been published [16–20]. As an *in vivo* applicable method the axial transmission technique is best validated measuring the ultrasound velocity along the axis of long bones such as the radius or the tibia. The squared velocity in a medium (in this case bone) is directly related to the effective elastic modulus in the linear propagation regime [21]. Therefore, velocity can be used to estimate the elasticity. In an effort to measure additional fragility-relevant properties of cortical bone we have developed a new QUS device with the aim to estimate cortical porosity at the human tibia [22]. Mineralization and porosity of the bone both influence ultrasound velocity [23,24] but it is not possible to discriminate between these properties with a single measurement. However, simulation studies indicate that the ultrasound velocity in tangential direction (perpendicular to the axis) is stronger influenced by porosity changes than the velocity in axial direction [25–30], e.g. Bossy et al. [25] found that a 15% porosity results in a decrease in compressional velocity along the pores of 300 m/s and of 600 m/s perpendicular to the pores. We hypothesize that the (squared) ratio of the two velocities correlates with the porosity and, hence, a device measuring the velocity in both directions might be a useful tool for the *in vivo* estimation of cortical porosity. In a previous approach we developed a device to measure these velocities (in axial and tangential direction) simultaneously [22]. For axial transmission measurements a minimum transducer distance is required to receive the ultrasound wave propagating through the bone earlier than the ultrasound wave propagating through the soft tissue only. It turned out that the limited widths of the human tibiae make a bidirectional transmission in tangential direction difficult because not in all bones the minimal required transducer separation can be achieved. To pursue this purpose the new device exploits the effect of the cosine behavior of velocity. Because bone is a transverse isotropic medium the velocity profile follows a cosine curve with its maximum in axial direction and its minimum in tangential direction [31]. Our device is capable of measuring ultrasound velocities in five different paths with three of them parallel to each other and two tilted by an angle of 37.5°. With these velocities measured under different angles it should be possible to estimate the velocity in tangential direction. In combination with the axial velocity, which will be measured along the axis of the bone, an anisotropy index could be calculated which is expected to correlate with cortical porosity. The calibration curve of this correlation should be obtained on human tibia bones *ex vivo*. Measuring velocities on long bones may be subject to additional error sources e.g. due to variable curvature of the surface of the bone. The aim of the study presented in this paper was to present a new device and method to estimate porosity from ultrasonic measurements and to evaluate its capabilities regarding the sensitivity to porosity and the impact of error sources like positioning and curvature. For this two sets of isotropic phantoms were measured: the first set exhibits varying porosities and the second differing curvatures. These data provide the basis to derive measurement protocols and analysis algorithms suited for the assessment of cortical porosity on human bones. The here found influence of porosity on ultrasound velocities in different directions has been presented previously [32].

2. Materials and method

2.1. Measurement method

The cortical compartment of long bones is usually measured using the axial transmission method [33]. For this method at least one emitter and one receiver placed on the same side of the bone are required. The emitter excites an ultrasonic wave which passes through the coupling medium (e.g. soft tissue, water) and impinges on the specimen (e.g. bone). The part of the wave which impinges under the critical angle travels along the surface of the specimen and constantly emits energy back into the coupling medium which can be detected by the receiver. A minimum distance between emitter and receiver is crucial to receive the ultrasound wave travelling through the specimen prior to the ultrasound wave passing through the coupling medium. This distance d is determined by the ratio of the coupling medium velocity SOS_{CM} (Speed of Sound, approximately 1480 m/s) to the specimen velocity SOS_S and the thickness of the coupling medium h:

$$d > h * \frac{2}{\cos(\alpha)} * \left(1 + \frac{SOS_{CM}}{SOS_S}\right) \tag{1}$$

with α being the critical angle: $\sin(\alpha) = SOS_{CM}/SOS_S$. For a rough estimation, the distance has to be 4 times as large as the coupling medium thickness for SOS_S = 2770 m/s and 3 times as large for SOS_S = 3900 m/s.

To eliminate the influence of the thickness of the coupling medium on the velocity measurement, at least two receivers in line with the emitter are necessary. The difference in time of flight (TOF) of the signals received is used in combination with the distance between the receivers s for SOS calculation:

$$SOS = s/\Delta TOF \tag{2}$$

To improve the accuracy of the measurements with regard to an inconstant coupling medium thickness a bidirectional axial transmission technique is used. As described in [34], a second emitter is placed opposite of the first one in line with the receivers, so that SOS in a given direction (+) and the opposite direction (−) are measured. The harmonic mean of the two SOS values measured using both emitters is less susceptible to an inclination angle than each SOS value on its own:

$$SOS = 2 * (1/SOS^{+} + 1/SOS^{-}) \tag{3}$$

2.2. The device

The device consists of a PC, new electronics developed in our lab and the probe. The probe was developed in cooperation with Smart Material GmbH (Dresden, Germany). Six emitters and receivers are arranged in a unique design to allow the measurement of different