Ultrasonic Scattering Models for Cancellous Bone

Pacs reference : 43.80.Qf (Medical diagnosis with acoustics)

PADILLA Frédéric ; JENSON Frédéric, LAUGIER Pascal
Laboratoire d'Imagerie Paramétrique CNRS UMR 7623 – Université Paris 6
15 rue de l'Ecole de Médecine
75006 PARIS
France
Tel : 33 1 44 41 49 60
Fax : 33 1 46 33 56 73
e-mail : padilla@lip.bhdc.jussieu.fr

ABSTRACT
Quantitative ultrasound (QUS) in transmission has played a growing role in the assessment of osteoporosis. It is generally accepted that transmission QUS represents a surrogate marker for bone mineral density. Scattering techniques may be useful for the assessment of bone micro-architecture, an independent predictor of fracture risk. We will review recent experimental data (*in vitro* and *in vivo*) as well as theoretical modeling of ultrasound scattering by cancellous bone. Good agreement between experimental data and predictions has been reported for the frequency-dependent backscatter coefficient. In addition, *in vivo* data showed that the ultrasound backscatter was significantly associated with fracture risk.

1. INTRODUCTION

Cancellous bone is a highly porous and inhomogeneous medium, composed of a solid matrix (mineralized collagen) of interconnected trabeculae with diameter ranging from 50 to 200 µm filled with marrow. Cancellous bone loss due to aging or osteoporosis leads to increased porosity, thinning or even total disappearance of some trabecular elements and disruption of structure continuity. The complex micro architecture of trabecular bone plays an important role in the biomechanical properties of bone. Hence, the ability to non destructively characterize the micro architecture of the trabecular network would be useful for the evaluation of bone pathologies like osteoporosis that affect this component of bone. In past years, considerable efforts have been devoted to developing new methods to assess non-invasively bone micro-architecture, among these, magnetic resonance microimaging [1-4], high resolution peripheral quantitative computed tomography [5] and radiographic image processing techniques [6-11].

Quantitative ultrasound (QUS) is increasingly used for non invasive assessment of osteoporotic fracture risk. Measurements of bone velocity and slope of attenuation are performed in transmission at peripheral skeletal sites, the calcaneus being the most frequently used measurement site [12]. In earlier views, QUS techniques have been advocated to have the potential to measure bone quality (i.e., micro architecture and material properties). To date the ability to characterize bone micro architecture independently of bone mineral density (BMD) in a way that could be of any significance in clinical measurements has been rather disappointing (Measurement of Bone Mineral Density or BMD is the reference technique for the diagnosis of osteoporosis. It relies on a measurement of absorption of the X rays by bone tissues). The relationships of quantitative ultrasound variables and micro architecture of trabecular bone have been the source of several independent investigations [13-20]. Most of these studies concluded that ultrasonic measurements in transmission performed on human cancellous bones reflected primarily bone quantity rather than structural parameters [14-17,19]. All these results suggest

that there is only very limited room for structural factors to play a role in current QUS measurements performed in transmission (i.e., BUA and SOS) [19].

Transmission measurements only partially exploit the information related to the interaction between the elastic wave and bone micro architecture. Ultrasonic backscatter measurements at the calcaneus have recently been introduced for their potential to directly assess the micro structure of trabecular bone, e.g. trabecular thickness and trabecular number density [21,22]. Based on the experience with measurements in soft tissue, ultrasonic tissue characterization using the analysis of backscattered signals has shown the potential to provide the information needed for the characterization of tissue microstructure [23,24]. Ultrasonic waves are affected by obstacles or inhomogeneities, such as discontinuity in density and/or elasticity. Small obstacles give rise to a scattered wave radiated in all directions. Cancellous bone can be considered as a highly inhomogeneous scattering medium. The quantity used for measuring scattering from biological tissue is the backscatter coefficient. Because the backscatter coefficient is related to medium characteristics such as the average density number (i.e., number of scatterers per unit volume), size, separation, orientation, and scattering strength (i.e, material properties) of scatterers, this parameter may be sensitive to micro architectural changes.

The general idea of the present paper is to review recent experimental data (*in vitro* and *in vivo*) as well as theoretical modeling of ultrasound scattering by cancellous bone. We will show that initial *in vivo* measurements have demonstrated the potential of backscatter measured at the calcaneus to assess bone status and to discriminate normal from osteoporotic patients. We will also see that new approaches to model ultrasonic scattering from cancellous bone have opened perspectives for the application of such approaches to non-invasive assessment of bone micro architecture.

2. EXPERIMENTAL RESULTS

2.1 *In vitro* measurements

Since a few years, the scattering properties of trabecular bone have been revealed by different groups with measurements of ultrasonic backscatter coefficient [20,21,25-27].

In a recent study [28], we have measured in vitro the backscatter coefficient on calcanei samples. Bone specimens were obtained from human calcanei by slicing off the cortical lateral faces to leave a 1 cm thick slice of pure trabecular bone. They were defatted and saturated with water. The ultrasound beam propagated perpendicular to the faces in the medio-lateral direction (perpendicular to the main orientation direction of the trabeculae), as with the clinical devices for transmission measurements. The experimental procedure is summarized by Fig. 1.

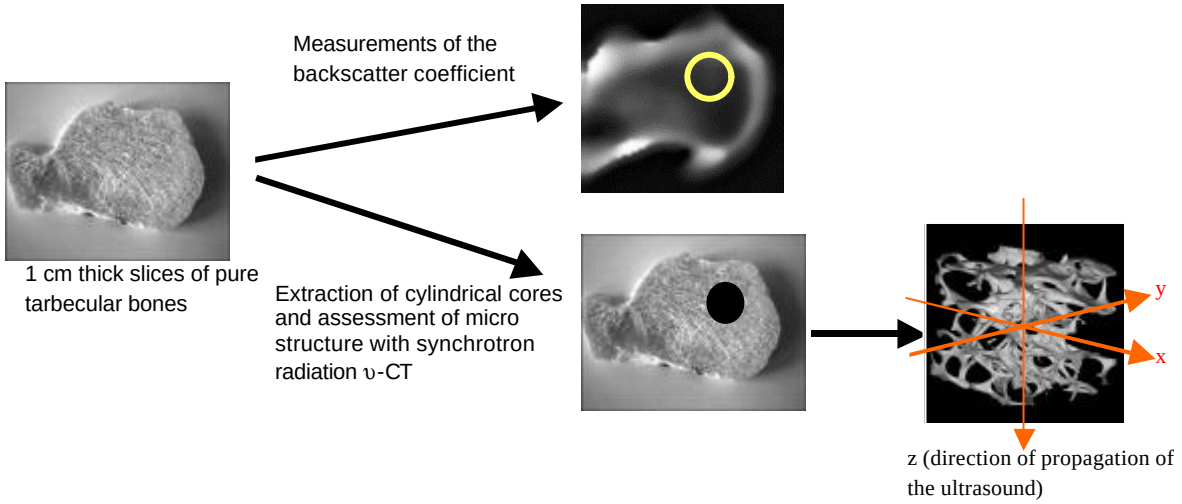

Figure 1 : Experimental procedure.

Measurements of both the ultrasonic attenuation and backscatter coefficients were performed with two focused transducers of 1 MHz central frequency, in a frequency range of 0.4–1.2 MHz. Classical substitution methods were used to obtain the two coefficients. Corrections were made to compensate for the transducer characteristics. Two-dimensional scans were performed on the bone specimens, with steps of 1 mm. Finally, 19 regions of interest (ROIs) of 7*7 mm^2 were selected, containing 49 measurement points. For each ROI, averaged attenuation and backscatter coefficients were calculated by spatially averaging the values obtained at each point of the scan. The experimental procedure has been described in a previous paper [29].

It was found that the frequency dependence of the backscatter coefficient was on average over the 19 specimen : $f^{3.4}$. This takes place between the Rayleigh scattering regime by a cylinder (f^3) and by a sphere (f^4). This results suggests that scattering could be due to the trabeculae, and we will discuss this point in the theoretical section.

In a second step, cylindrical cores were extracted from the specimen, corresponding to the location of the selected ROIs. Then the 3D micro architecture of the cores was analyzed with synchrotron radiation μ–CT at ESRF in Grenoble, France. It resulted in 3D numerical images of the trabeculae micro architecture [28] with a spatial resolution of 10 μm (Fig. 1). From these models, several micro structural parameters have been computed, like the mean trabecular thickness (Tb.Th=78±17 μm), the mean trabecular spacing (Tb.Sp=0.76±0.2 mm) or the mean porosity (β=0.92±0.03).

Based on these experimental results, the correlation between the QUS parameters and the micro structural parameters have been studied [20]. The association of the ultrasonic variables with density and micro architecture was assessed using simple and multivariate linear regression techniques. For all ultrasonic variables, a strong association was found with density (BMD) (r = 0.84-0.90). We also found that, with the exception of connectivity, all micro structural parameters correlated significantly with density, with r values of 0.54-0.92. For most micro structural parameters there was a highly significant correlation with ultrasonic parameters (r = 0.33-0.91). However, the additional variance explained by micro structural parameters compared with the variance explained by BMD alone was small (Delta r(2) = 6% at best). In particular, no significant independent association was found between microstructure and backscatter coefficient after adjustment for density. This last result may be explained by the strong correlation between micro structural parameters and density.

2.2 *In vivo* measurements

Initial *in vivo* measurements have demonstrated the potential of backscatter measured at the calcaneus to assess bone status and to discriminate normal from osteoporotic patients [22,30,31]. In a recent study [31], we have examined 210 postmenopausal women (including 60 with osteoporotic fractures) and 30 healthy premenopausal controls and shown that integrated backscatter coefficient (also called BUB for Broadband Ultrasound Backscatter) has adequate ability to discriminate osteoporotic patients from controls.

However, the clinical utility of BUB at the os calcis, in addition to usual ultrasound parameters (BUA and SOS), is not yet proven. This may be due to a lack of scattering models needed to address the inverse scattering problem in order to provide quantitative measurements of micro structural and material features of bone.

3. THEORETICAL RESULTS

The estimation of tissue micro architectural features from backscatter data belongs to the class of inverse problems and has been successfully addressed in the field of soft tissue characterization [24,32]. This approach requires the development of specific appropriate scattering models : Estimates of scatterers characteristics, such as scatterer size or scattering strength, are obtained by a least-squares fit of the scattering model to experimental data. It has been successfully applied to estimate structural characteristics of normal and pathological

human tissues such as the kidney [33,34], the liver [35,36] or the eye [36]. Recent developments of theoretical scattering models for cancellous bone have opened perspectives for the application of such approaches to non-invasive assessment of bone micro-architecture.

Two different approaches have been proposed to model ultrasonic scattering from cancellous bone, both assuming single scattering.

The first approach, proposed by Wear [27], consists in solving the differential propagation equations in the ambient fluid and in the scatterers, and then to use the appropriate boundary conditions at the interface between fluid and scatterers. Analytical solutions can be derived for canonical geometries. In Wear's model, the trabecular network is represented by an assembly of randomly distributed identical parallel cylindrical scatterers, aligned perpendicular to the direction of propagation of the incident wave. Assuming no multiple scattering, the backscatter coefficient of a collection of scatterers is obtained by the summation of the backscatter coefficient of each scatterer. The backscatter cross-section of individual scatterers was computed using the analytical model of Faran [37]. The model proposed by Wear has given predictions of the frequency dependence of the backscatter coefficient which were in good agreement with experimental observations in the low frequency range.

The second approach consists in considering the medium as a fluid random continuum. The inhomogeneities are described as source terms which perturb the homogeneous wave equation in the ambient fluid. With the help of a Green function, the scattered pressure field is calculated by integrating the contribution of each source over a volume containing the scatterers. This scattered pressure can be expressed as a function of the spatial Fourier transform of a function describing the random inhomogeneities in density and compressibility [24]. This approach usually assumes weak scattering (Born hypothesis). For statistically homogeneous systems, one may perform an average of the values of the backscatter coefficient at different positions (equivalent to an average over different realizations of the process), and then relate the backscatter coefficient to the autocorrelation function of the medium. This method is classically used to describe scattering by inhomogeneities in soft tissues [24]. In order to apply such a model to bone, Strelitzki [38] and Nicholson [39] have suggested to model trabecular bone as a two-phase mixture. In their approach, fluctuations in sound speed accounted for scattering and an exponential autocorrelation function was used to describe the statistical properties of the random medium. The authors have shown that the order of magnitude of the model predictions was similar to some experimental values published by others, but no accurate comparison with experimental data was provided in their work.

We have developed a similar approach, but instead of using an exponential autocorrelation function to describe the medium, we have used data provided by high-resolution synchrotron radiation micro-computed tomography (μ-CT). First, these data allow the reconstruction of 2D and 3D bone micro architecture with a spatial resolution of 10 μm. Second, an autocorrelation function was derived from two dimensional micro-computed tomography reconstructions of bone micro-architecture [28] and was used to compute the frequency dependence of the backscatter coefficient. This has resulted in close agreement between theoretical prediction of the frequency dependence of the backscatter coefficient and experimental data. One potential advantage of the random continuum approach over the discrete cylindrical model of Wear is a greater flexibility in representing the actual bone micro-architecture by using the data derived from the now available powerful high resolution micro-imaging techniques such as synchrotron radiation or Xray μ-CT. In particular, the calculation can be achieved individually for each bone specimen, by taking into account the specific micro-architecture derived from μ -CT of each specimen under study.

Recently, we have improved this model [40]. Assuming that the Born approximation is valid, the backscatter coefficient may be related to the spatial Fourier transform of the spatial fluctuations in density and compressibility. For the computations, the geometrical characteristics of the medium were obtained directly from an analysis of the 3D images of micro structure, and the following values were assumed : ρ_w = 1000 kg/m^3 and c_w = 150 m/s in water, ρ_b = 1980 kg/m^3 and c_b = 3200 m/s in bone. The result is presented on the figure 2. The predictions of the frequency dependence and for the first time of the magnitude of the backscatter coefficient are in good agreement with experimental values. This validates the weak sacttering approximation

a posteriori. However, The limit of this approach lies in the fact that the micro architecture has to be perfectly known in order to compute the backscatter coefficient.

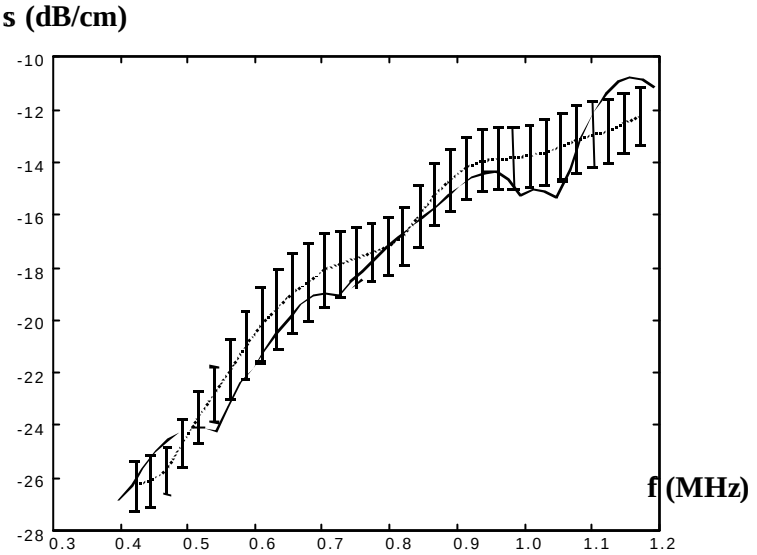

Figure 2 : Averaged backscatter coefficient over the 19 ROIs as a function of the frequency. Plain line : simulation, dashed line : experiment. Error bars : standard error.

Finally, in order to address this inverse problem, we proposed to use the weak scattering model and to express the backscatter coefficient in terms of analytical autocorrelation function of the medium [41]. Different autocorrelation functions (Gaussian, exponential and dense media) were used to compute the backscatter coefficient. Comparison was made with experimental data obtained on 19 human specimens of calcanei and for frequency ranging from 0.4 to 1.2 MHz. For each specimen a non-linear regression was performed and the mean trabecular thickness was estimated. Experimental and modeled data were averaged over the 19 specimens. Good agreement between experimental data and predictions was found for the magnitude and the frequency dependence of the backscatter coefficient. A seen on Fig.3, we also found a good agreement between the experimental mean trabecular thickness (Tb-Th=130±6.5 µm) derived from the 3D images of microarchitecture (high resolution micro tomography) and theoretical predictions (d_{Gauss}=140±10 µm, $d_{exponential}$=153±12.5 µm and d_{dense}=138±6.5 µm). These results open interesting prospects for the assessment of bone micro architecture from ultrasonic backscattering measurements.

4. CONCLUSION

In the context of assessment of bone status with ultrasound, the potential of backscatter coefficient measurement to discriminate normal from osteoporotic patients has been demonstrated. Its clinical utility, however, in addition to usual ultrasound parameters measured in transmission (BUA and SOS), is not yet proven.

As it has been done in the studies of soft tissues, the actual works are orientated towards the propagation models, in order to solve the inverse scattering problems. A first estimation of trabecular thickness has been obtained, and further work should be done to improve these predictions and to determine the sensitivity of the model.

Another interesting point of the future developments is the simulation of « virtual » osteoporosis by means of image processing on 3D images of bone micro architecture. Computing the backscatter coefficient on these images should allow to test different models and to determine which signal processing has to be apply to in vivo data in order to extract information on bone micro architecture from ultrasound measurements.

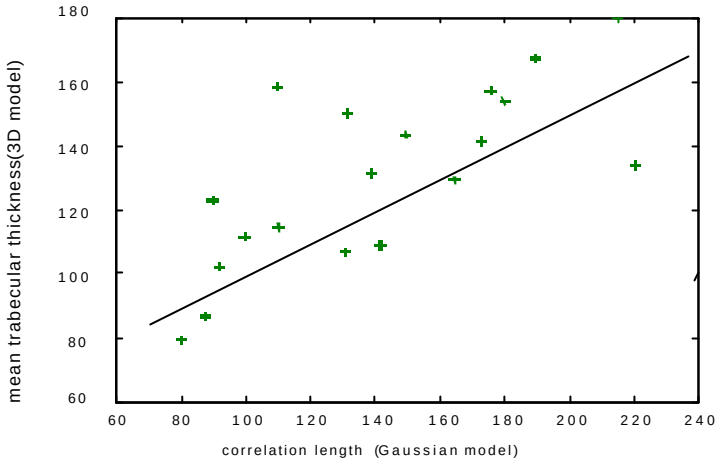

Figure 3 : Mean trabecular thickness computed on the 3D images of the samples, as a function of the correlation length estimated for each sample with the weak scattering medium model and Gaussian autocorrelation function. Straight line : regression line.

5. BIBLIOGRAPHY

1. Gordon *et al.* Med. Phys. 24:585-593; 1997.
2. Link *et al.* J. Bone Miner. Res. 13:1175-1182; 1998.
3. Majumdar *et al.* Osteoporosis Int. 6:376-385; 1996.
4. Majumdar *et al.* J. Bone Miner. Res. 12:111-118; 1997.
5. Müller *et al.* J. Bone Miner. Res. 11:1745-1750; 1996.
6. Benhamou *et al.* J. Bone Miner. Res. 9:1909-1917; 1994.
7. Caligiuri *et al.* Med. Phys. 21:503-508; 1994.
8. Cortet *et al.*. Osteoporosis Int. 9:410-419; 1999.
9. Geraets *et al*. Bone 22 : 165-173; 1998.
10. Lespessailles *et al.* Rev. Rhum. [Eng Ed] 63:337-343; 1996.
11. Pothuaud *et al.* Osteoporosis Int. 8:618-625; 1998.
12. Njeh, Hans, Fuerst, Glüer, Genant. *Quantitative ultrasound: assessment of osteoporosis and bone status*. London:Martin Dunitz; 1999.
13. Glüer *et al.* Osteoporosis Int. 3: 185-191;1993.
14. Glüer *et al*. Calcif. Tissue Int. 55: 46-52; 1994.
15. Hans *et al*. Bone 16:295-300; 1995.
16. Hans *et al*. Calcif. Tissue Int. 64: 18-23; 1999.
17. Häusler *et al*. Calcif. Tissue Int. 64:477-480; 1999.
18. Nicholson *et al*. Phys. Med. Biol. 39: 1013-1024; 1994.
19. Nicholson *et al*. Bone, 23:425-431; 1998.
20. Chaffai *et al*. Bone. 2002 Jan;30(1):229-37.
21. Roberjot *et al*. Schneider, S. C., Levy, M., and McAvoy B.R., Eds. IEEE 1997 Ultrasonics Symposium proceedings. New York : Institute of Electrical and Electronic Engineers; 1996; 1123-1126.
22. Wear and Garra. Ultrasound Med. Biol. 24:689-695; 1998.
23. Insana *et al*. J. Acoust. Soc. Am. 87:179-192; 1990.
24. Shung and Thieme. *Ultrasonic scattering in biological tissues*. Boca Raton : CRC Press; 1993.
25. Wear IEEE UFFC,47, 777-780, 2000.
26. Wear J. Acoust. Soc. Am., 107, 3474-3479, 2000.
27. Wear. J. Acoust. Soc. Am., 106, 3659-3664, 1999.
28. Chaffaï *et al*. J. Acoust. Soc. Am., 108, 2403-2411, 2000.
29. Chaffai *et al*., J. Acoust. Soc. Am., 108, 1281-1289, 2000.
30. Laugier *et al*. Schneider, S. C., Levy, M., and McAvoy B.R., Eds. IEEE 1997 Ultrasonics Symposium proceedings. New York : Institute of Electrical and Electronic Engineers; 1997; 1101-1103.
31. Roux et al., J. Bone Miner. Res., 16, 1353-1362, 2001.
32. Nassiri and Hill. J. Acoust. Soc. Am., 76, 2048-2054, 1986.
33. Insana, J. Acoust. Soc. Am., 97, 649-655, 1995.
34. Insana *et al.* Ultrasound Med. Biol. 17, 613-626, 1991.
35. Waag *et al.* J. Acoust. Soc. Am., 85, 423-431, 1989.
36. Lizzi et al. IEEE UFFC, 33, 319-329,1986.
37. Faran, J. Acoust. Soc. Am., 23, 405-418, 1951.
38. Sreelitzki et al. Physiol. Meas., 19, 189-196, 1998.
39. Nicholson *et al*. J. Biomech., 33, 503-506, 2000.
40. Padilla *et al*. Submitted to J. Acoust. Soc. Am., 2002.
41. Jenson *et al*. Submitted to Ultrasound Med. Biol, 2002.