1. J. R. Soc. Interface (**2009**) 6, 97–109

The influence of mesoscale porosity on cortical bone anisotropy. Investigations via asymptotic homogenization

William J. Parnell and Quentin Grimal

Recently, the **mesoscale of cortical bone** has been given particular attention in association

with novel experimental techniques such as nanoindentation, micro-computed X-ray

tomography and quantitative scanning acoustic microscopy (SAM).

A need has emerged for **reliable mathematical models to interpret the related microscopic and mesoscopic data in terms of effective elastic properties**. In this work, a new model of **cortical bone elasticity** is developed and used to **assess the influence of mesoscale porosity** on the induced anisotropy of the material. **Only the largest pores** (Haversian canals and resorption cavities), characteristic of the mesoscale, are considered.

The input parameters of the model are derived from typical mesoscale experimental data (e.g. SAM data). We use the **method of asymptotic homogenization** to determine the **local effective elastic properties** by modelling the **propagation of low-frequency elastic waves** through an **idealized material** that models the local mesostructure. We use a novel **solution of the cell problem** developed by Parnell & Abrahams.

This **solution is stable** for the physiological range of variation of mesoscopic porosity and elasticity found in bone. Results are **computed** **efficiently** (in seconds) and the

solutions can be implemented easily by other workers. Parametric studies are performed in

order to assess the influence of mesoscopic porosity, the assumptions regarding the material inside the mesoscale pores (drained or undrained bone) and the shape of pores. Results are shown to be in **good qualitative agreement** with existing schemes and we describe the potential of the scheme for future use in modelling more complex microstructures for cortical bone. In particular, the scheme is shown to be a useful tool with which to predict the qualitative changes in anisotropy due to variations in the structure at the mesoscale.

1. Bone Volume 49, Issue 5, November **2011**, Pages 1020-1026

Change in porosity is the major determinant of the variation of cortical bone elasticity at the millimeter scale in aged women

Mathilde Granke, Quentin Grimal et al.

At the **mesoscale** (i.e. over a few millimeters), **cortical bone** can be described as two-phase composite material consisting of **pores** and a **dense mineralized matrix**. The cortical porosity is known to influence the mesoscopic elasticity.

Our objective was to determine whether the **variations of porosity** are sufficient to predict the **variations of bone mesoscopic anisotropic elasticity** or if change in bone matrix elasticity is an important factor to consider.

We measured **21 cortical bone specimens** prepared from the mid-diaphysis of 10 women donors (aged from 66 to 98 years). A 50-MHz scanning acoustic microscope (SAM) was used to evaluate the bone matrix elasticity (reflected in impedance values) and porosity. Porosity evaluation with SAM was validated against Synchrotron Radiation μCT measurements. A standard contact ultrasonic method was applied to determine the mesoscopic elastic coefficients. Only matrix impedance in the direction of the bone axis correlated to mesoscale elasticity (adjusted R2 = [0.16–0.25], p < 0.05). The mesoscopic elasticity was found to be highly correlated to the cortical porosity (adj-R2 = [0.72–0.84], p < 10−5). Multivariate analysis including both matrix impedance and porosity did not provide a better statistical model of mesoscopic elasticity variations. Our results indicate that, for the elderly population, the elastic properties of the mineralized matrix do not undergo large variations among different samples, as reflected in the low coefficients of variation of matrix impedance (less than 6%). This work suggests that **change in the intracortical porosity accounts for most of the variations of mesoscopic elasticity**, at least when the analyzed porosity range is large (3–27% in this study). The trend in the variation of mesoscale elasticity with porosity is consistent with the predictions of a micromechanical model consisting of an anisotropic matrix pervaded by cylindrical pores.

Highlights

► Cortical bone is a material consisting of pores and a mineralized matrix.

► Our goal was to identify the **determinants of elasticity at the millimeter scale** (mesoscale).

► Elasticity at meso and microscale and porosity were measured using ultrasound and SRCT.

► We found that **porosity explains most of the variations of mesoscopic elasticity.**

► The results are consistent with the predictions of a simple mechanical model.

1. Biomech Model Mechanobiol (**2012**) 11:883–901

Analytical methods to determine the effective mesoscopic and macroscopic elastic properties of cortical bone

William J. Parnell · M. B. Vu · Q. Grimal · S. Naili

We compare **theoretical predictions** of the **effective elastic moduli** of **cortical bone** at both the **meso- and macroscales**. We consider the efficacy of **three alternative approaches**: the method of asymptotic homogenization, the Mori–Tanaka scheme and the Hashin–Rosen bounds. The methods concur for specific engineering moduli such as the axial Young’s modulus but **can vary for others**. **In a past study**, the effect of porosity alone on mesoscopic properties of cortical bone was considered, taking the **matrix to be isotropic**.

Here, we consider the additional **influence of the transverse isotropy of the matrix**. We make the point that micromechanical approaches can be used in two alternative ways to predict either the **macroscopic** (size of cortical bone sample) or **mesoscopic** (in between micro- and macroscales) effective moduli, depending upon the choice of representative volume element size. It is widely accepted that the mesoscale behaviour is an important aspect of the mechanical behaviour of bone but models incorporating its effect have started to appear only relatively recently. Before this only macroscopic behaviour was addressed.

Comparisons are drawn with experimental data and simulations from the literature for macroscale predictions with particularly good agreement in the case of dry bone. Finally, we show how predictions of the effective mesoscopic elastic moduli can be made which retain dependence on the well-known **porosity gradient** across the thickness of cortical bone.

1. Biomech Model Mechanobiol (**2016**) 15:97–109

Elasticity–density and **viscoelasticity**–density relationships at the tibia mid-diaphysis assessed from resonant ultrasound spectroscopy measurements

Simon Bernard · Joannes Schneider · Peter Varga · Pascal Laugier ·Kay Raum · Quentin Grimal

**Cortical bone** tissue is an anisotropic material characterized by typically five independent elastic coefficients (for **transverse isotropy**) governing shear and longitudinal deformations in the different anatomical directions.

It is well established that the **Young’s modulus** in the direction of the bone axis of long bones has a strong relationship with **mass density**. It is not clear, however, whether relationships of similar strength exist for the other elastic coefficients, for they have seldom been investigated, and the results available in the literature are contradictory.

The objectives of the present work were to document the **anisotropic elastic properties of cortical bone** at the tibia mid-diaphysis and to elucidate their **relationships with mass density**. Resonant ultrasound spectroscopy (**RUS**) was used to measure the transverse isotropic stiffness tensor of **55 specimens** from 19 donors.

Except for Poisson’s ratios and the non-diagonal stiffness coefficient, strong linear correlations between the different elastic coefficients (0.7 < r 2 < 0.99) and between these coefficients and density (0.79 < r 2 < 0.89) were found. Comparison with previously published data from femur specimens suggested that the strong correlations evidenced in this study may not only be valid for the mid-tibia. **RUS also measures the viscous part of the stiffness tensor**. An anisotropy ratio close to two was found for damping coefficients. **Damping increased as the mass density decreased.** The data suggest that a relatively accurate estimation of all the mid-tibia elastic coefficients can be derived from mass density. This is of particular interest

(1) to **design organ-scale bone models** in which elastic coefficients are mapped according to Hounsfield values from computed tomography scans as a surrogate for mass density and

(2) to **model ultrasound propagation at the mid-tibia**, which is an important site for the in vivo assessment of bone status with axial transmission techniques.

1. J. Acoust. Soc. Am. 138 (1), July **2015** JASA-EL

Ultrasonic wave properties of human bone marrow in the femur and tibia

Satoshi Kawasaki, Ryohei Ueda, et al

Ultrasonic wave properties of **human bone marrow** obtained in the **femur** and **tibia** were measured using an **ultrasound pulse technique**.

The measured frequency range was **4–10 MHz**, and the temperature range was **30 C–40 C.**

The sound velocity was **1410 m/s**, and the attenuation coefficient was **4.4 dB/cm** at 36 C (**10 MHz**).

These values decreased with temperature. Site dependence and individual differences in elderly human bone marrow were negligible.

The **slopes of the attenuation coefficient** were estimated by a power law. The values of the exponent *n* were **2.0** (30 C–38 C) and 2.3 (40 C).

Note : see figure 2 *α* = *α*0 *f* n

*α* = *β f =>*

*n* between 2 and 2.3 y *α*0 about 0.04 dB cm-1 MHz -*n*

at **0.1 MHz**  *β* about 2\*0.04\*0.1 about 8 10-3 less than 1% about 0.01 dB cm-1 MHz -1

at **1 MHz**  *β* about 2\*0.04\*01 about 8 10-2 about 8% about 0.1 dB cm-1 MHz -1

*β* about 0.1 dB cm-1 MHz -1 = 0.01 dB mm-1 MHz -1 = 1.15 10-3 Np mm-1 MHz -1

with v = 1.4 mm.µs-1

at **0.1 MHz**

at **1 MHz**

at **0.5 MHz**

1. J Mech Behav Biomed Mater. **2015** October ; 50: 299–307.

Mechanics of Intact Bone Marrow

Lauren E. Jansen, Nathan P. Birch, et al

The current knowledge of bone marrow mechanics is limited to its **viscous properties**, **neglecting the elastic** contribution of the **extracellular matrix**.

To get a more complete view of the mechanics of marrow, we characterized intact **yellow porcine bone** marrow using three different, but complementary techniques: **rheology, indentation, and cavitation.**

Our analysis shows that **bone marrow is elastic**, and has a large amount of intra- and inter-sample heterogeneity, with an effective Young’s modulus ranging from **0.25–24.7 kPa** at physiological temperature.

Each testing method was consistent across matched tissue samples, and each provided unique benefits depending on user needs.

We recommend bulk rheology to capture the effects of temperature on tissue elasticity and moduli, indentation for quantifying local tissue heterogeneity, and cavitation rheology for mitigating destructive sample preparation.

We anticipate the knowledge of bone marrow elastic properties for building in vitro models will elucidate mechanisms involved in disease progression and regenerative medicine.

1. Am J Hematol. **2018** March ; 93(3): 430–441.

The Role of Extracellular Matrix Stiffness in Megakaryocyte Development and Function

Orly Leiva, Catherine Leon, et al …

*abstract*

The **extracellular matrix (ECM)** is a key acellular structure in constant remodeling to provide tissue cohesion and rigidity. Deregulation of the balance between matrix deposition, degradation and crosslinking results in fibrosis.

**Bone marrow fibrosis (BMF)** is associated with several malignant and nonmalignant pathologies severely affecting blood cell production. BMF results from abnormal deposition of collagen fibers and enhanced lysyl oxidase-mediated ECM crosslinking within the marrow, thereby increasing marrow stiffness.

**Bone marrow stiffness** has been recently recognized as an important regulator of blood cell development, notably by modifying the fate and differentiation process of hematopoietic or mesenchymal stem cells.

This review surveys the different components of the ECM and their influence on stem cell development, with a focus on the impact of the ECM composition and stiffness on the megakaryocytic lineage in health and disease. Megakaryocyte maturation and the biogenesis of their progeny, the platelets, are thought to respond to environmental mechanical forces through a number of mechanosensors, including integrins and mechanosensitive ion channels, reviewed here.

*in the text*

Bone Marrow ECM Stiffness: Measurement and Natural Contributors

Several ECM components in the BM contribute to the stiffness of the tissue. This property is

typically assessed by methods such as **rheometry and atomic force microscopy**. Rheometry involves measuring the **viscoelastic properties** of a substance by looking at the

relationship between deformations and stresses in order to calculate **Young’s modulus**, a

measurement for stiffness.

1. Bone Joint Res **2018**;7:524–538.

Standardizing compression testing for measuring the stiffness of human bone

S. Zhao et al.

**Objectives**

The ability to determine **human bone stiffness** is of clinical relevance in many fields, including bone quality assessment and orthopaedic prosthesis design. Stiffness can be measured using **compression testing**, an experimental technique commonly used to test bone specimens in vitro. This systematic review aims to determine how best to perform compression testing of human bone.

**Methods**

A keyword search of all English language articles up until December 2017 of compression testing of bone was undertaken in Medline, Embase, PubMed, and Scopus databases. *Studies using bulk tissue, animal tissue, whole bone, or testing techniques other than compression testing* ***were excluded.***

**Results**

A total of 4712 abstracts were retrieved, with 177 papers included in the analysis; **20 studies directly analyzed the compression testing technique to improve the accuracy of testing**. Several influencing factors should be considered when testing bone samples in compression. These include the method of data analysis, specimen storage, specimen preparation, testing configuration, and loading protocol.

**Conclusion**

Compression testing is a widely used technique for measuring the stiffness of bone but there

is a **great deal of inter-study variation in experimental techniques** across the literature. Based on best evidence from the literature, suggestions for bone compression testing are made in this review, although further studies are needed to establish standardized bone testing techniques **in order to increase the comparability and reliability of bone stiffness studies.**

**Article focus**

To provide a **comprehensive review** on the **experimental technique** of **compression testing of bone**.

To provide r**ecommendations** on how best to perform compression testing of bone in the future.

**Key messages**

There is a great deal of **inter-study variatio**n in the experimental technique for compression testing of bone.

Factors such as specimen preparation, specimen geometry, testing configuration, and strain rate can affect the measurement of bone stiffness.

Further studies looking specifically at aspects of the compression testing technique are required in order to establish a **standardized method for bone**.

**Strengths and limitations**

This review followed guidelines suggested by the Cochrane and Preferred Reporting Items for Systematic Reviews and Meta-Analyses organizations.

This review of compression testing can help to develop a standardized experimental bone testing technique in the future.

9) Journal of Biomechanics Volume 49, Issue 13, 6 September **2016**, Pages 2748-2755

Prevalent role of porosity and osteonal area over mineralization heterogeneity in the fracture toughness of human cortical bone

Mathilde Granke, Alexander J. Makowski et al.

Changes in the distribution of bone mineralization occurring with aging, disease, or treatment have prompted concerns that **alterations in mineralization heterogeneity may affect the fracture resistance of bone**. Yet, so far, studies assessing bone from hip fracture cases and fracture-free women have not reached a consensus on how heterogeneity in tissue mineralization relates to skeletal fragility.

Owing to the **multifactorial nature** of toughening mechanisms occurring in bone, we assessed the **relative contribution of heterogeneity in mineralization** to **fracture resistance** with respect to **age**, **porosity**, and **area fraction of osteonal tissue**.

The latter parameters were extracted from **quantitative backscattered electron imaging** of human cortical bone sections following R-curve tests of single-edge notched beam specimens to determine **fracture toughness properties**.

Microstructural heterogeneity was determined as the width of the mineral distribution (bulk) and as the sill of the variogram (local).

In univariate analyses of measures from 62 human donors (21 to 101 years), local but not bulk heterogeneity as well as pore clustering negatively correlated with fracture toughness properties. With age as covariate, heterogeneity was a significant predictor of crack initiation, though local had a stronger negative contribution than bulk. When considering all potential covariates, age, cortical porosity and area fraction of osteons explained up to 50% of the variance in bone׳s crack initiation toughness. However, including heterogeneity in mineralization did not improve upon this prediction.

The findings of the present work **stress the necessity to account for porosity and microstructure** when evaluating the potential of matrix-related features to affect skeletal fragility.

10) Bone Reports Volume 11, December **2019**, 100213

MRI-derived bone porosity index correlates to bone composition and mechanical stiffness

Abigail L. Hong, Mikayel Ispiryan et al

The **MRI-derived porosity index (PI)** is a non-invasively obtained biomarker based on an ultrashort echo time sequence that images both bound and pore water protons in bone, corresponding to water bound to organic collagenous matrix and freely moving water, respectively.

This measure is known to **strongly correlate** with the **actual volumetric cortical bone porosity**. However, it is unknown whether PI may also be able to directly quantify **bone organic composition** and/or **mechanical properties**.

We investigated this in **human cadaveric tibiae** by comparing PI values to **near infrared spectral imaging** (NIRSI) **compositional** data and **mechanical compression** data.

Data were obtained from a cohort of eighteen tibiae from male and female donors with a mean ± SD age of 70 ± 21 years. Biomechanical **stiffness** in compression and NIRSI-derived **collagen and bound water** content all had **significant inverse correlations with PI** (r = −0.79, −0.73, and −0.95 and p = 0.002, 0.007, and <0.001, respectively).

The MRI-derived bone PI alone was a moderate predictor of bone stiffness (R2 = 0.63, p = 0.002), and multivariate analyses showed that neither cortical bone cross-sectional area nor NIRSI values improved bone stiffness prediction compared to PI alone. However, NIRSI-obtained collagen and water data together were a moderate predictor of bone stiffness (R2 = 0.52, p = 0.04).

Our data validates the **MRI-derived porosity index** as a strong predictor of organic composition of bone and a **moderate predictor of bone stiffness**, and also provides preliminary evidence that NIRSI measures may be useful in future pre-clinical studies on bone pathology.

11) Computers in Biology and Medicine, Volume 114, November **2019**, 103457

Artificial neural network to estimate micro-architectural properties of cortical bone **using ultrasonic attenuation:** A 2-D numerical study

Kaustav Mohanty, Omid Yousefian et al.

The goal of this study is to estimate **micro-architectural parameters of cortical porosity** such as **pore diameter** (φ), **pore density** (ρ) and **porosity** (ν) of **cortical bone** from **ultrasound frequency dependent attenuation** using an artificial neural network (ANN).

First, heterogeneous structures with **controlled pore diameters and pore densities** (mono-disperse) were generated, to mimic simplified structure of cortical bone. Then, more **realistic structures** were obtained from high resolution CT scans of human cortical bone.

**2-D finite-difference time-domain simulations** were conducted to calculate the frequency-dependent attenuation in the **1–8 MHz range**. An ANN was then trained with the ultrasonic attenuation at different frequencies as the input feature vectors while the output was set as the micro-architectural parameters (pore diameter, pore density and porosity).

The ANN is composed of three fully connected dense layers with 24, 12 and 6 neurons, connected to the output layer. The dataset was trained over 6000 epochs with a batch size of 16. The trained ANN exhibits the ability to predict the micro-architectural parameters with high accuracy and low losses. ANN approaches could potentially be used as a tool to help inform physics-based modelling of ultrasound propagation in complex media such as cortical bone. This will lead to the solution of inverse-problems to retrieve bone micro-architectural parameters from ultrasound measurements for the non-invasive diagnosis and monitoring osteoporosis.

12) Journal of the Royal Society Interface (**2019**) 16(151)

Homogenization of cortical bone reveals that the organization and shape of pores marginally affect elasticity

Cai X, Brenner R, Peralta L et al.

With ageing and various diseases, the vascular pore volume fraction (porosity) in cortical bone increases, and the morphology of the pore network is altered. Cortical bone elasticity is known to decrease with increasing porosity, but the effect of the microstructure is largely unknown, while it has been thoroughly studied for trabecular bone.

Also, popular micromechanical models have disregarded several micro-architectural features, idealizing pores as cylinders aligned with the axis of the diaphysis.

The aim of this paper is to quantify the relative effects on **cortical bone anisotropic elasticity of porosity** and other descriptors of the **pore network micro-architecture** associated with **pore number,** **size** and **shape**.

The five stiffness constants of bone assumed to be a transversely isotropic material were measured with **resonant ultrasound spectroscopy** in 55 specimens from the femoral diaphysis of 29 donors.

The pore network, imaged with **synchrotron radiation X-ray micro-computed tomography**, was used to **derive the pore descriptors and to build a homogenization model** using the fast Fourier transform (FFT) method. The model was calibrated using experimental elasticity.

A detailed analysis of the computed effective elasticity revealed in particular that **porosity explains most of the variations of the five stiffness constants** and that the **effects of other micro-architectural features are small** compared to usual experimental errors.

We also have evidence that modelling **the pore network as an ensemble of cylinders yields biased elasticity values** compared to predictions based on the real micro-architecture.

The FFT homogenization method is shown to be particularly efficient to model cortical bone.

13) May **2020** Materialia 11:100730

Anisotropic elastic properties of human cortical bone tissue inferred from inverse homogenization and resonant ultrasound spectroscopy

X Cai et al

Abstract

**Bone extravascular matrix** (EVM) elasticity at several tens micrometer scale plays a key role in the mechanical behavior of bone at different length scales with implications on bone biology through mechanotransduction.

The elastic properties of cortical bone EVM have been evaluated by several experimental methods, including nanoindentation, scanning acoustic microscopy (SAM) and mechanical testing on μm sized bone specimens. Nevertheless, these methods hardly give access to elastic anisotropy.

In this work, we propose **a novel inverse homogenization method** to evaluate the **anisotropic elastic properties of cortical bone EVM** based on the transverse isotropic elastic tensor of millimeter-sized bone specimens measured by using **resonant ultrasound spectroscopy** and Fast Fourier Transform homogenization method.

With the inverse homogenization method, the anisotropic EVM stiffness constants were evaluated on 50 human femoral cortical bone specimens from an elderly group. To our knowledge, this is the first time that the whole set of the EVM stiffness tensor is evaluated on the same specimen and on a large number of samples.

Further comparison with the results from **SAM** and the **degree of mineralization** of bone (DMB) showed the potential of this method. Empirical laws between DMB and EVM anisotropic stiffness constants were also provided for the first time. With the anisotropic elasticity evaluated by the proposed method, more accurate models can be developed to better understand bone mechanics and biology, such as mechanotransduction.

14) May **2020** Bone 137:115446

Cortical thinning and accumulation of large cortical pores in the tibia reflect local structural deterioration of the femoral neck

G Iori et al

**Introduction:** Cortical bone thinning and a rarefaction of the trabecular architecture represent possible causes of increased femoral neck (FN) fracture risk. Due to X-ray exposure limits, the bone microstructure is rarely measurable in the FN of subjects but can be assessed at the tibia. Here, we studied whether changes of the tibial cortical microstructure, which were previously reported to be associated with femur strength, are also associated with structural deteriorations of the femoral neck.

**Methods**: The cortical and trabecular architectures in the FN of 19 humans were analyzed ex vivo on **3D microcomputed tomography images with 30.3 μm voxel size**. Cortical thickness (Ct.Thtibia), porosity (Ct.Potibia) and pore size distribution in the tibiae of the same subjects were measured using **scanning acoustic microscopy (12 μm pixel size)**. Femur strength during sideways falls was simulated with homogenized voxel finite element models.

**Results**: Femur strength was associated with the total (vBMDtot; R² = 0.23, p < 0.01) and trabecular (vBMDtrab; R² = 0.26, p < 0.01) volumetric bone mineral density (vBMD), with the cortical thickness (Ct.ThFN; R² = 0.29, p < 0.001) and with the trabecular bone volume fraction (Tb.BV/TVFN; R² = 0.34, p < 0.001), separation (Tb.SpFN; R² = 0.25, p < 0.01) and number (Tb.NFN; R² = 0.32, p < 0.001) of the femoral neck. Moreover, smaller Ct.Th tibia was associated with smaller Ct.ThFN (R² = 0.31, p < 0.05), lower Tb.BV/TVFN (R² = 0.29, p < 0.05), higher Tb.SpFN (R² = 0.33, p < 0.05) and lower Tb.NFN (R² = 0.42, p < 0.01). **A higher prevalence of pores with diameter > 100 μm in tibial cortical bone** (relCt.Po100μm-tibia) indicated higher Tb.SpFN (R² = 0.36, p < 0.01) and lower Tb.NFN (R² = 0.45, p < 0.01).

**Conclusion**: **Bone resorption and structural decline of the femoral neck** may be identified in vivo by measuring cortical bone thickness and large pores in the tibia.

15) Bone Volume 114, September **2018**, Pages 50-61

BMD-based assessment of local porosity in human femoral cortical bone

Gianluca Iori, Frans Heyer, Vantte Kilappa et al

<https://doi.org/10.1016/j.bone.2018.05.028>

* HR-pQCT provided reliable cortical porosity estimates in vitro.
* Local BMD was used to overcome the resolution-limit of conventional threshold-based cortical porosity estimations.
* A BMD-based multiparameter model can improve the cortical porosity assessment.
* The BMD inhomogeneity is a stronger porosity predictor than average BMD.

Abstract

Cortical pores are determinants of the elastic properties and of the ultimate strength of bone tissue. An increase of the overall cortical porosity (Ct.Po) as well as the local coalescence of large pores cause an impairment of the mechanical competence of bone. Therefore, Ct.Po represents a relevant target for identifying patients with high fracture risk. However, given their small size, the in vivo imaging of cortical pores remains challenging. The advent of modern high-resolution peripheral quantitative computed tomography (HR-pQCT) triggered new methods for the clinical assessment of Ct.Po at the peripheral skeleton, either by pore segmentation or by exploiting local bone mineral density (BMD). In this work, we compared BMD-based Ct.Po estimates with high-resolution reference values measured by scanning acoustic microscopy. A calibration rule to estimate local Ct.Po from BMD as assessed by HR-pQCT was derived experimentally. Within areas of interest smaller than 0.5 mm2, our model was able to estimate the local Ct.Po with an error of 3.4%. The incorporation of the BMD inhomogeneity and of one parameter from the BMD distribution of the entire scan volume led to a relative reduction of the estimate error of 30%, if compared to an estimate based on the average BMD. When applied to the assessment of Ct.Po within entire cortical bone cross-sections, the proposed BMD-based method had better accuracy than measurements performed with a conventional threshold-based approach.

17) Osteoporosis International volume 26, pages 2137–2146 (**2015**)

Measurement of cortical porosity of the proximal femur improves identification of women with nonvertebral fragility fractures

L. A. Ahmed, R. Shigdel, R. M. Joakimsen, O. P. Eldevik, E. F. Eriksen, A. Ghasem-Zadeh, Y. Bala, R. Zebaze, E. Seeman & Å. Bjørnerem

Summary

We tested whether **cortical porosity of the proximal femur measured using StrAx1.0 software** provides additional information to areal bone mineral density (aBMD) or Fracture Risk Assessment Tool (FRAX) in differentiating women with and without fracture. Porosity was associated with fracture independent of aBMD and FRAX and identified additional women with fractures than by osteoporosis or FRAX thresholds.

Introduction

Neither aBMD nor the FRAX captures cortical porosity, a major determinant of bone strength. We therefore tested whether combining porosity with aBMD or FRAX improves identification of women with fractures.

Methods

We quantified femoral neck (FN) aBMD using dual-energy X-ray absorptiometry, FRAX score, and femoral subtrochanteric cortical porosity using StrAx1.0 software in 211 postmenopausal women aged 54–94 years with nonvertebral fractures and 232 controls in Tromsø, Norway. Odds ratios (ORs) were calculated using logistic regression analysis.

Results

Women with fractures had lower FN aBMD, higher FRAX score, and higher cortical porosity than controls (all p < 0.001). Each standard deviation higher porosity was associated with fracture independent of FN aBMD (OR 1.39; 95 % confidence interval 1.11–1.74) and FRAX score (OR 1.58; 1.27–1.97) in all women combined. Porosity was also associated with fracture independent of FRAX score in subgroups with normal FN aBMD (OR 1.88; 1.21–2.94), osteopenia (OR 1.40; 1.06–1.85), but not significantly in those with osteoporosis (OR 1.48; 0.68–3.23). Of the 211 fracture cases, only 18 women (9 %) were identified using FN aBMD T-score < −2.5, 45 women (21 %) using FRAX threshold >20 %, whereas porosity >80th percentile identified 61 women (29 %). Porosity identified 26 % additional women with fractures than identified by the osteoporosis threshold and 21 % additional women with fractures than by this FRAX threshold.

Conclusions

Cortical porosity is a risk factor for fracture independent of aBMD and FRAX and improves identification of women with fracture.

16) Bone Volume 97, April **2017**, Pages 233-242

Intrinsic material property differences in bone tissue from patients suffering low-trauma osteoporotic fractures, compared to matched non-fracturing women

S.Vennin, A.Desyatova, J.A. Turner et al

<https://doi.org/10.1016/j.bone.2017.01.031>

Highlights

While bone density is important**, the intrinsic material property of bone is needed to understand** fracture risks in women.

**Nano indentation** testing provides information on intrinsic material properties of bone tissue.

**Women with fractures (Cases) had less heterogeneity** in their intrinsic material properties of cortical bone than Controls.

Abstract

Osteoporotic (low-trauma) fractures are a significant public health problem. Over 50% of women over 50 yrs. of age will suffer an osteoporotic fracture in their remaining lifetimes. While current therapies reduce skeletal fracture risk by maintaining or increasing bone density, additional information is needed that includes the intrinsic material strength properties of bone tissue to help develop better treatments, since measurements of bone density account for no more than ~ 50% of fracture risk. The hypothesis tested here is that postmenopausal women who have sustained osteoporotic fractures have reduced bone quality, as indicated with measures of intrinsic material properties compared to those who have not fractured. Transiliac biopsies (N = 120) were collected from fracturing (N = 60, Cases) and non-fracturing postmenopausal women (N = 60, age- and BMD-matched Controls) to measure intrinsic material properties using the nano-indentation technique. Each biopsy specimen was embedded in epoxy resin and then ground, polished and used for the nano-indentation testing. After calibration, multiple indentations were made using quasi-static (hardness, modulus) and dynamic (storage and loss moduli) testing protocols. Multiple indentations allowed the median and variance to be computed for each type of measurement for each specimen. Cases were found to have significantly lower median values for cortical hardness and indentation modulus. In addition, cases showed significantly less within-specimen variability in cortical modulus, cortical hardness, cortical storage modulus and trabecular hardness, and more within-specimen variability in trabecular loss modulus. Multivariate modeling indicated the presence of significant independent mechanical effects of cortical loss modulus, along with variability of cortical storage modulus, cortical loss modulus, and trabecular hardness. These results suggest mechanical heterogeneity of bone tissue may contribute to fracture resistance. Although the magnitudes of differences in the intrinsic properties were not overwhelming, this is the first comprehensive study to investigate, and compare the intrinsic properties of bone tissue in fracturing and non-fracturing postmenopausal women.

[Abueidda et al., 2017](https://www.sciencedirect.com/science/article/pii/S2352187219300191?via%3Dihub#bbb0005)

D.W. Abueidda, F.A. Sabet, I.M. Jasiuk**Modeling of stiffness and strength of bone at nanoscale**

J. Biomech. Eng., 139 (5) (2017)

[Google Scholar](https://scholar.google.com/scholar_lookup?title=Modeling%20of%20stiffness%20and%20strength%20of%20bone%20at%20nanoscale&publication_year=2017&author=D.W.%20Abueidda&author=F.A.%20Sabet&author=I.M.%20Jasiuk)

[Ahmed et al., 2015](https://www.sciencedirect.com/science/article/pii/S2352187219300191?via%3Dihub#bbb0010)

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