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# Canalicular Intrinsic Permeability in Human Femoral Cortical Bone assessed by 3D Synchrotron Nano-CT

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## 1. Introduction

Bone mechanobiology is known to be based on fluid flow within its multi-scale porous network. The development of pressure gradient within bone porosity promotes interstitial fluid flow. A fluid-flow induced shear stress is then transduced by the cells into mechanobiological mediators of bone modeling or remodeling. The osteocytes, which play a major role in bone mechanobiology, are particularly subjected to this mechanotransductive mechanism. Osteocytes are closely trapped within bone mineralized matrix inside the interconnected lacunocanalicular network (LCN). But due to its submicrometric nature, understanding how fluids circulate within this LCN is a real challenge. LCN fluid flow is mainly evaluated using computational modelling. Fluid flow through porous media is generally modelled using the Darcy's law. In this law, the ability of a fluid to circulate within a porous material is related to its viscosity and to the intrinsic permeability of the medium. In current computational models of LCN fluid flow, the

determination of these two parameters can be questioned. This is mainly due to the difficulty to characterize both the fluid and the porous network at the submicrometric scale. Recently, the LCN from 27 human femoral diaphyses were observed through Synchrotron Radiation Phase nano-Computed Tomography (Gauthier et al., 2023). Such data set allows to characterize the lacunar and canalicular morphology over large volumes of interest (up to  $10^7 \mu\text{m}^3$ ). In the present study, this data set was used to estimate the intrinsic permeability of human canalicular network.

## 2. Methods

In the current study, cortical bones samples were harvested from human femoral diaphyses (12 females (50 – 95 y.o.) and 9 males (66 – 89 y.o)). The samples have been scanned on line ID16B at the European Synchrotron Radiation Facility (Grenoble, France). Volumes of  $256 \times 256 \times 205 \mu\text{m}^3$  were reconstructed. The lacunae and canaliculi were segmented according to a previous published protocol (Yu et al., 2021). The canalicular network was converted into a network topology defined by links (canaliculi) connected at nodes (canalicular ramifications) (Weinkamer et al., 2019). A watershed algorithm was applied based on the 3D distance map of the canalicular volume, to create a tessellation in which each unit contains one canalicular. The intrinsic permeability of each canalicular was then calculated as (Lemaire et al., 2012):

$$\kappa = \frac{\eta_f \delta^2}{32\theta^2} (m^2), \quad \text{Eq.1}$$

where  $\eta_f$  (%) is the local volume fraction of the canalicular in its unit cell,  $\delta$  is the canalicular averaged diameter, and  $\theta$  is the canalicular tortuosity (geodesic length / straight length). Additionally, the density of canaliculi was calculated as the number of links (canaliculi) divided by the bone volume.

## 3. Results and discussion

The results showed a large heterogeneity in terms of canalicular intrinsic permeability within bone structure (Figure 1). The values obtained for the permeability in one sample ranged from  $10^{-14}$  to  $10^{-21} m^2$ . Qualitatively, the canalicular permeability seems higher close to the vascular canal and to the osteocytic lacunae. Such heterogenous distribution will have an influence on fluid velocity and pressure developed within the canalicular network during loading. It is hence relevant to consider it in further computational model of LCN fluid flow.

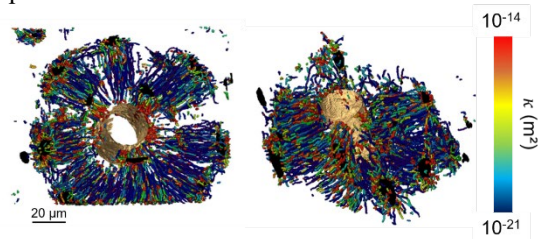


Figure 1: Permeability distribution in an osteon. Lacunae are in black.

For each sample, a permeability distribution was obtained over the total number of canaliculi. The three quartiles of this distribution, averaged over the whole population are provided in Table 1.

Table 1 Averaged permeability quartiles over the whole population and canalicular density.

Parameters	Q <sub>1</sub> (SD)	Q <sub>2</sub> (SD)	Q <sub>3</sub> (SD)
$\kappa$ ( $10^{-18} \text{ m}^2$ )	3.5 (1.7)	13.3 (6.0)	46.1 (16.8)
Density of canaliculi ( $10^6 \text{ mm}^{-3}$ )	$7.3 \pm 3.3$		

The permeability values are in accordance with what can be estimated with analytical methods (Lemaire et al., 2012). But the estimated value of bone LCN permeability is generally lower ( $< 10^{-18} \text{ m}^2$ ) (Benalla et al., 2014). This may be due to the fact that in the current study, the presence of a pericellular matrix within the canaliculi was not considered. This matrix decreases the permeability of the canaliculi. It is hence important to state that the current study is limited to a morphological-based LCN permeability.

It was measured that the permeability median ( $Q_2$ ) is significantly correlated to the donors' age ( $r_{\text{pearson}} = -0.64$ ,  $p\text{-value} = 0.001$ ). This means that it is more difficult to promote fluid flow within the LCN from older donors. This result is mostly due to an increasing tortuosity and decreasing canalicular volume fraction with age as validated by Pearson's correlation analyses ( $p\text{-value} = 0.006$  and  $0.001$  for tortuosity and volume fraction respectively).

This decrease in LCN permeability is in accordance with a less active bone remodeling with age. Evaluating the ability to promote fluid flow within the LCN with different permeabilities distribution might be of great interest to better understand the relation with remodeling and LCN fluid flow.

#### 4. Conclusions

One major insight provided by the current study is the large heterogeneous distribution of canalicular intrinsic permeability within bone structure. Furthermore, permeability has been shown to decrease with age. This provides new avenues of research concerning the understanding of bone remodelling mechanotransduction through the embedded osteocytic network according to patient specificities.

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