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**Is cortical porosity associated with degraded material quality ?** Aurelien Gourrier<sup>\*1</sup>, Delphine Farlay<sup>2</sup>, Helene Follet<sup>2</sup>, Georges Boivin<sup>2</sup>. <sup>1</sup>LIPHY CNRS Université Grenoble Alpes, France, <sup>2</sup>INSERM UMR 1033 Université de Lyon, France

The mineral nanoscale structure and organization are intrinsic determinants of bone quality. While these material characteristics have been shown to be altered in severe pathological state (e.g. fluorosis, OI), the extent of the fluctuations in healthy individuals is still not fully understood. This study aims to analyze the extent of nanoscale fluctuations that can be expected in a group of healthy individual which main morphological variability is cortical porosity. Transverse sections of 100  $\mu\text{m}$  in thickness were prepared from the lateral quadrant of the femoral mid-diaphysis of 26 donors aged 50–95 (12 men, 14 women). The samples were analyzed by quantitative scanning small-angle X-ray scattering (qsSAX-SI) using a synchrotron beam of 20  $\mu\text{m}$  in diameter which allowed resolving histological features. Images of the mineral nanoparticle thickness and organization were thus reconstructed with nanoscale resolution over the full cortical shell (up to 5 x 11 mm<sup>2</sup>). The global

mineral nanoparticle thickness distributions reported in fig.1a fall in a range of 3.5 – 4.1 nm (interquartile range), in good agreement with values found in the literature. Significant shifts in average thickness were found between samples, but these remain in a limited range (0.2 – 0.3 nm) as compared to known pathological modifications (e.g. > 1 nm for fluorotic bone). However, a closer examination of the images reveals spatial fluctuations well correlated with histology. In particular, lower thickness values are encountered in the vicinity of the cortical pores/voids. Furthermore, significant perturbations of the mineral organization (higher interparticle distance and shorter correlation length) were also observed (fig.1b) indicating ultrastructural tissue modifications. Our preliminary analysis tends to indicate that cortical bone porosity may be associated with a degraded material quality. While the limited changes in nanoparticle thickness suggests that the global mineralization mechanisms are essentially conserved, the perturbation in their organization indirectly points to alterations of the structure and/or organization of the tissue at the microfibril level. Because microfibrils have been shown to be the main determinants of microelasticity at the lamellar level, these tissue modifications should have an impact on the micro- to macroscopic biomechanical properties. Fig.1: (a) nanoparticle thickness (SAXS) vs age; (b) short range order ( $2\pi/a$ ) vs interparticle distance ( $2\pi/\beta$ ).

