ESRF	**Experiment title:** Osteolysis in arthroplasty: The influence of metal exposure in peri-implant bone on the osteocyte lacuno-canalicular network.	**Experiment number**: md1314
Beamline: ID16b	**Date of experiment**: from: 26/05/2022 to: 28/05/2022	**Date of report**: 6/9/2023
Shifts: 6	**Local contact(s)**: **Julie Villanova**	*Received at ESRF:*

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Report:

Background: In a recent study, we found that cobalt and chromium released from arthroplasty implants integrate into peri-implant bone [1]. Peri-implant metal exposure can induce sterile inflammation which leads to imbalanced bone remodeling and consequently to bone loss. It remains elusive whether metal integration into bone directly alters bone tissue (re-)modeling and homeostasis of calcium and phosphorus. These processes are mainly orchestrated by osteocytes. The bone cells with their complex network of dendrites are located in the lacunar-canclicular-network (LCN). Recent studies revealed mineral exchange at the LCN interfaces. A well-adjusted level of mineralization of bone tissue is achieved in healthy bone but may be altered under pathological conditions such as the above-mentioned peri-implant metal exposure.
The proposed project aims to perform nanoCT analyses of human ex vivo specimens to systematically investigate the influence of metal exposure on osteocyte lacunae and the lacunar-canalicular network. Nano-resolution, high sensitivity to mass density fluctuations a high sample throughput and sophisticated 3D image analyses are mandatory to understand the role of the LCN in the disturbed mineral homeostasis. The obtained results will provide new insights regarding the pathogeneses of metal exposure-induced peri-implant osteolysis an potential treatment strategy in the future. By learning more about the consequences of metal release from orthopedic implants we follow the overall aim to keep patients' safety at the highest possible level.

Experimental part: In total we have performed 112 scans from 22 individual samples. The X-ray energy was set to 29.6 keV. Of each sample, we have collected two to three single-distance scans at 240 nm voxelsize, 64 scans in total. For 48 of those, a high resolution scan at 50 nm spatial resolution was acquired. The high-resolution scans were obtained through collection of tomograms at 4 different sample detector distances as described previously [2]. The acquisition time per frame was 30 ms for each of the 3000 projections. The phase retrieval and reconstruction was performed as described previously [2].

Results: We could reconstruct all data and all data are largely exploitable. Some regions suffer from motion artefacts, probably induced by the X-ray dose during the scanning. The data are currently being analysed as described in the initial proposal: the morphology of the lacunar-canalicular network is quantified and related to the peri-iplant related metal release. Due to the complex segmentation of the LCN, this analysis is still ongoing. In Figure 1 the impact of the metal exposure on the LCN morphology can be seen. In the control bone (a), the osteocytes are interconnected with other osteocytes, but also canalicular connections to the osteoblasts at the trabcular rim are visible. This rim is lost after metal exposure (b). The osteoloytic sample nicely shows the particle exposure (lower right), as well as the loss of the interconnetivity of the LCN.

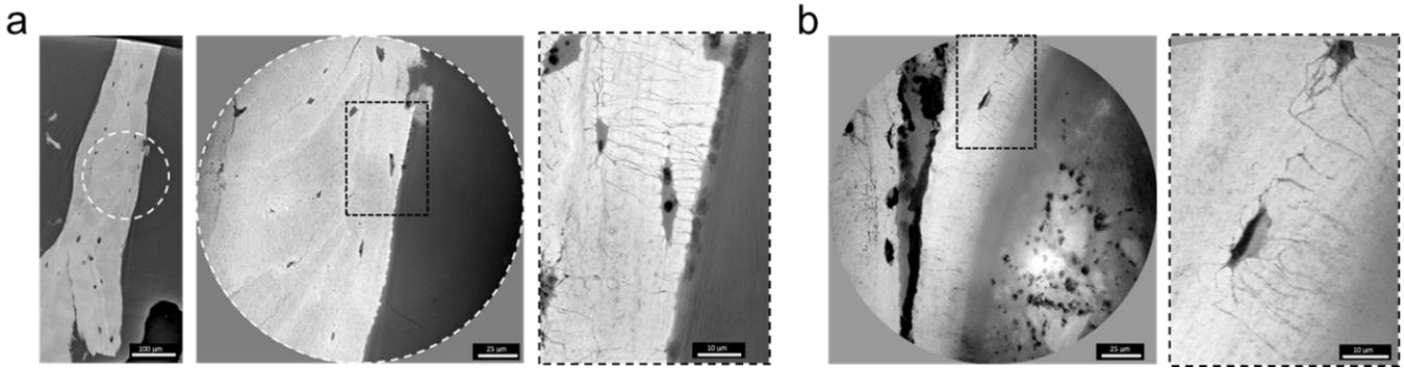

Figure 1: Comparison of 2D slices of nanoCT scans of a) a control sample and b) trabecular bone of an osteolytic sample.

In some of the data we observe bizare bone structures (Figure 2 left) with a high heterogenity between adjacent tissue (black and white arrows). Those unaffected and pathological regions are well seperated by cement lines, this is visible in the 240 nm scans as well as in the 50 nm scans (right). Here, we observe alterations of the cellular shape and interconnection which is going to be quantified.

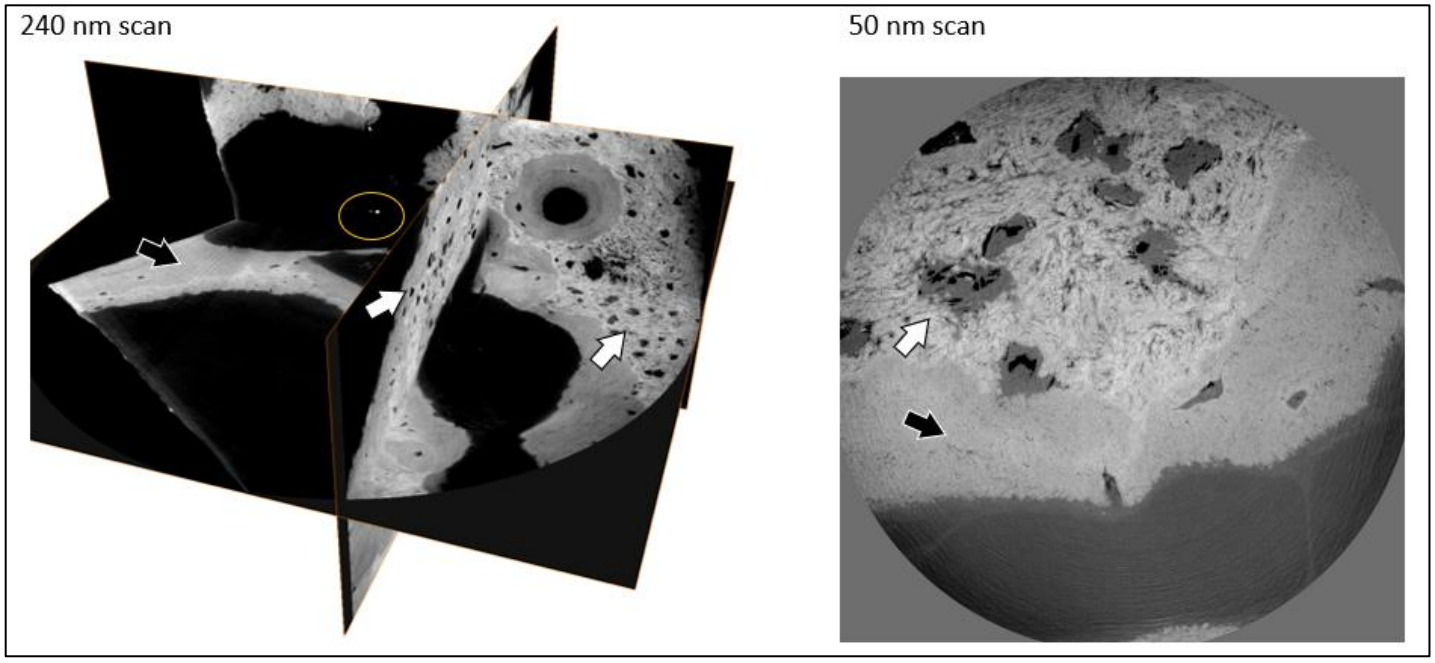

Figure 2: 240nm scan (left) and 50 nm scan (right) of the same sample. The three orthoslices in the left image show the 3D distribution of the osteolytic bone (white arrow). A metal particle is highlighted with a yellow circle. The disorganized regions are also found in the high resolution scans where the osteocytes seem bigger and less organized. There is a clear boundary to typical regions (black arrows). Also, there are more non-mineralized or delaminated regions (dark fiber-like structures).

References:

[1] J. Schoon, B. Hesse et al., Metal-Specific Biomaterial Accumulation in Human Peri-Implant Bone and Bone Marrow, Adv Sci (Weinh) 7(20) (2020) 2000412

[2] B. Hesse et al., Canalicular network morphology is the major determinant of the spatial distribution of mass density in human bone tissue: evidence by means of synchrotron radiation phase-contrast nano-CT, Journal of bone and mineral research 30(2) (2015) 346-56.