**Quantification of the Photon Counting CT Reproducibility And Its Implication For Detecting Bone Remodeling**

For the quantification of localized bone strength and bone changes, volumetric methods such as quantitative CT are to be preferred over conventional techniques such as DXA. This due to DXA being a two-dimensional technique, which is dependent on body frame [1]. However, the low resolution of conventional clinical CT limits direct implementation in health care. Photon Counting CT (PCCT) shows potential to overcome this limitation thanks to its higher resolution and better image contrast. The aim of this study was to quantify the reproducibility of PCCT and determine the least-detectable change in volumetric bone density.

Using PCCT (NAEOTOM Alpha, Siemens Healthineers), eighth cadaveric wrists were scanned twice with repositioning. For each wrist, the eight carpal bones were delineated. Images were registered onto each other and the difference image was calculated by voxel-wise subtraction. In parallel, a phantom was scanned and a linear relation was fitted, expressing volumetric bone density as a function of Hounsfield Unit (HU). Bone remodeling was defined as all voxels in the difference image that surpassed a predefined threshold and that were part of a cluster of at least 5 voxels.

Averaged over all samples, estimated mean intensity difference is 1.75 HU, and estimated standard deviation 142 HU. For a threshold of 250 mgHA/cm³, the total amount of falsely detected remodeling amounts to 0.31% (formation 0.14% +- 0.17%; resorption 0.17% +- 0.39%; Fig.1). This is an acceptable error, hence differences above this threshold are likely to be physiological in nature.

Our results compare well to HRpQCT. In a similar *ex vivo* study with HRpQCT, Christen et al. [2] reported 0.4% remodeling for a threshold of 225 mgHA/cm³. Using the same threshold in an *in vivo* analysis, remodeling increased to > 5%, due to motion artifacts. For *in vivo* analyses we hypothesize that PCCT may outperform HRpQCT because of the shorter acquisition time which limits these artifacts.

In conclusion, PCCT shows an excellent reproducibility when used for the quantification of volumetric bone density and results are comparable to HRpQCT. This study considers bone remodeling based on image intensity only; however, also voxel size plays an important role, which could favor HRpQCT. In future studies we will 1) repeat the analysis with *in vivo* measurements and 2) use PCCT for a follow-up study in patients.

[1] Alawi et al., Cureus 13(2) : e13261, 2021.

[2] Christen et al., PLoS One 13: e0191369, 2018.