3D UTE MRI derived porosity index as a practical approach to assess cortical bone porosity in human subjects

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Purpose: Increased intracortical and endocortical bone porosity has direct adverse affect on bone's mechanical competence and thus fracture resistance [1]. Since the majority of the pores in cortical bone (CB) are below the resolution limit achievable in vivo [2,3], microstructure of pores cannot be resolved even with the state of the art bone imaging methods such as high-resolution pQCT and MRI. One method relying on ultrashort echo time (UTE) imaging that has shown promise makes use of the much longer T2* of pore water relative to bound water (milliseconds versus several hundred microseconds for the latter) [4]. The method requires to invert the T2* signal decay to extract the two components. The method is laborious as it requires data collection for a large range of echo times. Here, we pursue a related approach by collecting only two echoes, one at the shortest possible TE and a second echo at much longer TE as part of a single 3D UTE scan, the idea being that the first echo contains essentially all water, the second predominantly pore water. The method was evaluated in specimens of human cortical bone against porosity derived from high-resolution μCT and the pore volume fraction obtained by bi-component analysis of multi-echo T2* decay signal. The reproducibility was tested in healthy volunteers.

Methods: _Bone Samples_—Cadaveric human whole cross-sectional cortical bone segments of thickness 36 mm from the 38% site of the tibia diaphysis were harvested from 9 female donors (age 27-97 years). _UTE imaging_—3D UTE imaging was performed using a 4-channel surface coil in a 3T whole-body MRI scanner (Siemens, Erlangen, Germany) with the following parameters: FOV = $160\times160\times160$ mm^3, TR = 12 ms, FA = 12° with 20 μs hard pulse duration, 50000 half-projections distributed uniformly within a sphere [5], 190 readout points per projection, gradient ramp time = 240 μs, readout bandwidth = 125 kHz. Twenty three UTE images were acquired using a series of TEs between TE=50μs to 7790 μs. Total imaging time was 115 minutes. _Reconstruction_—Using a 3D non-uniform fast Fourier transform, images were reconstructed on to a $320\times320\times320$ matrix corresponding to isotropic 0.5-mm voxel size. Cortical bone region was selected by delineating the endosteal and periosteal boundaries using a semiautomatic segmentation method on the 50-μs image and automatically extracting matching analysis regions from all echoes. _Porosity Index (PI)_—A marker of cortical porosity was defined as the ratio of the intensity in the 2000-μs image to that of 50-μs image in a voxel-wise manner. The 50-μs TE value was chosen to obtain the maximum combined proton signal resulting from bound water (T2*~300 μs) and pore water (T2* > 1 ms) [4, 6]. At 2000-μs TE, on the other hand, the detected proton signal is essentially from water residing in pore spaces because the shorter-T2* components should have negligible amplitude (<5%) at TE = 2000 μs. _Bi-component fitting_—To further investigate the association between cortical porosity and bone water, voxel-wise bi-exponential fitting was performed on the multi-echo UTE data assuming a two-compartment model of bound and pore water involving two T2* time constants. _Micro-CT Imaging and analysis_—To assess the cortical bone's microstructure, the same bone samples were scanned by micro computed tomography (μCT, Bruker, Kontich, Belgium) using the following parameters: source voltage 100 kV, source current 100 μA, exposure time 5.89 seconds, angular increment 0.04°, 4877 views, scan time ~ 50 hours, and isotropic voxel size 8.63 μm. The solid phase of cortical bone was segmented from the background and pore spaces by selecting a threshold value. Cortical bone porosity was calculated as the ratio of total pore volume over total volume. _Bone Density Measurements_—To test the association between MRI-derived porosity index and bone density, apparent cortical bone mineral density (CBMD) was measured by peripheral quantitative computed tomography (pQCT) using 2.3 mm axial slices to cover the entire 36-mm sample at 0.4 mm in-plane voxel size on a Stratec XCT 2000 pQCT scanner (Orthometrix, White Plains, NY). _Reproducibility in human subjects_—To investigate the suitability of using porosity index as a marker of cortical porosity in a clinical setting, 5 healthy volunteers (2 female and 3 male, age range 26-41 years) were imaged three times within 5 days in different scanning sessions using the same UTE parameters and RF coil described above but restricting the number of echoes to only two (TE=50 μs and 4600 μs) obtained is a single acquisition (total scan time 10 mins). PI was computed as described above and reproducibility was assessed in terms of the coefficient of variation and intraclass correlation coefficient.

Results: Micro-CT-derived porosity showed strong positive association with MRI-derived porosity index (R^2= 0.79), T2* of pore water (R^2= 0.75), and pore-water fraction (R^2= 0.73) (**Fig. 1**). PI, pore-water T2*, and pore-water fraction are positively associated with age (R^2= 0.53, 0.42, and 0.52 respectively) and negatively with CBMD (R^2= 0.61, 0.62, and 0.64 respectively). PI was found to correlate strongly with pore volume fraction obtained by bi-component analysis (R^2= 0.81). Increased cortical bone porosity is visually apparent in the micro-CT images and MRI-derived porosity-index maps of the cortical bone obtained from older donors compared to younger donors (**Fig. 1**). For repeated measurements in healthy volunteers, the average CV for the porosity index was 2.6% and the intra-class correlation coefficient was 0.98, indicating good reproducibility.

Discussion: Data suggest that cortical bone porosity associated with the Haversian system and endocortical bone loss in the tibia diaphysis can be assessed using a simple UTE MRI protocol that is clinically practical, requiring only 10 mins scan time, providing the spatial distribution of cortical porosity. Correlation with pore volume fraction derived by bicomponent analysis show that PI provides essentially the same information.

Conclusion: The data presented suggest that the UTE PI, an easily derived marker for cortical porosity, is strongly correlated with actual porosity and can reliably be measured in vivo. The method should be straightforward to extend to actual fracture sites such as the femoral neck.
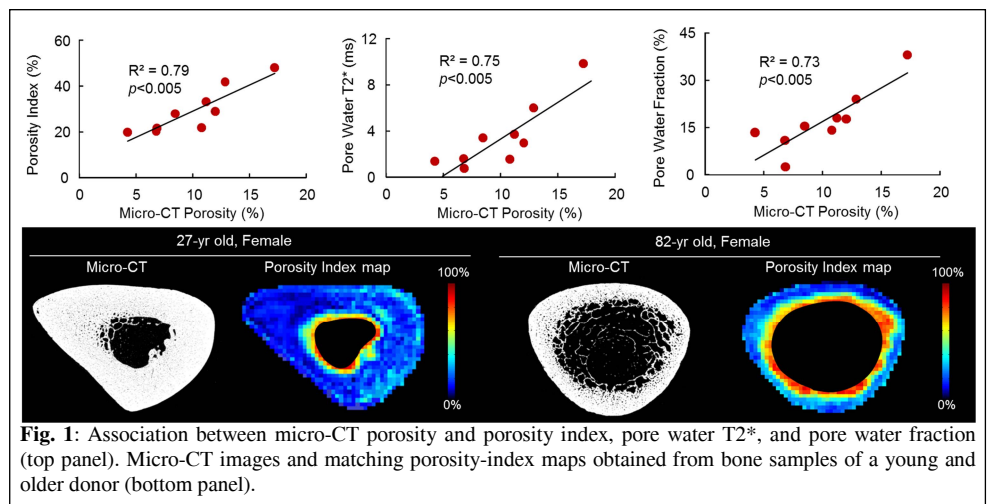

Fig. 1: Association between micro-CT porosity and porosity index, pore water T2*, and pore water fraction (top panel). Micro-CT images and matching porosity-index maps obtained from bone samples of a young and older donor (bottom panel).

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