## EQUIPMENT

### HIGH-RESOLUTION PERIPHERAL QUANTITATIVE COMPUTED TOMOGRAPHY (HR-pQCT)

Images of the non-dominant distal/diaphyseal radius and distal/diaphyseal tibia will be acquired using the Scanco XtremeCT II High-Resolution peripheral Quantitative Computed Tomography (**HR-pQCT**) scanner (Scanco Medical AG Bruttisellen, Switzerland) with an isotropic voxel size of 61$\mu$m and a radiation dose of <5$\mu$Sv per scan per anatomical site. Distal acquisitions will be used to measure volumetric bone mineral density (**vBMD**), bone microarchitecture and geometry in the cortical and trabecular bone compartments, as well as to estimate bone strength using micro-finite element analysis (***μ*FEA**). Diaphyseal acquisitions will be used to measured cortical vBMD and cortical porosity. The distal acquisitions aim to capture both trabecular and cortical bone, while the diaphyseal acquisitions increase the sensitivity of assessments of cortical porosity.

The XtremeCT II scanner is located at the Outpatient Clinical Translational Research Center (**CTRC**) at the University of Colorado Anschutz. The scanner was acquired through a successful S10 Shared Instrumentation Grant application to the NIH (NIGMS) in June 2019 (S10 OD028453) and is operated by the HR-pQCT Imaging Core, including the Faculty Director, Dr. Julio Carballido-Gamio, Medical Director, Dr. Christine Swanson, and Technical Director, Dr. R. Dana Carpenter. It has been available for clinical research studies at the University of Colorado Anschutz since October 2022. Quality control phantom scans are performed daily and weekly per manufacturer specifications. This second-generation device has high reproducibility in published reports with short-term ranges of root mean square coefficients of variation ($CV_{RMS}$) of <0.6% for vBMD, <0.8% for bone size, 0.7-3.2% for trabecular bone microarchitecture, 10.3-15.4% for cortical porosity, and 1.8-2.9% for estimated failure load at distal sites. Regarding diaphyseal sites, the reported reproducibility is <0.6% for vBMD, <0.8% for bone size, 4.6-6.7% for cortical porosity, and <1% for estimated failure load.[1] The scan-rescan reproducibility of measurements with repositioning at our imaging center was assessed in 11 women and men and aligns with published data ($CV_{RMS}$ for the distal tibia and distal radius in table below).

| **Cortical Compartment: Presented as $CV_{RMS}$ in percent (%)** | | | | | | |
|---|---|---|---|---|---|---|
| | Ct.Ar | Ct.vBMD | Ct.Pm | Ct.Po | Ct.Th | Ct.Po.Dm |
| Distal Radius | 0.79 | 0.28 | 0.18 | 12.06 | 0.77 | 2.44 |
| Distal Tibia | 0.45 | 0.20 | 0.06 | 11.63 | 0.67 | 4.33 |
| **Trabecular Compartment: Presented as $CV_{RMS}$ in percent (%)** | | | | | | |
| | Tot. vBMD | Tb.Ar | Tb. vBMD | Tb. BV/TV | Tb.N | Tb.Th | Tb.Sp |
| Distal Radius | 0.29 | 0.20 | 0.35 | 0.69 | 2.47 | 0.95 | 1.49 |
| Distal Tibia | 0.15 | 0.11 | 0.37 | 0.43 | 2.35 | 0.87 | 1.19 |

Imaging will be performed using the recommended relative offset protocol, which ensures consistent scan placement across participants of varying height.[2,3] Prior to scanning, limb lengths will be measured with an anthropometric tape using standard anatomical landmarks.[2] Limb measurements at baseline will be used for the follow-up exams. Images will be graded for motion artifacts using the artifact grading scheme of the manufacturer (1=no motion artifacts to 5=extreme motion artifacts) and acquisitions will be repeated up to 3 times per region, if necessary. Scans with a grading of 4 or higher, known to influence structural indices, will be eliminated from analysis. Trabecular and cortical bone parameters of density, geometry and microstructure, and estimated measures of apparent bone strength ($\mu$FEA) will be calculated using the *in vivo* analysis protocol provided by the manufacturer. Briefly, bone voxels in the binary image stack of each HR-pQCT scan will be directly converted to 8-node, hexahedral elements using Scanco FE-software (v1.16). The linear-elastic FE solver from Scanco determines the element-wise strain values for boundary conditions that simulated high-friction, axial compression loading of the bone segment at an apparent strain of 1%. A homogeneous elastic tissue modulus of 10 GPa will be assigned to all bone elements (n = 0.3). The μFEA-derived estimated failure load is the reaction force that causes 5% of the bone volume to exceed 0.010 equivalent strain (μFEA-B).[4] These modulus values and failure criteria are commonly used in clinical studies.


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2. Bonaretti S, Majumdar S, Lang TF, Khosla S, Burghardt AJ. The comparability of HR-pQCT bone measurements is improved by scanning anatomically standardized regions. Osteoporos Int. 2017;28(7):2115-28. Epub 2017/04/10. doi: 10.1007/s00198-017-4010-7. PubMed PMID: 28391447; PMCID: PMC5526099.
3. Whittier DE, Boyd SK, Burghardt AJ, Paccou J, Ghasem-Zadeh A, Chapurlat R, Engelke K, Bouxsein ML. Guidelines for the assessment of bone density and microarchitecture in vivo using high-resolution peripheral quantitative computed tomography. Osteoporos Int. 2020;31(9):1607-27. Epub 2020/05/28. doi: 10.1007/s00198-020-05438-5. PubMed PMID: 32458029; PMCID: PMC7429313.
4. Arias-Moreno AJ, Hosseini HS, Bevers M, Ito K, Zysset P, van Rietbergen B. Validation of distal radius failure load predictions by homogenized- and micro-finite element analyses based on second-generation high-resolution peripheral quantitative CT images. Osteoporos Int. 2019;30(7):1433-43. Epub 20190417. doi: 10.1007/s00198-019-04935-6. PubMed PMID: 30997546; PMCID: PMC6614386.