

Automated Scan Prescription For HR-pQCT: A Multi-Atlas Prospective Registration Approach

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Bone density and geometry vary dramatically along the distal radius. Consequently, the prescription of a scan by an operator introduces a significant—but under-appreciated—source of variability in HR-pQCT measurements, increasing the scatter in cross-sectional and normative datasets, and complicating the translation of HR-pQCT to multicenter studies. To address this issue, we developed an automatic technique to *prospectively* prescribe patient HR-pQCT scans by automatically mapping scanning landmarks of a set of reference atlas radiographs of the forearm to their scout radiographs.

Scan-reposition-rescans of 60 radii of adult men and women from two different imaging centers were used to quantify root mean square coefficients of variation (RMSCVs) of integral BMD, Ct.Th and Tb.N, and slice-wise offsets between baseline and repeat scans for subvolumes identified by manual prescription in the scouts, and by the default *post hoc* slice-matching registration method—assumed to reflect ideal positioning. Repeat 330-slice scans of 5 cadaveric radii were used to validate the subvolume identification using the prospective method and similar metrics. Five atlases were generated, each based on ten scout radiographs randomly selected from a normative population. The automatic positioning of the scanning landmarks was computed with affine and nonlinear transformations between the scout radiographs and the atlases (Fig. 1A-E). Sub-volumes for bone quantification were identified by retrospectively applying the registrations to the scout radiographs.

Based on RMVCVs and mean slice offsets, a single atlas performed better than the others, however, values were also calculated for different atlas combination strategies. The *ex vivo* manual mean slice offset was 0.5 mm (93% overlap), with RMSCVs exceeding 9% for Ct.Th. The prospective mean slice offset was 0.1 mm (99% overlap) with RMSCVs equivalent to slice-matching (Fig. 1F).

True precision errors (*in vivo* and *ex vivo*) for BMD and Ct.Th in HR-pQCT are greater than previously reported (Fig. 1F) once variability due to operator positioning is considered. Results indicate that scan prescription by prospective atlas-based image registration can minimize this error and potentially improve standardization of HR-pQCT acquisitions. While mainly advantageous for cross-sectional studies, standardized positioning would also benefit longitudinal studies where periosteal bone changes make the default slice-matching method undesirable.