High Resolution Peripheral Quantitative CT Detects Marked Differences in Hand and Forearm Bone Microstructure and Volumetric Bone Mineral Density in Early Rheumatoid Arthritis.

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Background

- Despite improvements in clinical management of rheumatoid arthritis (RA), many people with early disease are still at high risk for developing periarticular erosions and osteopenia, as well as generalized systemic bone loss.
- Radiography, MR and CT imaging can only detect changes after permanent macro-structural bone damage has already occurred. Therefore, it is essential to develop new approaches to assess early changes in volumetric bone mineral density and microstructure in the hand and distal forearm bones in people with early RA before permanent macro-structural bone damage occurs[2-4].
- High Resolution Peripheral Quantitative CT (HR-pQCT) may provide a solution as it is a novel imaging system that images bone density and microstructure at the thickness of a human hair (82 μm, isotropic resolution).

Purpose

To determine if our adapted HR-pQCT (XtremeCT, Scanco Medical AG) imaging protocol[20] can characterize bone density or microstructural differences in the metacarpal head, metacarpal mid-shaft and ultra-ultra-distal radius in people diagnosed with RA in the previous 12 months, relative to age and gender matched counterparts.

Methods

Design, Setting and Participants

- **Design**: Cross-sectional cohort study. **Setting**: Community-based.
- **Participants**: 19 years or older. 1) RA Participants (n=30) - Diagnosed in previous 12 months with RA. 2) Non-RA Controls (n=30) - Age (mean 53.3 ± 21 to 73) and gender (80% matched), with no inflammatory arthritis.

Image Acquisition and Image Analyses

- **Standard in-vivo imaging parameters** [82 μm, 60 kVp, 900 μA, 100 ms].
- **Five regions of interest**: 1) **ultra-ultra-distal radius** (UUDr); 2) **Metacarpal Head** (MH) 2 and 3; and 3) **Metacarpal Mid-Shaft** (MS) 2 and 3. Figure 1A.

**Primary Outcomes and Statistical Analysis**

- **Excluded Images**: 2.5 % (8/325) images excluded from analyses due to image motion artifact grade > 3 (n=6) or scanner mechanical problems (n=2).
- **Primary Outcomes**
  - Whole, trabecular and cortical bone apparent volumetric bone density (vBMD - mgHA/cm³) and bone volume fraction (BV/TV - %).
  - Trabecular region - structural model index (SMI).
  - Cortical region - thickness (CTh - mm) and material vBMD (mgHA/cm³).
  - MS - marrow space diameter (Msd - mm).
- **Analysis**: Paired Student T-test (no correction for multiple analyses).

**Results**

- **RA Group**: 73% Rheumatoid Factor or anti-CCP positive; mean 8 months (SD:5) since diagnosis and 13 months (SD:8) since symptom onset; HAQ-DI mean 0.6 (SD:0.6).
- **Imaging**: RA participants had significantly different microstructure and density in peri-articular (MH and UUDr) and extra-articular (MS) bone locations, including: 1) thinner and less dense cortical bone, 2) fewer, thinner, less connected and less dense trabecular bone, 3) bigger and more variable sized spaces between the trabecular, and 4) larger MS marrow space diameter. Table 1 and Figure 2.

**Discussion**

- The changes in bone microstructure detected in the RA group 1-year after symptoms onset are consistent with microstructural bone deterioration that occurs normally with aging[7], however, with aging microstructural changes generally develop at a much slower pace[20].
- The marked microstructural bone changes occurring early on in RA disease may relate to an accelerated systemic inflammatory mediated catabolic imbalance in normal bone homeostatic resorption and remodeling[7,16].

**CONCLUSION**: HR-pQCT is a new imaging technology that can be used to identify and monitor the progression of early systemic inflammatory mediated microstructural bone disease, as well as the effects of treatments on microstructural bone health in early RA.

**RELEVANCE**: Microstructural bone changes are potentially modifiable if identified and managed with medications and active lifestyle interventions at the early stages of RA.