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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WELL IN HAND

Imaging Hand Bone Health in Early RA

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[1-4].
- 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[5] 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 y, 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.

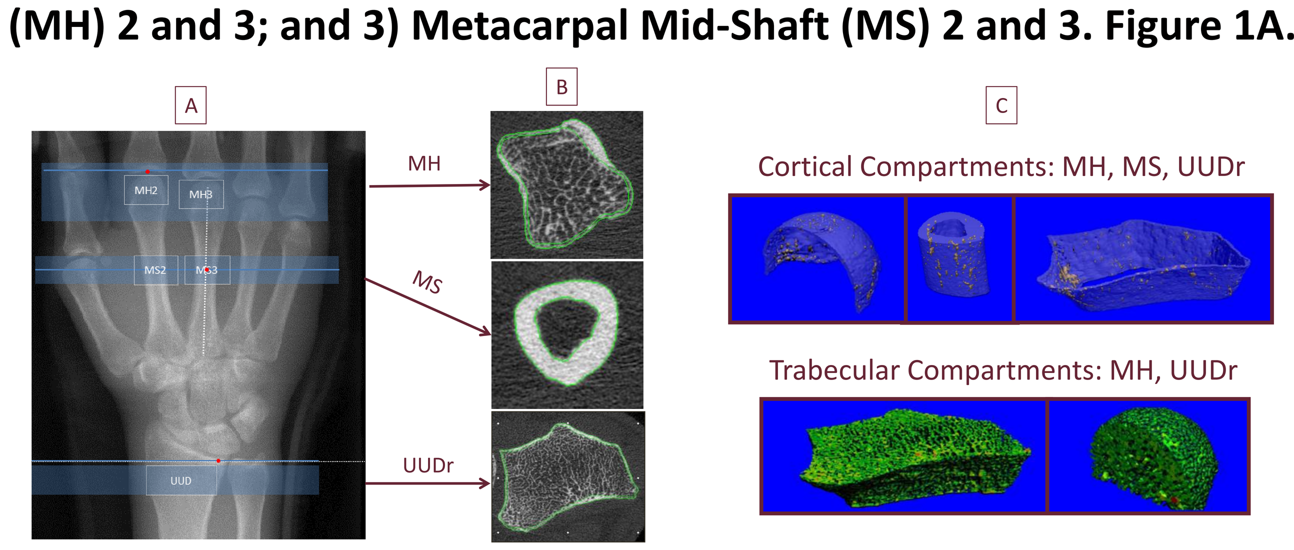

Figure 1: A) Scout view, MH, MS & UUDr scan locations. B) Cortical & trabecular compartment contours (green outlines). C) 3-D reconstruction of cortical (cortex - transparent blue, Pores – pink) and trabecular (Green) bone segmentation.

- Standard semi-automated contouring of periosteal bone surface.
- Modified semi-automated cortical & trabecular compartments extraction with modified MH boundary conditions[6]. Figure 1B,C.
- Whole, cortical and trabecular bone compartment analysis using direct transformation method evaluation scripts.

Primary Outcomes and Statistical Analysis

- Excluded Images: 2.5 % (8/325) images excluded from analyses due to image motion artifact graded > 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 (CtTh - 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 trabeculae, 3) bigger and more variable sized spaces between the trabeculae, and 4) larger MS marrow space diameter. Table 1 and Figure 2.

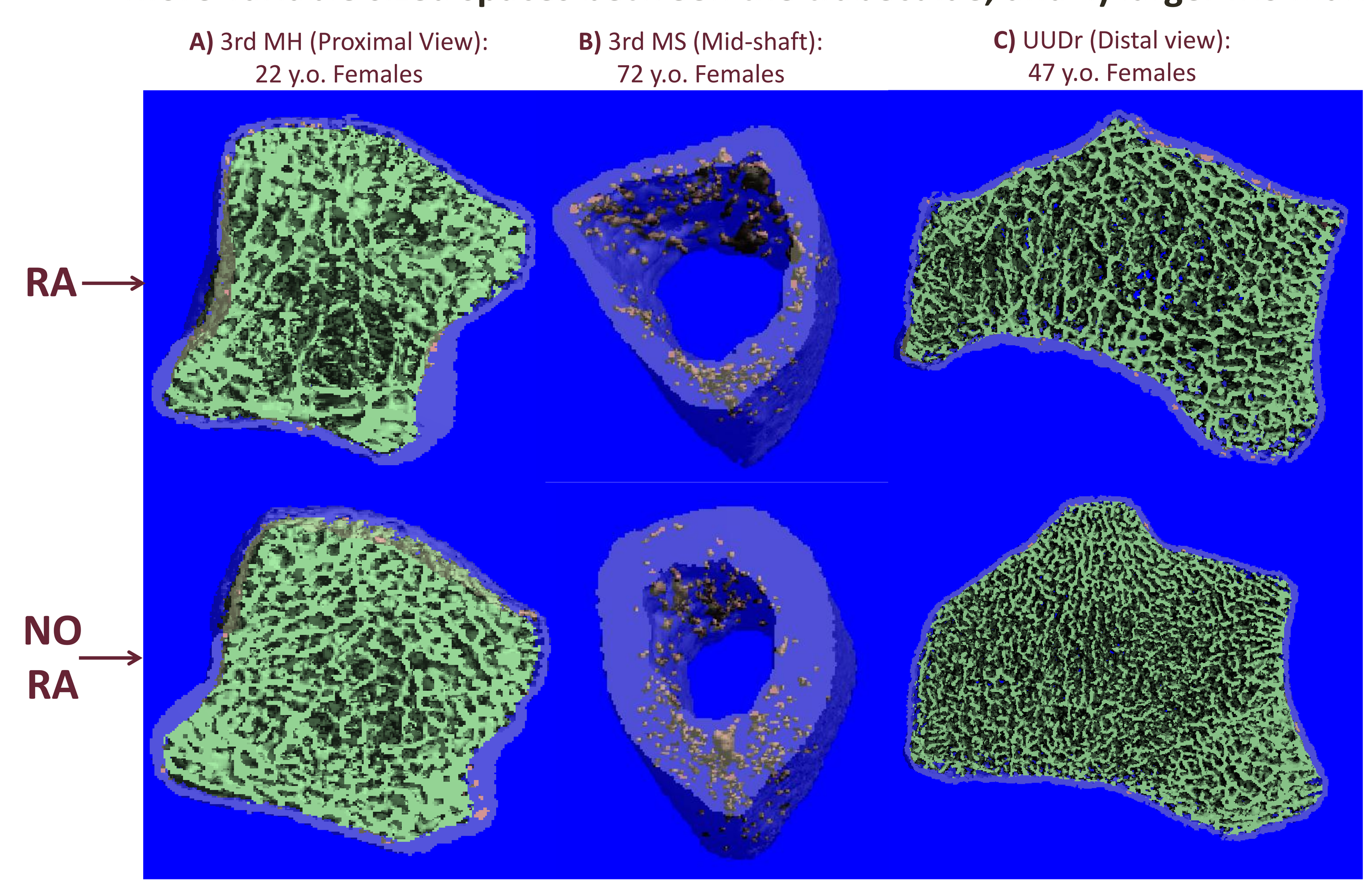

Figure 2: 3-D reconstructions of A) 3rd MH, B) 3rd MS and C) UUDr regions. Showing microstructural differences in RA participants (top row) compared to age an and gender matched controls (bottom row).

Table 1: Comparison of Volumetric Density and Microstructural Outcomes for UUDr, MH3 and MS2 ROIs

Ultra-Ultra-Distal Radius ROI (n=54, 27 Pairs)		RA [Mean (SD)]	Non-RA [Mean (SD)]	Difference (%)
Whole Bone	Apparent vBMD (mgHA/cm³)	262.26 (53.27)	281.52 (44.41)	-7%
Trabecular Region	* Apparent vBMD (mgHA/cm³)	167.30 (34.74)	187.70 (36.26)	**-11%**
Cortical Region	Apparent vBMD (mgHA/cm³)	760.25 (93.2)	785.52 (74.9)	-3%
	Material vBMD (mgHA/cm³)	942.28 (41.83)	949.81 (35.29)	-0.8%
Whole Bone	Bone Volume Fraction - BV/TV (%)	36.70 (4.9)	38.33 (4.5)	-6%
Trabecular Region	* Bone Volume Fraction - BV/TV (%)	26.88 (0.9)	29.39 (0.9)	**-9%**
	* Structural Model Index -SMI	1.87 (0.38)	1.60 (0.37)	**17%**
Cortical Region	Bone Volume Fraction - BV/TV (%)	90.49 (5.3)	91.47 (5.3)	-1%
	Thickness - CtTh (mm)	0.56 (0.14)	0.58 (0.11)	-1%
3rd Metacarpal Head ROI (n=54, 27 Pairs)		**RA [Mean (SD)]**	**Non-RA [Mean (SD)]**	**Difference (%)**
Whole Bone	* Apparent vBMD (mgHA/cm³)	290.28 (47.16)	316.96 (40.72)	**-9%**
Trabecular Region	* Apparent vBMD (mgHA/cm³)	241.78 (31.32)	262.56 (33.02)	**-8%**
Cortical Region	* Apparent vBMD (mgHA/cm³)	542.42 (73.31)	592.91 (72.49)	**-8%**
	* Material vBMD (mgHA/cm³)	817.34 (72.49)	843.87 (45.04)	**-3%**
Whole Bone	* Bone Volume Fraction - BV/TV (%)	42.32 (4.6)	44.91 (3.7)	**-7%**
Trabecular Region	* Bone Volume Fraction - BV/TV (%)	35.74 (4.4)	37.99 (3.2)	**-6%**
	* Structural Model Index -SMI	0.88 (0.45)	0.60 (0.42)	**47%**
Cortical Bone	* Bone Volume Fraction - BV/TV (%)	42.32 (4.6)	44.91 (3.7)	**-7%**
	* Thickness - CtTh (mm)	0.35 (0.09)	0.39 (0.07)	**-13%**
2nd Metacarpal Shaft ROI (n=52, 26 Pairs)		**RA [Mean (SD)]**	**Non-RA [Mean (SD)]**	**Difference (%)**
Cortical Bone	* Apparent vBMD (mgHA/cm³)	1033.79 (34.57)	1050.48 (21.78)	**-2%**
	* Material vBMD (mgHA/cm³)	1079.82 (27.78)	1091.87 (18.30)	**-1%**
Whole Bone	* Apparent vBMD (mgHA/cm³)	796.84 (112.32)	843.17 (79.35)	**-5%**
Cortical Region	* Bone Volume Fraction - BV/TV (%)	97.96 (1.2)	98.48 (0.61)	**-1%**
	* Thickness - CtTh (mm)	1.93 (0.36)	2.08 (0.29)	**-7%**
Whole Bone	* Bone Volume Fraction - BV/TV (%)	72.68 (9.7)	76.63 (6.9)	**-5%**
	Marrow Space Diameter - MSd (mm)	2.79 (0.61)	2.67 (0.51)	4%

Bold Difference (%) & * = p < 0.05 (Paired T-Test, no adjustment for multiple comparisons).
NOTE: MH2 and MS3 similar results, not shown

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[8].
- 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[9,10].

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.

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