Quantitative Analysis of RA imaged by HR-pQCT

The SPECTRA Consortium

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Limitations of Radiography for RA

- **Ordinal Scales by Reader**
  - subjective and time consuming
  - not sensitive to subtle changes

- **Computerized Quantitative Approaches**
  - estimating distance between complex, curved surfaces
  - radiographic super-position

→ Monitoring interval ≈ 1 year
SPECTRA Goals for Quantitative Imaging

Develop comprehensive standardized analysis pipelines for evaluating boney features of joint disease

- **Erosions**
  - number, volume, shape, boney margin

- **Joint Space Narrowing**
  - volume, width (min/max/mean), variance, asymmetry

- **Bone Quality**
  - cortical/trabecular density, microstructure, geometry, and strength
Erosions
Erosions: structural damage detected by HR-pQCT over a short observation interval

Burghardt and Li, UCSF
Semi-Automated Volumetric analysis of Erosions

Töpfer et al, Rheumatology, 2015
IPL-Based Segmentation of Erosions

Geusens et al, Nat Rev Rheumatol, 2014
Validation: reader reliability vs. $\mu$CT

Scharmga et al, BMC Muskuloskelet Disord, 2016
Validation: erosion or vascular channel?

Boutroy et al, Arthritis & Rheumatology, 2015
Joint Space Narrowing
3D DT Analysis of Joint Space Width

Variability in Joint Space Morphology in RA

Longitudinal changes in JSW: Anti-TNF

Baseline vs 3 months:
- JSV: +5.8%
- JSW: +2.1%
- JSW.MIN: +5.6%
- JSW.MAX: -3.4%
- JSW.SD: -34.5%

Burghardt, UCSF
Comparison of Three JSW Algorithms

- **AIM**: Establish a SPECTRA-driven consensus for a standard HR-method to measure 3D JSW using HR-pQCT

- **METHOD**: OMERACT filters:
  - *Truth*: is there a best algorithm for accurate results?
  - *Discrimination*: do the algorithms work on a spectrum of disease?
  - *Feasibility*: are the algorithms user-friendly? Can they be implemented into daily clinical practice?
  - *Pathophysiological Manifestations*: reduction in joint space width with disease

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Calgary (CLG)  San Francisco (SFR)  Lyon (LYN)
Comparison of Three JSW Algorithms

1. Disease spectrum: 30 MCP2 and 30 MCP3 joints
2. Scan/rescan: 45 MCP2 joints scanned twice with re-positioning
3. XT vs. XTII: 10 MCP2 joints each scanned on two machines

For all:
- Scanned using SPECTRA protocol
- All data pre-processed using an independent lab so all differences are specific to the JSW algorithms only
- Three JSW algorithms compared
Comparison of Three JSW Algorithms

<table>
<thead>
<tr>
<th></th>
<th>JSW</th>
<th>JSW.Min</th>
<th>JSW.Max</th>
</tr>
</thead>
<tbody>
<tr>
<td>ICC Consistency</td>
<td>0.991</td>
<td>0.994</td>
<td>0.843</td>
</tr>
<tr>
<td>ICC Abs Agreement</td>
<td>0.973</td>
<td>0.994</td>
<td>0.340</td>
</tr>
<tr>
<td>RMSE [mm]</td>
<td>0.04</td>
<td>0.03</td>
<td>0.30</td>
</tr>
<tr>
<td>RMSCV [%]</td>
<td>2.25%</td>
<td>5.64%</td>
<td>12.64%</td>
</tr>
</tbody>
</table>
Comparison of Three JSW Algorithms

CLG vs. SFR vs. LYN

JSW

specimen
Comparison of Three JSW Algorithms

CLG vs. SFR vs. LYN

JSW Max
JSW Precision
Scan-Rescan with complete repositioning

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Units</th>
<th>Description</th>
<th>SDD (RMSCV %)</th>
</tr>
</thead>
<tbody>
<tr>
<td>JSV</td>
<td>[mm³]</td>
<td>Joint Space Volume</td>
<td>11.8 (3.5%)</td>
</tr>
<tr>
<td>JSW</td>
<td>[mm]</td>
<td>Mean Joint Space Width</td>
<td>0.10 (2.1%)</td>
</tr>
<tr>
<td>JSW.MIN</td>
<td>[mm]</td>
<td>Minimum Joint Space Width</td>
<td>0.21 (5.9%)</td>
</tr>
<tr>
<td>JSW.MAX</td>
<td>[mm]</td>
<td>Maximum Joint Space Width</td>
<td>0.12 (2.0%)</td>
</tr>
<tr>
<td>JSW.SD</td>
<td>[mm]</td>
<td>Variance of Joint Space Width</td>
<td>0.06 (9.8%)</td>
</tr>
<tr>
<td>JSW.AS</td>
<td>[ ]</td>
<td>Joint Space Asymmetry (Max/Min)</td>
<td>0.38 (7.2%)</td>
</tr>
</tbody>
</table>

 Comparable to precision for 2D Radiography JSW

Comparison XtremeCT to XtremeCT II

ICC: 0.915
## Variation with Flexion Angle

<table>
<thead>
<tr>
<th>Positioned Angle</th>
<th>0°</th>
<th>5°</th>
<th>10°</th>
<th>15°</th>
<th>20°</th>
<th>25°</th>
<th>30°</th>
</tr>
</thead>
<tbody>
<tr>
<td>JSW(mm)</td>
<td>1.85</td>
<td>1.74</td>
<td>1.75</td>
<td>1.88</td>
<td>1.84</td>
<td>1.91</td>
<td>1.94</td>
</tr>
<tr>
<td>JSW.MIN (mm)</td>
<td>0.77</td>
<td>0.66</td>
<td>0.71</td>
<td>0.79</td>
<td>0.79</td>
<td>0.87</td>
<td>0.85</td>
</tr>
<tr>
<td>JSW.MAX (mm)</td>
<td>2.56</td>
<td>2.48</td>
<td>2.41</td>
<td>2.55</td>
<td>2.48</td>
<td>2.52</td>
<td>2.62</td>
</tr>
<tr>
<td>JSV (mm³)</td>
<td>134.56</td>
<td>135.07</td>
<td>134.30</td>
<td>139.28</td>
<td>139.47</td>
<td>143.48</td>
<td>147.04</td>
</tr>
</tbody>
</table>

Barnabe et al, ACR 2014, Poster 2146
Bone Quality
Distal Radius

Zhu et al, JBMR 2014

Metacarpal density and structure

Profile of Tb.BMD along the Metaphysis

Zhu et al, ACR 2010
Standardized Analysis Requires MC Length

Yang et al, Int J Rheum Dis 2015
Priorities

To be addressed for future OMERACT Meetings

- Work towards consensus and standardization of methods
  - JSW, erosions, density/structure
  - XT/XTII harmonization
- Robust comparisons to existing diagnostics
  - Radiography, MRI, US
- More longitudinal data with quantitative outcome measures
  - Preferably including short observation intervals
  - Matching standard practice measures
Radiocarpal and Radioulnar Joints

Wrist: Anti-TNF Responder

Baseline

3 Months

[SPECTRA: Quantitative Analysis of RA by HR-pQCT]

19-Oct-16
The Ankle (Tibiotalar Joint)

* Collected for the MrOS study on XtremeCT II at 61µm
Metatarsals and MTP Joints

Sode et al, ORS 2016
Metatarsals and MTP Joints: Positioning

Sode et al, ORS 2016
Elbow: Humeroulnar Joint

Sada et al, ASBMR 2016

Dominant  Non-Dominant
Operator variability in scan positioning is a major component of HR-pQCT precision error and is reduced by standardized training

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