Detection of marginal osteophytes and their association with pain: diagnostic performance of digital tomosynthesis compared with conventional radiography

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Authors: A. Guermazi, D. Hayashi, D. J. Hunter, L. Li, N.-K. Kabutey, F. W. Roemer; Boston, MA/US
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Purpose

- Conventional radiographs are currently the standard for establishing a radiographic diagnosis of knee osteoarthritis (OA).
- Hallmarks of the disease include the presence of marginal osteophytes in the tibiofemoral joint. Radiographic tibiofemoral OA is defined as Kellgren-Lawrence (KL) grade 2, i.e. the presence of a definite marginal osteophyte on the anteroposterior (AP) weight-bearing radiograph[1].
- Studies have shown osteophytes are associated with radiographic joint space narrowing and subchondral sclerosis [2], pain [3]and cartilage defects [4, 5]. However, detection of osteophytes with conventional radiography may be difficult due to overlapping of normal bony contour. MRI, with its tomographic nature, is highly sensitive to the detection of osteophytes.
- Digital tomosynthesis (DTS) is a multi-slice imaging technique which allows visualization of anatomy at 1mm slice intervals.
- Its potential clinical application includes detection of thoracic, breast, abdominal and skeletal abnormalities.
- The aims of this study were to test the hypotheses that: (1) DTS is superior to XR in the detection of marginal osteophytes (OPs) using semiquantitative MRI scoring as the reference standard; (2) prevalent OPs on DTS are associated with pain.
Methods and Materials

Subjects:

40 subjects aged >40 years were recruited irrespective of knee pain, stiffness, or knee OA. They volunteered to have both knees imaged by DTS, plain radiography and MRI (i.e. total 80 knees) were included.

Subjects were excluded if they had a history of Paget's disease, rheumatoid arthritis, gout, systemic lupus erythematosus, other inflammatory knee joint disease or major knee trauma or surgery.

All subjects recruited from the local community in Boston, MA. Written informed consent from all subjects and IRB approval from Boston University and New England Baptist Hospital obtained.

Radiographic and DTS assessments:

All subjects underwent weight-bearing postero-anterior fixed flexion view knee radiographs using the SynaFlexer™ positioning frame (Synarc, San Francisco, CA), and weight-bearing DTS imaging using the VolumeRAD™ imaging apparatus (General Electric Healthcare, Milwaukee, WI).

A single musculoskeletal radiologist (AG) scored marginal osteophytes on plain radiographs and DTS images using OARSI grading scheme (0=none, 1=small, 2=medium, 3=large).

Results of the readings were dichotomized into either a lesion is 'present (grade#1)' or 'absent (grade 0) in the following compartments: medial femoral, lateral femoral, medial tibial, and lateral tibial (Fig. 1).

MRI Acquisition:

All subjects had both knees imaged using 3.0T MRI scanner (Intera™, Philips Medical Systems, Andover, MA).

Coronal proton density-weighted (PDw) fat-suppressed (FS) (TR=9000 ms, TE=10 ms, Echo number=1, Slice thickness=2.5 mm, Spacing=2.5 mm, Echo train=8, Matrix=256 x 256, FOV=140 mm); Sagittal and axial PDw FS (TR=7650 ms, TE=10 ms, Echo
MRI Assessment:

A single musculoskeletal radiologist (AG) read all MRIs, which were scored for marginal osteophytes using WORMS scale. Marginal osteophytes were scored for each subregion from 0 to 7 (0=none; 1=equivocal; 2=small; 3=small-moderate; 4=moderate; 5=moderate-large; 6=large; 7=very large)

Results of the readings are then dichotomized into either the lesion was 'present (grade#1)' or 'absent (grade 0)'.

We used the readings from the following subregions: medial femoral central, lateral femoral central, medial tibial central, and lateral tibial central (Fig. 2).

Pain Assessment:

Pain was assessed using WOMAC pain subscale (range 0-20) and subjects were dichotomized into those with (score>0) or without (score 0) pain.

Statistical analysis:

Prevalence of marginal osteophytes detected by radiography and DTS was compared to that detected by MRI in each compartment.

Sensitivity, specificity and accuracy for osteophyte detection were calculated, using MRI as the reference.

A majority of subjects had WOMAC scores of zero in our study (i.e. skewed distribution of WOMAC scores) and both left and right knee were measured for each subject, which means that each subject was observed twice.

Thus, Zero-inflated Poisson regression model with random effects was used to test the relationship between the presence of osteophytes and pain by taking the effect of clustering into account.
Fig. 0: AP radiograph of the knee showing the 4 compartments: Lateral femoral (LF), medial femoral (MF), lateral tibial (LT) and medial tibial (MT) compartments.

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Fig. 0: Subregions of the knee as defined by the Whole Organ Magnetic Resonance Imaging Score (WORMS). We used the subregions annotated by the circles. L=lateral, M=medial, S=subspinous, A=anterior, C=central, P=posterior.

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Results

Participant Characteristics:

80 knees from 40 subjects were imaged. The mean age of subjects was 57 (SD±11) years, 30 (75%) were women, 35 (88%) were White, 31 (78%) had a body mass index #25 kg/m2 and 45 (57%) knees were Kellgren-Lawrence grade #2. 19 subjects (29 knees) had WOMAC pain score>0 (range 0-14, median 0)

Study Results:

Total 171 marginal osteophytes detected by MRI (Fig. 1)

DTS had a significantly better sensitivity in both femoral compartments and lateral tibial compartment (Fig. 2,3, 5-7).

No difference in the specificity was observed (Fig. 2).

Association between DTS-detected osteophytes and pain was seen in all compartments (Fig. 4).

However, X-ray-detected osteophytes appeared to be more stongly associated with pain in all compartments (Fig. 4).
### Images for this section:

<table>
<thead>
<tr>
<th>Compartments</th>
<th>Left knee</th>
<th>Right knee</th>
<th>All</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>N (%)</td>
<td>N (%)</td>
<td>N (%)</td>
</tr>
<tr>
<td>Central Lateral Femoral</td>
<td>24 (60)</td>
<td>24 (60)</td>
<td>48 (60)</td>
</tr>
<tr>
<td>Central Medial Femoral</td>
<td>21 (53)</td>
<td>18 (45)</td>
<td>39 (49)</td>
</tr>
<tr>
<td>Central Lateral Tibial</td>
<td>22 (55)</td>
<td>23 (58)</td>
<td>45 (56)</td>
</tr>
<tr>
<td>Central Medial Tibial</td>
<td>21 (53)</td>
<td>18 (45)</td>
<td>39 (49)</td>
</tr>
</tbody>
</table>

**Fig. 0:** Number of osteophytes detected by MRI

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<table>
<thead>
<tr>
<th>Compartments</th>
<th>Prevalence</th>
<th>Sensitivity</th>
<th>Specificity</th>
<th>Accuracy</th>
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<tr>
<td></td>
<td>N (%)</td>
<td></td>
<td></td>
<td></td>
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<tr>
<td><strong>X-ray</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Lat Fem</td>
<td>35 (44)</td>
<td>0.73</td>
<td>1.00</td>
<td>0.79</td>
</tr>
<tr>
<td>Med Fem</td>
<td>31 (39)</td>
<td>0.79</td>
<td>1.00</td>
<td>0.90</td>
</tr>
<tr>
<td>Lat Tib</td>
<td>42 (53)</td>
<td>0.87</td>
<td>0.91</td>
<td>0.89</td>
</tr>
<tr>
<td>Med Tib</td>
<td>42 (53)</td>
<td>0.90</td>
<td>0.83</td>
<td>0.86</td>
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<tr>
<td><strong>DTS</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Lat Fem</td>
<td>48 (60)</td>
<td>0.98*</td>
<td>0.97</td>
<td>0.98</td>
</tr>
<tr>
<td>Med Fem</td>
<td>39 (49)</td>
<td>0.97*</td>
<td>0.98</td>
<td>0.98</td>
</tr>
<tr>
<td>Lat Tib</td>
<td>49 (61)</td>
<td>1.00*</td>
<td>0.89</td>
<td>0.95</td>
</tr>
<tr>
<td>Med Tib</td>
<td>42 (53)</td>
<td>1.00</td>
<td>0.93</td>
<td>0.96</td>
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</table>

**Fig. 0:** Prevalence of marginal osteophytes.

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<table>
<thead>
<tr>
<th>Compartments</th>
<th>No. of OPs on DTS</th>
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<tr>
<td></td>
<td>Grade 1</td>
<td>Grade 2</td>
<td>Grade 3</td>
<td></td>
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<tr>
<td>Lateral Femoral</td>
<td>9</td>
<td>2</td>
<td>2</td>
<td></td>
</tr>
<tr>
<td>Medial Femoral</td>
<td>8</td>
<td>0</td>
<td>0</td>
<td></td>
</tr>
<tr>
<td>Lateral Tibial</td>
<td>9</td>
<td>0</td>
<td>0</td>
<td></td>
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<tr>
<td>Medial Tibial</td>
<td>5</td>
<td>0</td>
<td>0</td>
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</tbody>
</table>

**Fig. 0:** The number and grades of osteophytes that were not detected by X-ray (grade 0) but detected by DTS (grade 1 or above).

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<table>
<thead>
<tr>
<th>Compartments</th>
<th>X-ray Odds ratio (p-value)</th>
<th>DTS Odds ratio (p-value)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Lateral Femoral</td>
<td>5.0 (0.0037)</td>
<td>4.4 (0.0095)</td>
</tr>
<tr>
<td>Medial Femoral</td>
<td>8.4 (0.0005)</td>
<td>6.4 (0.0011)</td>
</tr>
<tr>
<td>Lateral Tibial</td>
<td>5.9 (0.0019)</td>
<td>4.2 (0.011)</td>
</tr>
<tr>
<td>Medial Tibial</td>
<td>6.3 (0.0012)</td>
<td>5.7 (0.0023)</td>
</tr>
</tbody>
</table>

**Fig. 0:** Relationship between the presence of marginal osteophytes and pain (WOMAC score >0).

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Fig. 0: Plain radiograph shows no obvious osteophyte in the right lateral femur (arrow).

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Fig. 0: DTS reveals an OARSI grade 2 osteophyte in the same compartment (arrow).

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Fig. 0: Coronal proton density-weighted MRI confirms the presence of the osteophyte (white arrow, WORMS grade 4). A focal cartilage defect is also noted (yellow arrow).

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Conclusion

- DTS offers higher sensitivity for detection of osteophytes in both femoral and lateral tibial compartments.
- Both DTS and X-ray osteophytes are associated with pain although the association is stronger for x-ray. This suggests that the additional osteophytes that TDS detects may be less clinically important.
- DTS offers superior detection of osteophytes than plain X-rays, and thus may potentially be used to establish the radiographic diagnosis of osteophytes in a clinical and research setting.
Personal Information

• We thank all the participants of this study.
• This study was funded by a research grant from GE Healthcare, but the sponsor did not have any role in the data interpretation and analysis presented herein.
• Ali Guermazi is the President of Boston Imaging Core Lab (BICL) LLC. He is a consultant to Facet solutions, Merckserono, Genzyme, Novartis, and Stryker.
• Frank W Roemer is a shareholder of BICL.
• No other authors declared potential conflict of interests.