SUPPLEMENTARY MATERIAL

S1. Full methodology

At the initial task force meeting, members contributed clinically relevant questions related to key aspects of the use of imaging in JIA. The research questions were agreed by consensus and 11 final research questions were selected which encompassed the role of imaging in making a diagnosis of JIA, detecting inflammation and damage, predicting outcome and response to treatment, the use of guided treatment, monitoring disease progression, and remission (see online supplementary text, research questions, S2).

A systematic search of articles was performed and the bibliographies of included papers were manually searched for evidence of other studies for inclusion. A hand search was performed of the conference proceedings for the American College of Rheumatology (ACR) and the European League against Rheumatism (EULAR) annual general meetings for 2012-13 to identify unpublished studies. Specific medical subject headings (MeSH) and additional keywords were used to identify all relevant studies (see online supplementary text, details of search strategy, S3).

Titles and abstracts of all citations identified were screened, and potentially relevant articles were reviewed in full text using predetermined inclusion and exclusion criteria. Studies, published in English, on the use of imaging in all patients with a clinical diagnosis of JIA were included. Imaging modalities included were X-ray described as conventional radiology (CR), ultrasound (US), magnetic resonance imaging (MRI), computed tomography (CT), scintigraphy and positron emission tomography (PET); study types included randomised controlled trials, controlled clinical trials, cohort studies, case-control studies, diagnostic studies and case series where n≥10. Studies were considered for inclusion when they provided information on the role of imaging in making a diagnosis of JIA, detecting inflammation and damage, predicting outcome and response to treatment, the use of guided treatment, monitoring disease progression, and remission. Included studies were evaluated for risk of bias and applicability using the Quality Assessment of Diagnostic Accuracy Studies (QUADAS)-2 tool.

Following presentation of the data from the literature review, the experts produced points to consider (the evidence was not deemed strong enough to produce recommendations) based on the 11 clinical questions with final agreement by a process of discussion and consensus. The available evidence for each recommendation was scored according to the Oxford Centre for Evidence-based medicine (CEBM) level of evidence, which gives studies a score for “level of evidence” (1a-5) and for “grade of recommendation” (A-D). The experts anonymously scored their perceived level of agreement for each proposition using a 0–10 numerical rating scale (0=do not agree at all, 10=fully agree). Scores reflected both research evidence and clinical expertise.
An agenda for future research was agreed by consensus following presentation of the literature review.

Given the unique challenges of asking children or young adults to attend consensus meetings in Zurich with the task force members, a separate Patient and Public Involvement (PPI) event was arranged following the second task force meeting where the process and results were presented and all comments were recorded. The meeting was attended by three patients (one child and two young adults with a diagnosis of JIA), two parents of children with JIA, two consultant rheumatologists including task force epidemiologist CJE and, one with a special interest in paediatric rheumatology, a paediatric rheumatology nurse specialist and a paediatric research senior nurse. At this meeting all proposed points to consider were reviewed by the patients and any alternations made as required.
S2. Research questions

Q1 - What is the evidence for the differential diagnostic value of individual imaging modalities for JIA?

Q2 - What is the evidence for the diagnostic value above clinical criteria of individual imaging modalities for JIA?

Q3 - What is the evidence for the added value (sensitivity, specificity etc) of individual imaging modalities in detecting inflammation (synovitis, tenosynovitis, osteitis, bursitis, enthesitis) above clinical evaluation according to age?

Q4 - What is the evidence for the added value above clinical examination for the comparative value (sensitivity, specificity etc) of individual imaging modalities in detecting age-related structural abnormalities and damage in JIA (bone, cartilage, tendons, ligaments)?

Q5 - What is the evidence for the prognostic (prediction of therapeutic response) value of individual imaging modalities for JIA?

Q6 - What is the evidence for the prognostic (prediction of outcome) value of individual imaging modalities for JIA?

Q7 - When (time), where (which joints), how often and with what imaging modality should we monitor JIA disease inflammation?

Q8 - When (time), where (which joints), how often and with what imaging modality should we monitor age-related structural abnormalities and damage in JIA?

Q9 - What is the role of imaging for the monitoring of systemic treatment (corticosteroids, synthetic and biological DMARDs) and the targeted delivery of local treatments such as intra-articular injections?

Q10 - What is the relationship between individual imaging modalities and clinical remission in JIA?

Q11 - What is the impact with respect to outcome of imaging-detected inflammation /damage in the patient in clinical remission?
S3. Details of search strategy performed using MEDLINE (1946 to November 2013); EMBASE (1980 to November 2013); and the Cochrane Central Register of Controlled Trials (CENTRAL, The Cochrane Library, third quarter 2013) without language restrictions. The Cochrane Database of Systematic Reviews (CDSR) and the Database of Abstracts of Reviews of Effects (DARE) were also searched to ensure all potential studies were identified.

Search Strategy, MEDLINE

1. exp Arthritis, Juvenile Rheumatoid/
2. (juvenile$ adj3 arthrit$).tw.
3. jia.tw.
4. or/1-3
5. exp ARTHRITIS/
6. arthrit$.tw.
7. (still$ adj disease).tw.
8. Oligoarthrit$.tw.
10. or/5-9
11. exp Child/
12. Adolescent/
13. child$.tw.
14. adolesc$.tw.
15. juvenile$.tw.
16. teenage$.tw.
17. youth$.tw.
18. or/11-17
19. 10 and 18
20. 4 or 19
21. exp Diagnostic Imaging/
22. magnetic resonance.tw.
23. mri$.tw.
24. (ultrasonic adj (diagnos$ or tomography or imaging$)).tw.
25. echotomograph$.tw.
26. echograph$.tw.
27. ultrasonograph$.tw.
28. ultrasound.tw.
29. sonograph$.tw.
30. exp Contrast Media/
31. (computed adj2 tomography).tw.
32. cat scan$.tw.
33. ct.tw.
34. X-Rays/
35. (xray$ or x-ray$).tw.
36. Arthograph$.tw.
37. radiograph$.tw.
38. radiolog$.tw.
40. (Scintigraph$ or scintiphograph$).tw.
41. ((gamma camera or radionuclide) adj imag$).tw.
42. radioisotope scan$.tw.
43. Positron emission tomograp$.tw.
44. (pet scan$ or pet-scan$).tw.
45. or/21-44
46. 20 and 45

Search Strategy, EMBASE
1. juvenile rheumatoid arthritis/
2. (juvenile$ adj3 arthrit$).tw.
3. jia.tw.
4. or/1-3
5. exp arthritis/
6. arthrit$.tw.
7. (still$ adj disease).tw.
8. Oligoarthrit$.tw.
10. or/5-9
11. child/
12. adolescent/
13. child$.tw.
14. adolesc$.tw.
15. juvenile$.tw.
16. teenage$.tw.
17. youth$.tw.
18. or/11-17
19. 10 and 18
20. 4 or 19
21. exp diagnostic imaging/
22. exp joint radiography/
23. exp nuclear magnetic resonance imaging/
24. magnetic resonance.tw.
25. mri$.tw.
26. exp echography/
27. (ultrasonic adj (diagnos$ or tomography or imaging$)).tw.
28. echotomograph$.tw.
29. echograph$.tw.
30. ultrasonograph$.tw.
31. ultrasound.tw.
32. sonograph$.tw.
33. exp computer assisted tomography/
34. exp contrast medium/
35. (computed adj2 tomography).tw.
36. cat scan$.tw.
37. ct.tw.
38. X ray/
39. (xray$ or x-ray$).tw.
40. Arthrograph$.tw.
41. radiograph$.tw.
42. radiolog$.tw.
43. (roentgen adj ray$).tw.
44. scintiscanning/
45. (Scintigraph$ or scintiphoto$graph$).tw.
46. ((gamma camera or radionuclide) adj imag$).tw.
47. radioisotope scan$.tw.
48. positron emission tomography/
49. Positron emission tomography$.tw.
50. (pet scan$ or pet-scan$).tw.
51. or/21-50
52. 20 and 51

Search Strategy, The Cochrane Library

#1 MeSH descriptor: [Arthritis, Juvenile Rheumatoid] this term only
#2 juvenile* near/3 arthrit*:ti,ab
#3 jia:ti,ab
#4 #1 or #2 or #3
#5 MeSH descriptor: [Arthritis] explode all trees
#6 arthrit*:ti,ab
#7 "still* disease":ti,ab
#8 Oligoarthrit*:ti,ab
#9 Polyarthrit*:ti,ab
#10 #5 or #6 or #7 or #8 or #9
#11 MeSH descriptor: [Child] explode all trees
#12 MeSH descriptor: [Adolescent] this term only
#13 child*:ti,ab
#14 adolesc*:ti,ab
#15 juvenile:ti,ab
#16 teenage*:ti,ab
#17 youth*:ti,ab
#18 #11 or #12 or #13 or #14 or #15 or #16 or #17
#19 #10 and #18
#20 #4 or #19
#21 MeSH descriptor: [Diagnostic Imaging] explode all trees
#22 "magnetic resonance":ti,ab
#23 mri*:ti,ab
#24 (ultrasonic next (diagnosis* or tomography or imaging*)):ti,ab
#25 echotomograph*:ti,ab
#26 echograph*:ti,ab
#27 ultrasonograph*:ti,ab
#28 ultrasound:ti,ab
#29 sonograph*:ti,ab
#30 MeSH descriptor: [Contrast Media] explode all trees
#31 computed near/2 tomography:ti,ab
#32 "cat scan"*:ti,ab or cat-scan*:ti,ab
#33 ct:ti,ab
#34 MeSH descriptor: [X-Rays] this term only
#35 xray*:ti,ab or x-ray*:ti,ab
#36 Arthrograph*:ti,ab
#37 radiograph*:ti,ab
#38 radiolog*:ti,ab
#39 "roentgen ray"*:ti,ab
#40 (Scintigraph* or scintiphotograph*):ti,ab
#41 ("gamma camera" or radionuclide) next imag*:ti,ab
#42 "radioisotope scan"*:ti,ab
#43 "Positron emission tomogr"*:ti,ab
#44 ("pet scan"* or pet-scan*):ti,ab
#45 #21 or #22 or #23 or #24 or #25 or #26 or #27 or #28 or #29 or #30 or #31 or #32 or #33 or #34 or #35 or #36 or #37 or #38 or #39 or #40 or #41 or #42 or #43 or #44
#46 #20 and #45
Figure S4. Flowchart showing the literature search of 13,277 articles, from which 433 articles were selected for detailed review; 204 articles met the inclusion criteria.
### Table S5. Number of included articles per question

<table>
<thead>
<tr>
<th>Question</th>
<th>No. of included articles</th>
</tr>
</thead>
<tbody>
<tr>
<td>Q1 - What is the evidence for the differential diagnostic value of individual imaging modalities for JIA?</td>
<td>4</td>
</tr>
<tr>
<td>Q2 - What is the evidence for the diagnostic value above clinical criteria of individual imaging modalities for JIA?</td>
<td>2</td>
</tr>
<tr>
<td>Q3 - What is the evidence for the added value (sensitivity, specificity etc) of individual imaging modalities in detecting inflammation (synovitis, tenosynovitis, osteitis, bursitis, enthesitis) above clinical evaluation according to age?</td>
<td>65</td>
</tr>
<tr>
<td>Q4 - What is the evidence for the added value above clinical examination for the comparative value (sensitivity, specificity etc) of individual imaging modalities in detecting age-related structural abnormalities and damage in JIA (bone, cartilage, tendons, ligaments)?</td>
<td>37</td>
</tr>
<tr>
<td>Q5 - What is the evidence for the prognostic (prediction of therapeutic response) value of individual imaging modalities for JIA?</td>
<td>1</td>
</tr>
<tr>
<td>Q6 - What is the evidence for the prognostic (prediction of outcome) value of individual imaging modalities for JIA?</td>
<td>13</td>
</tr>
<tr>
<td>Q7 - When (time), where (which joints), how often and with what imaging modality should we monitor JIA disease inflammation?</td>
<td>39</td>
</tr>
<tr>
<td>Q8 - When (time), where (which joints), how often and with what imaging modality should we monitor age-related structural abnormalities and damage in JIA?</td>
<td>57</td>
</tr>
<tr>
<td>Q9 - What is the role of imaging for the monitoring of systemic treatment (corticosteroids, synthetic and biological DMARDs) and the targeted delivery of local treatments such as intra-articular injections?</td>
<td>40</td>
</tr>
<tr>
<td>Q10- What is the relationship between individual imaging modalities and clinical remission in JIA?</td>
<td>16</td>
</tr>
<tr>
<td>Q11- What is the impact with respect to outcome of imaging-detected inflammation /damage in the patient in clinical remission?</td>
<td>5</td>
</tr>
</tbody>
</table>
### S6. Scores for risk of bias and applicability of the included studies according to QUADAS-2

<table>
<thead>
<tr>
<th>Point to consider</th>
<th>RoB</th>
<th>Applicability</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Patient selection</td>
<td>Index test</td>
</tr>
<tr>
<td>1. US and MRI are superior to clinical examination in the evaluation of joint inflammation; these techniques should be considered for more accurate detection of inflammation, both in diagnosis and assessing extent of joint involvement.</td>
<td>Low (%) 43</td>
<td>41.5</td>
</tr>
<tr>
<td></td>
<td>High (%) 0</td>
<td>6.2</td>
</tr>
<tr>
<td></td>
<td>Unclear (%) 56.9</td>
<td>52.3</td>
</tr>
<tr>
<td>2. When there is clinical diagnostic doubt, CR, US or MRI can be used to improve the certainty of a diagnosis of JIA above clinical features alone.</td>
<td>Low (%) 50</td>
<td>50</td>
</tr>
<tr>
<td></td>
<td>High (%) 0</td>
<td>0</td>
</tr>
<tr>
<td></td>
<td>Unclear (%) 50</td>
<td>50</td>
</tr>
<tr>
<td>3. If detection of structural abnormalities or damage is required, CR can be used. However MRI or US may be used to detect damage at an earlier time point than CR.</td>
<td>Low (%) 46.8</td>
<td>41.5</td>
</tr>
<tr>
<td></td>
<td>High (%) 0</td>
<td>0</td>
</tr>
<tr>
<td></td>
<td>Unclear (%) 53.2</td>
<td>56.4</td>
</tr>
<tr>
<td>4. In JIA imaging may be of particular benefit over routine clinical evaluation when assessing certain joints, particularly the use of MRI in detecting inflammation of the TMJ and axial involvement</td>
<td>Low (%) 38.8</td>
<td>39.5</td>
</tr>
<tr>
<td></td>
<td>High (%) 0</td>
<td>2.6</td>
</tr>
<tr>
<td></td>
<td>Unclear (%) 63.2</td>
<td>57.9</td>
</tr>
<tr>
<td>5. Imaging in JIA may be considered for use as a prognostic indicator. Damage on CR can be used for the prediction of further joint damage. Persistent inflammation on US or MRI may be predictive of subsequent joint damage.</td>
<td>Low (%) 46.2</td>
<td>46.2</td>
</tr>
<tr>
<td></td>
<td>High (%) 0</td>
<td>7.7</td>
</tr>
<tr>
<td></td>
<td>Unclear (%) 53.8</td>
<td>46.2</td>
</tr>
<tr>
<td>6. In JIA, US and MRI can be useful in monitoring disease activity given their sensitivity over clinical examination and good responsiveness. MRI should be considered for monitoring axial disease and TMJ.</td>
<td>Low (%) 43.6</td>
<td>33.3</td>
</tr>
<tr>
<td></td>
<td>High (%) 0</td>
<td>12.8</td>
</tr>
<tr>
<td></td>
<td>Unclear (%) 56.4</td>
<td>53.4</td>
</tr>
<tr>
<td>7. The periodic evaluation of joint damage should be considered. The imaging modality used may be joint dependent.</td>
<td>Low (%) 49.1</td>
<td>45.6</td>
</tr>
<tr>
<td></td>
<td>High (%) 0</td>
<td>3.5</td>
</tr>
<tr>
<td></td>
<td>Unclear (%) 50.9</td>
<td>50.9</td>
</tr>
<tr>
<td>8. US can be used for accurate placement of intra-articular injections.</td>
<td>Low (%) 47.6</td>
<td>19.0</td>
</tr>
<tr>
<td></td>
<td>High (%) 0</td>
<td>14.3</td>
</tr>
<tr>
<td></td>
<td>Unclear (%) 52.4</td>
<td>66.7</td>
</tr>
<tr>
<td>9. US and MRI can detect inflammation when clinically inactive disease is present; this may have implications for monitoring.</td>
<td>Low (%) 29.4</td>
<td>58.9</td>
</tr>
<tr>
<td></td>
<td>High (%) 0</td>
<td>5.9</td>
</tr>
<tr>
<td></td>
<td>Unclear (%) 70.6</td>
<td>35.3</td>
</tr>
</tbody>
</table>
S7. Reference list of included articles per point to consider

PTC 1. US and MRI are superior to clinical examination in the evaluation of joint inflammation; these techniques should be considered for more accurate detection of inflammation, both in diagnosis and assessing extent of joint involvement.


PTC 2. When there is clinical diagnostic doubt, CR, US or MRI can be used to improve the certainty of a diagnosis of JIA above clinical features alone.


**PTC 3. If detection of structural abnormalities or damage is required, CR can be used. However MRI or US may be used to detect damage at an earlier time point than CR.**


PTC 4. In JIA imaging may be of particular benefit over routine clinical evaluation when assessing certain joints, particularly the use of MRI in detecting inflammation of the TMJ and axial involvement.


**PTC 5. Imaging in JIA may be considered for use as a prognostic indicator.** Damage on CR can be used for the prediction of further joint damage. Persistent inflammation on US or MRI may be predictive of subsequent joint damage.


**PTC 6. In JIA, US and MRI can be useful in monitoring disease activity given their sensitivity over clinical examination and good responsiveness. MRI should be considered for monitoring axial disease and TMJ.**


**PTC 7. The periodic evaluation of joint damage should be considered. The imaging modality used may be joint dependent.**


**PTC 8. US can be used for accurate placement of intra-articular injections.**


**PTC 9. US and MRI can detect inflammation when clinically inactive disease is present; this may have implications for monitoring.**


### Specific comments on PTC:

None given. Read all and discussed but thought all sounded reasonable but clearly they were not for patients.

### General comments:

**POSITIONING:** Anything with JIA is very awkward and painful due to the positions you have to hold and for the length required

**INFORMATION GIVING:** Really important to be talked to as an adult and as someone with understanding of their illness; don’t just speak to mum; appropriateness of going to Children’s Outpatient Department surrounding by ‘kids’; ‘I like being talked to about my illness’

Understanding how a machine works makes it less scary

Best if imaging and rheumatology in the same physical space

Delay for appointments and travelling to hospital and within hospital is a problem so try to co-locate

Technology not worrying i.e. radiation from CR

Need dedicated imaging area for paediatrics

One stop shop is best to reduce time wasted

Always good to be shown scans (always shown US, sometimes CR, almost never shown MRI)

Need scanning to show joint inflammation as when you have pain for a long time you get used to it and may not notice it anymore

Having contrast (injection and needle) can be frightening

Position for CR and MRI can be painful particularly if you have to maintain the same position for a long time

Climbing onto couch for MRI or CR can be difficult/painful, as the couch is often at adult height.

CR and MRI environment can look very sparse and clinical for children

### CR specific comments:

At least this is quick

Parents can be frightened by the risk of CR radiation

### MRI specific comments:

It can take a long time to have an MRI and it is uncomfortable

Need clear information in advance about how long it will take, how noisy it is and what it looks like

Perceived high value of MRI for some joints (TMJ)

Music with MRI helps but is often not loud enough; noise of MRI very scary

MRI is often in an environment used by adults and children and can look frightening

You can sometimes see the faces of the MRI staff looking ‘puzzled’ at the pictures - this is a worrying experience for children/young people, especially as the staff don’t give any information at the time/after the MRI - you have to wait for your next clinic appointment which causes prolonged worry

Sometimes it’s difficult to even get up and off on the MRI ‘bed’, you need a wheelchair and they often don’t have the right equipment to help you get on and off the bed.

PARENTAL PERSPECTIVE: Would be beneficial to learn about the ‘loudness’ of the noise; it was a shock when first heard the loudness of the MRI; first MRI was a ‘traumatic experience’ but needed to ‘be brave for XXX’; some prior warning of just how loud it was would be very useful - perhaps an audio clip of the sound and of the scanner

### US specific comments:

Good because they can show you what’s going on at the time of the scan; you get instant feedback and they can show you the image and inflammation on the screen; even if that joint feels fine; it’s very visual and instant

US made guided injections less worrying, helped

US is easy to understand

Saw benefit of US as showed inflammation when it was not detected by clinical examination

US is real time so you can discuss as you go along, often a doctor you know is doing the scan

---

PTC, points to consider: CR, conventional radiography; US, ultrasound MRI, magnetic resonance imaging; TMJ, temporomandibular joint
## S9. PTC 4: Summary of the included studies comparing imaging and CE in the detection of TMJ damage and inflammation (references in S7, PTC 4)

### TMJ damage:

<table>
<thead>
<tr>
<th></th>
<th>US TMJ vs. CE (3 studies [21, 24, 30])</th>
<th>MRI TMJ vs. CE (10 studies [1, 6, 9, 11, 12, 13, 20, 21, 23, 30])</th>
<th>CR TMJ vs. CE (11 studies [3, 13-15, 17, 19, 23, 26-28, 31])</th>
<th>CT TMJ vs. CE (3 studies [8, 10, 25])</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Bony changes vs. abnormal CE</strong> (2 studies) [21, 30]</td>
<td>Detection rate, mean (range) US vs. CE 1.26-fold (0.41-1.69-fold)</td>
<td>Condylar damage in 81.6% asymptomatic jt</td>
<td>Bony changes vs. abnormal CE (4 studies) [3, 14, 27, 31] 1.54-fold (1.13-1.78-fold)</td>
<td>0.86-fold (0.72-1.0-fold) Increase in % pt with symptoms with increasing severity of CT changes</td>
</tr>
<tr>
<td><strong>Abnormal translation vs. facial asymmetry</strong> (1 study) [6]</td>
<td>1.20-fold</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Bony changes vs. reduced MIO</strong> (2 studies) [11, 23]</td>
<td>5.63-fold p 0.002</td>
<td>Bony changes vs. reduced MIO (4 studies) [15, 19, 23, 27] 1.75-fold (1.39-2.40) r -0.46, p&lt;0.001</td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Erosions vs. abnormal CE</strong> (1 study) [24]</td>
<td>Agreement: 81.9% kappa: 0.57</td>
<td>Erosions vs. abnormal CE (2 studies) [13, 17] 1.71-fold (0.67-2.78-fold)</td>
<td>Clinical indicators of CR TMJ arthritis (1 study) [26] reduced MIO, mandibular asymmetry, mandibular deviation: positive discriminator when all 3 factors combined in 86%</td>
<td>Correlation: 0.303 p&lt;0.05</td>
</tr>
</tbody>
</table>

**Detection rate, mean (range)**
- **US TMJ vs. CE**
- **MRI TMJ vs. CE**
- **CR TMJ vs. CE**
- **CT TMJ vs. CE**

**TMJ damage**

- **Bony changes vs. abnormal CE**
- **Abnormal translation vs. facial asymmetry**
- **Bony changes vs. reduced MIO**
- **Erosions vs. abnormal CE**

**Clinical indicators**

- reduced MIO, mandibular asymmetry, mandibular deviation: positive discriminator when all 3 factors combined in 86%

**Detection rate**
- 0.86-fold (0.72-1.0-fold)
- Increase in % pt with symptoms with increasing severity of CT changes

**Agreement**
- 81.9% kappa: 0.57

**Correlation**
- 0.303 p<0.05
<table>
<thead>
<tr>
<th>Synovitis/effusion (2 studies) [18, 21]</th>
<th>11.7-fold (0.35-23.0-fold)</th>
<th>Synovitis (6 studies) [12, 13, 20, 21, 30, 32]</th>
<th>2.46-fold (1.10-5.91-fold)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Synovitis vs. reduced MIO (4 studies) [1, 2, 20, 21]</td>
<td></td>
<td>Significantly correlated</td>
<td>Reduced MIO best predictor of active MRI changes</td>
</tr>
<tr>
<td>Acute changes (1 study) [30]</td>
<td></td>
<td>71% asymptomatic</td>
<td>63% normal CE</td>
</tr>
</tbody>
</table>

CE, clinical examination; CR, conventional radiography; MIO, maximal incisal opening; r, correlation coefficient
### Summary of Included Studies Describing the Role of Imaging for Guided IA Steroid Injections

<table>
<thead>
<tr>
<th>Reference</th>
<th>No. of subjects</th>
<th>Duration of follow-up (months)</th>
<th>Intervention</th>
<th>Imaging modality</th>
<th>Outcome assessed</th>
<th>Outcome</th>
</tr>
</thead>
<tbody>
<tr>
<td>Young 2012</td>
<td>198</td>
<td>Not specified</td>
<td>IA various joints</td>
<td>US-guided</td>
<td>Accuracy of needle placement</td>
<td>US allowed visualisation of point for injection for 1444 injections</td>
</tr>
<tr>
<td>Agarwal 2012</td>
<td>23</td>
<td>30</td>
<td>IA hip</td>
<td>US-guided</td>
<td>Clinical response</td>
<td>Clinical response in 71% after 1 injection; Mean duration of response (range): 7 (4-15) months</td>
</tr>
<tr>
<td>Boehnke 1994</td>
<td>26</td>
<td>18</td>
<td>IA hip</td>
<td>US-guided</td>
<td>US remission</td>
<td>US remission in 32%</td>
</tr>
<tr>
<td>Neidel 2002</td>
<td>48</td>
<td>24</td>
<td>IA hip</td>
<td>US-guided</td>
<td>Clinical remission; MRI remission</td>
<td>Clinical remission in 76.1%; MRI remission in 76.1%</td>
</tr>
<tr>
<td>Tynjala 2004</td>
<td>13</td>
<td>12</td>
<td>IA hip</td>
<td>US</td>
<td>Clinical remission; US remission</td>
<td>Clinical and US remission in 70% at 3 and 6 months, 50% at 12 months</td>
</tr>
<tr>
<td>Eich 1994</td>
<td>10</td>
<td>1</td>
<td>IA hip and knee</td>
<td>US; MRI</td>
<td>US inflammation; MRI inflammation</td>
<td>US: Hips – 100% improved; knees – no change; MRI: Hips - 75% improved; knees - 63.6% improved</td>
</tr>
<tr>
<td>Laurell 2012</td>
<td>11</td>
<td>1</td>
<td>IA wrist</td>
<td>US-guided</td>
<td>Clinical response; US response</td>
<td>Clinical response in 80%; US response in 91%; US enabled precise location of inflamed compartment which could not be established clinically</td>
</tr>
<tr>
<td>Laurell 2011</td>
<td>30</td>
<td>1</td>
<td>IA ankle</td>
<td>US-guided</td>
<td>US inflammation</td>
<td>Improvement in 87% (resolution in 55%, regression in 32%); US enabled precise location of inflamed compartment which could not be established clinically</td>
</tr>
<tr>
<td>Savage 2012</td>
<td>20</td>
<td>3</td>
<td>IA ankle</td>
<td>US-guided</td>
<td>Clinical response; US response</td>
<td>Clinical resolution in 81.6%; US resolution in 92.1%</td>
</tr>
<tr>
<td>Parra 2010</td>
<td>83</td>
<td>None</td>
<td>IA TMJ</td>
<td>US-guided</td>
<td>Accuracy of needle placement by CT</td>
<td>Acceptable needle placement in 91% (75% required no adjustment, 16% minor adjustment); Unacceptable needle placement in 9% (i.e. required major readjustment)</td>
</tr>
<tr>
<td>Habibi 2012</td>
<td>39</td>
<td>2</td>
<td>IA TMJ</td>
<td>US-guided</td>
<td>Clinical response</td>
<td>Clinical response in 92.1%</td>
</tr>
<tr>
<td>Arabshahi 2005</td>
<td>14</td>
<td>6-12</td>
<td>IA TMJ</td>
<td>CT-guided</td>
<td>Clinical response; MRI inflammation</td>
<td>Improvement in pain (77%), jaw locking (67%), MIO 43%; Resolution of effusion in 48%</td>
</tr>
<tr>
<td>Study</td>
<td>Patients</td>
<td>Follow-up (Months)</td>
<td>Site(s)</td>
<td>Imaging-guided</td>
<td>Clinical Response</td>
<td>Clinical Findings</td>
</tr>
<tr>
<td>---------------</td>
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<td>----------------------------------------------------------------------------------</td>
</tr>
<tr>
<td>Cahill 2007</td>
<td>15</td>
<td>15</td>
<td>IA TMJ</td>
<td>CT-guided</td>
<td>Clinical response</td>
<td>MRI inflammation</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>Clinical response in 58.3%</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>MRI inflammation</td>
<td>MRI improvement in 73%, stable in 20%, worse in 6.7%</td>
</tr>
<tr>
<td>Lochbuler 2013</td>
<td>33</td>
<td>6-12</td>
<td>IA vs. extra-articular TMJ</td>
<td>MRI</td>
<td>MRI inflammation</td>
<td>MRI improvement in 56% with IA injection, 17% with extra-articular injection</td>
</tr>
<tr>
<td>Saurenmann 2009</td>
<td>33</td>
<td>3</td>
<td>IA vs. extra-articular TMJ</td>
<td>MRI</td>
<td>MRI accuracy of needle placement</td>
<td>MRI confirmed injection accurately placed IA in 65%</td>
</tr>
<tr>
<td></td>
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<td></td>
<td>MRI inflammation</td>
<td>MRI improvement in 73% with IA injection, 15% with extra-articular injection</td>
</tr>
<tr>
<td>Stoll 2012</td>
<td>31</td>
<td>5.3</td>
<td>IA TMJ</td>
<td>MRI</td>
<td>MRI response</td>
<td>MRI improvement in 38.7% (resolution in 14.5%), deterioration in 24.2%, stable changes 12.9%, stable normal 24.2%</td>
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<tr>
<td>Fritz 2011</td>
<td>14</td>
<td>22</td>
<td>IA SIJ</td>
<td>MRI-guided</td>
<td>Clinical response</td>
<td>MRI inflammation</td>
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<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>100% of injections were accurately located</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>MRI inflammation</td>
<td>Clinical response in 79%</td>
</tr>
<tr>
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<td></td>
<td></td>
<td></td>
<td>MRI improvement in 59%</td>
</tr>
<tr>
<td>Huppertz 1995</td>
<td>21</td>
<td>13</td>
<td>IA knee, ankle, elbow</td>
<td>MRI</td>
<td>Clinical response</td>
<td>MRI inflammation</td>
</tr>
<tr>
<td></td>
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<td></td>
<td></td>
<td></td>
<td></td>
<td>At 7 weeks: clinical resolution in 76.2%, MRI improvement in 100%, resolution in 52.4%</td>
</tr>
<tr>
<td></td>
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<td></td>
<td></td>
<td></td>
<td>MRI inflammation</td>
<td>At 13 months: clinical resolution in 50%, MRI improvement in 100%</td>
</tr>
<tr>
<td>Beukelman 2006</td>
<td>38</td>
<td>1.5</td>
<td>IA ankle</td>
<td>Fluoroscopy-guided</td>
<td>Clinical response</td>
<td>Clinical response</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>Clinical response in 89%</td>
</tr>
<tr>
<td>Cahill 2007</td>
<td>38</td>
<td>1.5</td>
<td>IA ankle</td>
<td>Fluoroscopy-guided</td>
<td>Clinical response</td>
<td>Clinical response</td>
</tr>
<tr>
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<td></td>
<td></td>
<td></td>
<td></td>
<td>Clinical response in 89%</td>
</tr>
<tr>
<td>Sparling 1990</td>
<td>30</td>
<td>42</td>
<td>IA various joints</td>
<td>CR</td>
<td>Deterioration in damage</td>
<td>CR deterioration after IA steroid was unusual, but most common at the hip (deterioration in 33% by 2+ grades)</td>
</tr>
</tbody>
</table>

IA, intra-articular; MIO, maximal incisal opening
S11. Point to consider 9: Summary of included studies describing imaging findings in clinical remission

(references in S7, PTC 9)

<table>
<thead>
<tr>
<th>Reference</th>
<th>No. of subjects</th>
<th>Clinical assessment of remission</th>
<th>Imaging modality</th>
<th>Site</th>
<th>Outcome</th>
</tr>
</thead>
</table>
| Collado 2012                     | 44             | CRM CR                           | US synovitis (GS, PD) | 44-joints          | GS synovitis: 84.1% jt  
PD activity: 48.6% jt  
More in CRM than CR, p NS |
| Erik Nielsen 2013                | 62             | Clinically inactive joints       | US synovitis     | Multiple           | Subclinical synovitis: 56.1% pt |
| Halbwachs 2012                   | 13             | Clinically inactive joints       | US synovitis     | Multiple           | Subclinical synovitis: 94.1% jt |
| Magni-Manzoni 2013               | 39             | ID                              | US inflammation  | Multiple           | Synovial hyperplasia: 76.9% pt  
Effusion: 66.7% pt  
PD activity: 15.4% pt  
Tenosynovitis: 15.4% pt |
| Donati 2012                      | 100            | Wallace ID                       | US synovitis (SH, effusion, PD) | 72-joints          | US inflammation: 23% pt, 43/7200 (0.06%) jt  
All 3 US changes: 17/43 (32%) jt |
| Silva 2013                       | 35             | CRM CR                           | US synovitis (SH, PD) | 17-joints          | Subclinical US: 37.8% jt |
| Rebollo-Pollo 2011               | 28             | Clinical remission               | US synovitis (GS, PD) | Wrist              | GS: 57.1  
PD: 21.4  
Ankle: GS: 40  
PD: 6.7 |
| Bugni Miotto E Silva 2013        | 36             | Clinical remission               | US synovitis (GS, PD) | Multiple           | GS synovitis: 41.7% pt (3.1% jt)  
PD activity: 19.4% pt  
Subclinical synovitis more common with older disease onset (p 0.007), and in extended oligoarticular or pJIA (p 0.013) |
| Parsa 2011                       | 35             | ID, CRM, CR                      | US inflammation  | Knee               | Inflammation: 35% pt in ID, CRM or CR |
| Molina 2011                      | 11             | Clinical remission               | US synovitis     | Knee               | Synovitis: 36% pt |
| Doria 2001                       | 22             | Clinical remission vs. active disease | US effusion     | Knee               | Effusion in remission: 20% jt  
Effusion in active disease: 77.8% |
| Hemke 2013                       | 146            | Clinically inactive joints       | MRI inflammation | Knee               | Synovitis: 35.9% pt  
BM changes: 33.3% pt |
| Van Veenendaal 2012              | 16             | CRM CR                           | MRI synovitis    | Knee               | Synovitis, CRM: 30% pt  
Synovitis, CR: 25% pt |
| Van Veenendaal 2011              | 30             | CRM CR                           | MRI synovitis    | Knee               | Synovitis, CRM: 30% pt  
Synovitis, CR: 25% pt |
| Brown 2012                       | 11             | CRM CR                           | MRI inflammation | Hand/wrist         | Any MRI inflammation: 63% pt  
Synovitis: 45.5% pt  
BM oedema: 27.3% pt  
Tenosynovitis: 54.5% |
| Zwir 2010                        | 93             | Active disease vs. CRM and CR    | MRI synovitis    | TMJ                | Synovitis, active disease: 80% pt  
Synovitis, CRM: 70% pt  
Synovitis, CR: 65.6% |
CRM, clinical remission on medication; CR, clinical remission off medication; GS, grey scale; PD, power Doppler; NS, not significant; ID, inactive disease; SH, synovial hypertrophy; BM, bone marrow