Assessing structural changes in axial spondyloarthritis using a low-dose biplanar imaging system

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Abstract

Objectives. Patients with axial SpA experience repeated spine imaging. EOS is a new low-dose imaging system with significantly lower irradiation than conventional radiography (CR). The objective was to explore the EOS performances compared with CR for the classification and follow-up of SpA.

Methods. We performed an observational, cross-sectional, single-centre study including SpA patients (definite diagnosis by expert opinion) and control patients (definite chronic mechanical low back pain (cLBP)). All patients underwent pelvic and frontal and lateral CR of the entire spine and two-dimensional (2D) EOS imaging on the same day. Images were blindly assessed for sacroiliitis (modified New York criteria (mNY)) and for ankylosis of the spine (modified Stoke AS Spine Score (mSASSS)). Global ease of interpretation was rated on a scale of 0-10. The primary outcome was intermodality agreement, with an a priori defined non-inferiority limit of 0.7. Interobserver, intra-observer and intermodality agreement were measured by kappa, weighted kappa, intraclass correlation coefficient and Bland-Altman plots.

Results. Forty-eight SpA patients [mean age 47.6 years (s.d. 14.9), symptom duration 21.4 years (s.d. 13.3), 35 (70%) men] and 48 cLBP controls [mean age 49.1 years (s.d. 10.7), 9 (22.5%) men] were included. Intermodality agreement between EOS and CR was 0.50 (95% CI 0.26, 0.75) and 0.97 (95% CI 0.95, 0.98) for sacroiliitis and mSASSS, respectively. Ease of interpretation was greater for CR [8.2 (s.d. 0.9)] compared with EOS [7.2 (s.d. 0.8), P < 0.0001).

Conclusion. Our results suggest that EOS could replace CR for the follow-up of structural damage of the spine, but its place in the classification of sacroiliitis needs to be further explored.

Key words: radiography, spondyloarthritis, ankylosis, sacroiliitis, syndesmophytes, EOS.

Introduction

SpA is a chronic inflammatory disease that encompasses AS, PsA, reactive arthritis and IBD-related arthritis [1]. Over their lifetime, SpA patients are repeatedly exposed to conventional radiography (CR) for classification and follow-up. For classification, sacroiliitis is considered the hallmark of the disease, especially in axial forms [2]. Although the new criteria developed by the Assessment of SpondyloArthritis international Society (ASAS) include MRI as a classification modality for sacroiliitis [3], CR of the sacroiliac joints has been used for decades for the classification of SpA and is still widely used for
classification purposes. Usually when using CR to assess sacroiliitis, the modified New York (mNY) criteria are used to classify sacroiliitis defined by at least a grade II bilateral or grade III unilateral sacroiliitis [4].

Furthermore, while MRI is useful for detecting inflammation [5, 6], CR is considered superior for the detection of new bone formation such as syndesmophytes [7]. Follow-up of patients with axial involvement includes assessment of spinal ankylosis, in particular using the modified Stoke AS Spine Score (mSASSS), usually by CR [8, 9], and is recommended to be performed regularly, e.g. every 2–5 years [10, 11]. Therefore SpA patients are likely to be repeatedly exposed to X-rays during their lifetime. Since SpA appears when patients are young, this represents a major issue, especially when it has been acknowledged that radiation doses are linearly related to the corresponding additional attributable lifetime risk of cancer [12].

EOS is a biplane X-ray imaging system manufactured by EOS imaging (Paris, France) that is available in >10 countries worldwide, including France, the USA, the UK, Canada and Australia. EOS technology uses two perpendicular X-ray beams collimated in two very thin, horizontal, fan-shaped beams and two specific detectors, based on the Nobel prize-winning work of physicist Georges Charpak for his invention and development of particle detectors, in particular multiwire proportional chambers [13]. Fan-beam X-rays and detectors are mounted on a C-arm and scan all or part of the patient’s body. This allows frontal and lateral X-rays of a patient to be carried out simultaneously (4–6 s to scan the spine). The EOS system provides digital images of the skeleton without geometrical distortion and with significantly lower radiation than CR: a study reported a mean entrance surface radiation dose for the posteroanterior spine and lateral spine of 0.23 and 0.37 mGy, respectively, with EOS, compared with 1.2 and 2.3 mGy, respectively, for CR, resulting in a 5- to 6-fold reduction of radiation dose [14]. This imaging modality is mostly used in orthopaedics for studies of the spine, as it allows simultaneous lateral and posteroanterior images while the patient is in a standing position, capturing the entire spine in a single image [15]. Indications for this two-dimensional (2D) biplanar imaging technique may include pathologies where visualization of the entire spine is useful and exposure to X-rays is a concern (e.g. scoliosis in young patients). However, although the key advantage of a lower dose of radiation using this imaging modality has been well established [12, 16], the classification performance of this 2D biplanar imaging technique in SpA has yet to be evaluated and compared with CR [17].

Consequently, our aim was to establish whether EOS had similar performance characteristics to CR and could be considered a replacement for CR for the classification of SpA and/or follow-up. This was done by comparing EOS with CR for the assessment of sacroiliitis and structural changes in the spine.

Patients and methods

Study design

This was an observational, cross-sectional, single-centre study. Inclusion of cases was conducted from April to December 2011. The study was approved by the Ethics Committee of Cochin Hospital and all patients signed informed consent.

Patients

A total of 96 patients were included and had both imaging methods performed as planned. Inclusion criteria for SpA patients were age >18 years, definite axial SpA according to a rheumatologist and an indication for CR imaging for their follow-up (e.g. no CR performed for >2 years). The exclusion criteria were the presence of a contraindication to the performance of CR or EOS imaging (e.g. pregnancy), any disease affecting cognition or the absence of health care insurance. In order to assess specificity, control patients with definite mechanical chronic low back pain and age >18 years were included [18]. Exclusion criteria were identical.

Data collection

General data

Demographics (age, gender, BMI), disease characteristics [symptom duration, disease presentation (axial/peripheral), SpA features (psoriasis, uveitis, HLA-B27 positivity)] fulfilment of the Amor criteria, disease activity (BASDAI [19], CRP) and disease severity (BASFI [20]) data were collected.

CR technique

All patients underwent a posteroanterior pelvic CR and a lateral and anteroposterior CR of the full spine.

EOS imaging technique

All patients underwent full spine and pelvis 2D EOS imaging, which allows the acquisition of images while the patient is in an upright weight-bearing position. Posteroanterior and lateral images were taken simultaneously. Both imaging techniques were performed the same day or at least during the same week.

Data assessment

Readers

Two independent readers performed a blinded reading of both imaging modalities in the SpA patients. Reader 1 (V.F.) was a radiologist trained in musculoskeletal radiology and reader 2 (A.M.) was a rheumatologist specialized in the field of SpA. Readers were blinded to the diagnosis and medical files as well as to the other reader’s results and any previous imaging. Two weeks after imaging, reader 2 blindly read the pelvic imaging (EOS and CR) of the 29 patients in the SpA group with a radiographic sacroiliitis according to the medical file, pooled together with the pelvic imaging of the control group.
Prior to the study, three training sessions were performed and interreader agreement was high for the last session: the weighted kappa and 95% CI for sacroiliac joint scoring according to the mNY criteria (grade 0–4, blinded reading of 10 pelvic CRs) was 0.90 (0.73, 0.97), and the intraclass correlation coefficient (ICC) and 95% CI for spine scoring according to the mSASSS (blinded reading of 10 spine CRs) was 0.96 (0.87, 0.99).

Sacrolilits
Each sacroiliac joint of each pelvic CR or EOS imaging was scored from 0 to 4 according to the mNY score for sacroiliitis by both readers and definite sacroiliitis was defined as a grade 2 bilateral or unilateral grade 3 or 4 according to the mNY criteria [3].

Spine involvement
Both readers scored cervical and lumbar spine CR and EOS images according to the mSASSS system, which takes into account the presence of erosion, sclerosis, syndesmophytes and total bony bridging formation at each anterior site of the cervical spine from the lower border of C2 to the upper border of T1 and the lumbar spine from the lower border of T12 to the upper border of the sacrum only on a lateral view (range 0–72) [5].

Subjective ease of interpretation of imaging
Both readers gave a grade on a visual analogue scale (VAS) regarding the subjective visibility of the anatomic structures (0 being the lowest and 10 the optimal ease of interpretation) for each imaging modality and for each site of assessment.

Data analysis

Intermodality agreement
This was the primary outcome measure for the assessment of both the sacroiliac joints and the spine, with a defined a priori target of 0.70. Agreement was measured for the presence of definite sacroiliitis according to the mNY criteria (yes/no) by unweighted kappa coefficient of agreement and by weighted kappa for the agreement between each grade of the score for each sacroiliac joint. Agreement for the mSASSS was measured by ICC and a Bland–Altman plot and 95% limit of agreements. Intramodality, interreader and intrareader agreement were also assessed for both modalities and both sites (sacroiliac joint and spine).

Sacrolilits detection
The capacity of EOS and CR to classify a patient as radiographic axial SpA (i.e. detect sacroiliitis according to the mNY criteria) was evaluated by the calculation of sensitivity, specificity and positive likelihood ratio of each imaging modality. Here the gold standard was the medical diagnosis from the medical file [e.g. SpA with mNY sacroiliitis vs control chronic mechanical low back pain (cLBP) patients], thus for this analysis, only patients with mNY sacroiliitis from the SpA group were included (n = 29) and were compared with the 48 control cLBP patients. Reader 2 performed a blinded reading (for clinical condition, e.g. SpA vs cLBP) of all pelvic imaging by assessing the presence of sacroiliitis (yes/no).

Subjective ease of interpretation
The mean results for each modality at each site were compared by Wilcoxon test (SAS version 9.1; SAS Institute, Cary, NC, USA).

Results

Participants
Forty-eight SpA patients were included (Table 1). Thirty-one (64.5%) patients presented with mNY sacroiliitis according to medical files and 47 (97.9%) fulfilled either the ASAS or Amor criteria [21]. The control cLBP patients (n = 48) had a mean age of 49.1 years (S.D. 10.7); 9 were men and 39 were women.

Intermodality and inter- and intrareader agreement

Assessment of the sacroiliac joints
Intermodality agreement for the presence of sacroiliitis between EOS and CR was moderate with a kappa of 0.50 (95% CI 0.26, 0.75) and 0.50 (95% CI 0.16, 0.84) for reader 1 and reader 2, respectively, Interreader and intrareader agreement were fair and comparable for both modalities (Table 2).

Fig. 1 summarizes the sacroiliac joint analysis (mNY score) of both readers: more than half of the sacroiliac joints were identically scored by both techniques (56.9%) and none were scored as normal (grade 0) by one modality when definitely abnormal (grades 3 and 4) with the other modality. The weighted kappa coefficient of agreement was 0.66 (95% CI 0.59, 0.73).

Assessment of the spine
The mean mSASSS was 15.0 (S.D. 19.7) by CR versus 14.8 (S.D. 17.9) by EOS for reader 1 and 13.1 (S.D. 18.0) vs 12.8 (S.D. 17.9) for reader 2. Intermodality agreement was >0.90 for both readers [ICC 0.92 (95% CI 0.86, 0.95) and 0.97 (95% CI 0.95, 0.98) for reader 1 and reader 2, respectively; Table 2]. Interreader agreement was also >0.90 for both imaging modalities [ICC 0.94 (95% CI 0.89, 0.97) and 0.95 (95% CI 0.91, 0.97) for EOS and CR, respectively].

Bland–Altman plots and their 95% limits of agreement are presented in Fig. 2. Both EOS and CR interreader limits of agreement were rather wide, but the mean difference for both imaging modalities was low (−2.0).

Sacrolilits detection
Performance for sacroiliitis detection on pelvic imaging was identical with both techniques. Both had a sensitivity of 0.76 (range 0.58–0.88) and a specificity of 0.84 (range 0.71–0.91) identifying the presence of sacroiliitis in 22 of 29 patients (75.9%) within the SpA group and identifying 8 of 48 patients (16.7%) with sacroiliitis in the control group. The CR and EOS positive likelihood ratio was 4.65.
Subjective ease of interpretation

Subjective ease of interpretation was significantly higher for CR, particularly for the sacroiliac joint evaluation [VAS of the sacroiliac joint 6.7 (S.D. 1.1) vs 8.1 (S.D. 1.3) for EOS and CR, respectively; $P < 0.0001$], but also for evaluation of the spine (VAS 7.7 (S.D. 0.8) vs 8.3 (S.D. 0.8) for EOS and CR, respectively; $P < 0.0001$).

Discussion

This study provides evidence to suggest the possible use of EOS instead of CR for the follow-up of SpA patients at a lower radiation dose, as evaluation of spinal structural changes was satisfactory. Although EOS had a lower performance in evaluation of the sacroiliac joint, it was similar to CR, suggesting that further evaluation of the role of EOS in the classification of SpA is worthwhile.

Agreement between modalities in evaluation of the sacroiliac joints (i.e. sacroilitis) by EOS and CR was only moderate ($\kappa = 0.50$), and when looking individually at each sacroiliac joint scored, only grade 4 of the sacroiliac joint was consistently recognized between modalities (Fig. 1). The weighted kappa coefficient of agreement failed to reach 0.70. These results highlight the difficulty of scoring sacroiliac joints with EOS imaging, as well as with CR, the current gold standard [22, 33].

Intra-observer and interobserver agreement for the presence of sacroilitis according to the mNY criteria were as low as 0.40 and 0.33, respectively, but consistent for both modalities, reflecting again the difficulty of classifying sacroilitis by pelvic radiography, as has been reported in other previous studies, where intraobserver variation ranged from 0.07 to 1.0 [24] and interobserver variation ranged from 0.19 to 0.79 [6, 25].

The sensitivity for detection of sacroilitis was identical with EOS and CR. Sacroilitis recognition is crucial for the classification of axial SpA, but it is not always easy and requires experience. In this study we found lower sensitivities but higher specificities for both imaging modalities than those of van Tubergen et al. [16]. In any case, both sensitivity and specificity were comparable between the

Table 1: Demographic and disease characteristics of 48 SpA patients

<table>
<thead>
<tr>
<th>Measure</th>
<th>SpA patients</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age, mean (s.d.), years</td>
<td>47.6 (14.9)</td>
</tr>
<tr>
<td>Male, n (%)</td>
<td>35 (73)</td>
</tr>
<tr>
<td>Symptom duration, mean (s.d.), years</td>
<td>21.4 (13.3)</td>
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<tr>
<td>Diagnosis duration, mean (s.d.), years</td>
<td>16.8 (11.0)</td>
</tr>
<tr>
<td>HLA-B27 positive, n (%)</td>
<td>35/42 (83.3)</td>
</tr>
<tr>
<td>History of anterior uveitis, n (%)</td>
<td>16 (33.0)</td>
</tr>
<tr>
<td>History of psoriasis, n (%)</td>
<td>4 (8.3)</td>
</tr>
<tr>
<td>Fulfilling ASAS axial SpA criteria, n (%)</td>
<td>44 (91.7)</td>
</tr>
<tr>
<td>BASDAI (0–100), mean (s.d.)</td>
<td>25.2 (18.9)</td>
</tr>
<tr>
<td>BASFI (0–100), mean (s.d.)</td>
<td>23.8 (23.0)</td>
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<tr>
<td>CRP, mean (s.d.), mg/l</td>
<td>5.7 (10.0)</td>
</tr>
<tr>
<td>BMI, mean (s.d.), kg/m²</td>
<td>24.3 (4.3)</td>
</tr>
<tr>
<td>Anti-TNF-α therapy, n (%)</td>
<td>24 (63)</td>
</tr>
<tr>
<td>mNY sacroilitis according to medical record, n (%)</td>
<td>31 (64.5)</td>
</tr>
</tbody>
</table>

ASAS: Assessment in SpondyloArthritis international Society; mNY: modified New York criteria.

Table 2: Intermodality and interreader and intrareader agreement for evaluation of the sacroiliac joint and spine assessed in 48 SpA patients

<table>
<thead>
<tr>
<th>Imaging modality</th>
<th>Agreement for evaluation of the sacroiliac joint: presence of mNY sacroilitis, $\kappa$ (95% CI)</th>
<th>Agreement for evaluation of structural changes of the spine: mSASSS, ICC (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Intermodality</td>
<td>Reader 1: 0.50 (0.26, 0.75) Reader 2: 0.50 (0.16, 0.84)</td>
<td>0.92 (0.86, 0.95) Reader 1: 0.97 (0.95, 0.98) Reader 2: 0.94 (0.89, 0.97)</td>
</tr>
<tr>
<td>EOS</td>
<td>Interreader: 0.33 (0.10, 0.57) Intraobserver: 0.40 (–0.05, 0.85)</td>
<td>0.99 (0.98, 0.99) Intraobserver: 0.96 (0.91, 0.97)</td>
</tr>
<tr>
<td>CR</td>
<td>Interreader: 0.36 (0.09, 0.63) Intraobserver: 0.40 (–0.19, 0.99)</td>
<td>0.99 (0.99, 1.00) Intraobserver: 0.99 (0.99, 1.00)</td>
</tr>
</tbody>
</table>

mNY: modified New York criteria; mSASSS: modified Stoke Ankylosing Spondylitis Spine Score; ICC: intraclass correlation coefficient; CR: conventional radiography.
imaging modalities. This reinforces the idea that radiography might not be the ideal tool to assess sacroiliitis, but this imaging modality remains the initial classificatory tool in the evaluation of SpA [26], and EOS showed similar performance with less radiation.

On the other hand, agreement between the modalities in the evaluation of spinal involvement (e.g. ankylosis) was outstanding, with an interreader agreement of 0.95 for EOS and an intermodality agreement of >0.90 for both readers. Our results are consistent with previously published data where the ICC for interobserver agreement in mSASSS were found to be as high as 0.94 [27]. Thus EOS seems a viable imaging modality to follow-up SpA patients.

Subjective ease of interpretation was greater for CR compared with EOS, especially in evaluation of the sacroiliac joint. This might be explained by the different penetration of the X-rays, where abdominal anatomical structures might interfere with visualization of the sacroiliac joint. Another reason for this difference in interpretation might be familiarity with the technique. While CR has been used for >50 years in the detection of sacroiliitis, EOS is a brand new imaging technique, and readers might need time to become familiar with this new imaging modality.

This study has some weaknesses, but also some strengths. First, two independent readers performed the blinded reading of all CR and EOS images. Although the different backgrounds of the two readers (radiologist and rheumatologist) may be seen as a weakness and may explain the low agreement, especially for the evaluation of sacroiliitis, this reflects daily practice, as both radiologists and rheumatologists are confronted with the reading of pelvic CRs from SpA patients to establish the presence or not of sacroiliitis [6].

Moreover, reader 2 read the images of the 48 SpA patients and, 2 weeks later, performed the pooled blinded reading of the pelvic images of both the 29 SpA patients with sacroiliitis and the 48 control patients. This might have lead to a higher sensitivity for EOS, because of the larger number of readings performed by reader 2. However, this shows that with broader use and familiarization with this imaging modality, readers should be able to detect sacroiliitis with EOS imaging as well as with CR.

The small number of patients and the monocentricity of the study could be seen as a weakness. However, it is worth noting that the EOS imaging system is not widely available.

Our department is situated in a tertiary care setting and has expertise in SpA [28–30]. This addresses to some degree the absence of specific diagnostic criteria used to determine the SpA population, as patients were diagnosed based on expert opinion. Furthermore, demographic characteristics of the included patients are those expected in such a cohort.

The CI of the intermodality agreement for sacroiliitis detection was rather large, illustrating the difficulty of analysing the sacroiliac joint using EOS as well as CR. Moreover, different statistical techniques were used (kappa, weighted kappa coefficient, ICC and

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**Fig. 1** Comparison of the pooled scoring of the two readers of 181 sacroiliac joints according to mNY criteria by CR and EOS imaging modalities

<table>
<thead>
<tr>
<th></th>
<th>0 (7.2%)</th>
<th>1 (5.5%)</th>
<th>2 (2.2%)</th>
<th>3</th>
<th>0</th>
<th>0</th>
</tr>
</thead>
<tbody>
<tr>
<td>EOS</td>
<td>13</td>
<td>10</td>
<td>4</td>
<td>2</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>EOS</td>
<td>7 (3.9%)</td>
<td>13 (7.2%)</td>
<td>14 (7.7%)</td>
<td>2</td>
<td>2 (1.1%)</td>
<td>2 (1.1%)</td>
</tr>
<tr>
<td>EOS</td>
<td>1 (0.6%)</td>
<td>7 (3.9%)</td>
<td>19 (10.5%)</td>
<td>5</td>
<td>3</td>
<td>1 (1.7%)</td>
</tr>
<tr>
<td>EOS</td>
<td>0</td>
<td>1 (0.6%)</td>
<td>8 (4.4%)</td>
<td>16</td>
<td>6</td>
<td>2 (2.8%)</td>
</tr>
<tr>
<td>EOS</td>
<td>0</td>
<td>2 (1.3%)</td>
<td>1 (0.6%)</td>
<td>6</td>
<td>42 (23.2%)</td>
<td></td>
</tr>
</tbody>
</table>

- Differences of ≥ 3 grades in the scoring
- Differences in 2 grades in the scoring
- Agreement in the scoring

SIJ: sacroiliac joint; CR: conventional radiography; mNY: modified New York criteria.
This study suggests that EOS could replace CR for follow-up of SpA (e.g. progression of structural damage of the spine). Its place in the classification of sacroiliitis remains unclear because of the low interreader agreement, but this was comparable to CR, the current gold standard. Therefore it may be worth considering this technique for the classification of patients at a young age because of the reduced radiation, although this needs further evaluation.

**Disclosure statement:** The authors have declared no conflicts of interest.

**References**

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**Rheumatology key messages**

- EOS may be an alternative to conventional radiography (CR) for axial SpA follow-up.
- The agreement between EOS and CR was outstanding for the detection of spine involvement, but low for sacroiliitis detection.
- The sensitivity of EOS and CR was identical for sacroiliitis detection, with lower radiation with EOS.


