Workshop Report

Clinical Diagnosis and Imaging of Sacroiliitis, Innsbruck, Austria, October 9, 2003

Inflammation in the axial skeleton usually occurs as sacroiliitis and may result in chronic pain, increased comorbidity, and reduced working capacity[1]. These consequences have direct influence not only for the individual but also for society[2]. Therefore early diagnosis is considered a primary goal to prevent under- and misdiagnosis of sacroiliitis.

Confirmation of sacroiliitis in clinical practice is based on various imaging techniques. Sacroiliitis detected by radiography, magnetic resonance imaging (MRI), or computerized tomography (CT) in the presence of clinical manifestations is diagnostic of ankylosing spondylitis (AS)[3]. The cooperation between rheumatologists, radiologists, and nuclear medicine specialists can be crucial for future developments. The techniques currently used in the diagnosis of sacroiliitis are discussed in this review and an algorithm is proposed for the use in clinical practice.

CLINICAL DIAGNOSIS

In 1977, Calin defined a set of clinical symptoms useful to define patients with inflammatory low back pain[4]. Slow onset of symptoms, duration of more than 3 months, morning stiffness, improvement with exercise (or deterioration with rest), and age under 40 years at onset of symptoms are typical inflammatory signs, and fulfilment of 4 of the 5 signs has been shown to diagnose inflammatory low back pain with a sensitivity of 95% and a specificity of 85%[4]. Zeidler and colleagues added sleep disturbance (in the early morning hours), response to nonsteroidal antirheumatic drugs, and ischial pain referred from the gluteal region to the knee to the list of typical signs that would further support the diagnosis of inflammatory back pain[5].

The characteristics of pain symptoms suggested by Calin, *et al* are the only validated description available to diagnose inflammatory axial disease in the absence of radiographic evidence of sacroiliitis[4]. Tests of sacroiliac joint tenderness are poorly reproducible and inaccurate in distinguishing sacroiliitis from mechanical spinal conditions[6]. Therefore, the use of clinical signs is crucial to select patients with inflammatory back pain from the patients with other noninflammatory causes of spinal disease.

For assessment of disease activity in AS, the Bath Ankylosing Spondylitis Disease Activity Index (BASDAI) has been successfully introduced and evaluated since 1994[7–9]. It has been translated and adapted for the German patient[10]. This instrument has been shown to be easy to use, reliable, and sensitive to change in AS. In addition to other criteria, the BASDAI has also been used to define the patients with potential benefit from tumor necrosis factor (TNF)-blocking agents, and there is a broad consensus that a BASDAI score ≥ 4 is the major criterion to consider treatment of AS with TNF-α blockers. The effects of therapy can be evaluated by a reduction of 50% of the BASDAI score or a reduction of 2 points on a scale of 0 to 10 compared to the values before therapy was started[10].

However, for the indication of TNF-blocking agents and for research trials we need objective information to document the extent of inflammation and to estimate the structural changes in patients with inflammatory back pain[11]. In this situation the erythrocyte sedimentation rate (ESR) and other inflammatory serological measures may fail, as only 50% of patients with AS show an elevated ESR. Levels of C-reactive protein have only a minor role to play in the assessment of inflammatory axial disease (spondyloarthritis, SpA)[12-14]. Further, the presence of HLA-B27 has been shown to be helpful for the diagnosis of AS (with a sensitivity of 95% and specificity 20%), but is much less valuable in patients with psoriatic arthritis, reactive arthritis (Reiter's syndrome), colitis-associated SpA, or undifferentiated SpA[15].

Early diagnosis of milder cases to avoid inappropriate investigation and unhelpful nonspecific therapy may well be appropriate[4].

Therefore clearly defined documentation appears to be an important strategy to contribute to earlier diagnosis and followup of sacroiliitis. Apart from being an interesting research focus, there is a definite need for sensitive and specific imaging techniques, and the development of strategies to apply these imaging techniques in patients with inflammatory back pain.

IMAGING TECHNIQUES TO DETECT SACROILIITIS

Plain radiographs

The plain radiograph is the most widely accepted and available imaging method. It is the mainstay of radiological diagnosis and documentation of disease. It is relatively inexpensive, easy to obtain, and extremely helpful, when positive findings are present[16]. Evidence of sacroiliitis on radiograph is extremely frequent in AS, but it may not be a manifestation of every case, especially in early or atypical forms of the disease. Characteristic radiographic changes of AS begin in the sacroiliac (SI) joints and evolve slowly over many years to involve the rest of the spine.

Evaluation. Using anteroposterior radiographs of the pelvis, 5 grades can be differentiated from 0 (normal) to 4 (ankylosis) according to the modified New York classification of 1980:

Grade 0: normal; well defined margins, uniform regular rim.

Grade 1: suspicious; initial sclerosis, decreased focal thickness of articular space.

Grade 2: minimal sacroiliitis with loss of definitions of articular cartilage, subchondral osteoporosis, areas of sectoral reactive sclerosis and irregular pseudoenlargement.

Grade 3: moderate sacroiliitis with subchondral sclerosis of both articular margins predominantly at the iliac side, erosions, reduced articular space, and initial ankylosis.

Grade 4: complete ankylosis with residual sclerosis, which tends to decrease in time.

The diagnosis of grade 3 (clearly defined erosions, pseudodilatation of the joint space) or grade 4 is usually not a problem. The main difficulties relate to grade 1 (suspicious, unclear) and grade 2 (small erosions, hypersclerosis), where most of the diagnostic variability arises, with significant inter- and intraobserver variations either recognizing or grading sacroiliitis[16].

For cross-sectional and prospective studies of the vertebral column, radiographic findings of patients with AS have been defined by the Bath Ankylosing Spondylitis Radiology Index (BASRI) score[17]. The lumbar and cervical spine and hips were similarly graded 0–4. These scores were added together to give the BASRI-t (total), including BASRI-h (hip) and BASRI-s (spine). BASRI-s includes radiographs of the SI joints, lumbar spine, and the cervical spine[18]. The BASRI is easy and quick to use, and is an important outcome measure combined with the Bath AS Metrology Index (BASMI), Bath AS Functional Index (BASFI), BASDAI, and Bath AS General (BAS-G)[19]. Patients with hip involvement are reported to have more severe spinal disease than those without ($p < 0.0001$)[17].

Inter- and intraobservation showed between 73% and 82% and 73% and 88% complete agreement, respectively, with a specificity rate of 0.78–0.89. Thus, BASRI is a reliable and rapid method to grade radiographic changes in AS[17].

A limitation is that BASRI does not pick up minor radiological changes. Further, it always remains at grade 2, or mild disease, until there is a fusion between 2 vertebrae and 3 or more syndesmophytes[17]. Recently, the European OASIS group reported a newly validated scoring system for the cervical and lumbar spine, which is a modified Stoke Ankylosing Spondylitis Spine Score (mSASSS). The study authors concluded that the mSASSS is the most appropriate method for measuring radiographic outcome in randomized clinical trials in AS[18,19]. Although this score is more reproducible, it has been designed for scientific settings like the BASRI score[18–20].

Protocol. The anteroposterior radiograph is obtained with a 20° caudal tube tilt. Cranial angulation and conventional tomography do not increase sensitivity of the examination, and therefore a pelvic radiograph is recommended[21]. This multicenter study shows that the simple anteroposterior pelvic radiograph is equivalent for evaluating SI joints with the advantage of the additional evaluation of the hip joints. This seems important, as the hips become involved in about 25% of individuals and may predict a more severe outcome for the cervical spine. Therefore standardized pelvic radiographs should be obtained including the hip region, not only the region of the SI joints.

In summary, radiographs of the SI joints are quick and cheap to document AS and to differentiate AS from undifferentiated SpA.

Computed tomography (CT)

Changes are similar to those described for radiographs, but CT allows for a higher grading of sacroiliitis by using the same criteria as the modified New York criteria.

Early CT findings include cortical erosions, subchondral sclerosis, later joint space narrowing and bony ankylosis, sometimes together with additional findings such as pseudodilatation ("Buntes Bild"). Further findings can be bone marrow sclerosis (increased density), fat accumulation in bone marrow (decreased density), an irregular surface, or new bone formation at the enthesis[22].

CT can easily overdiagnose sclerosis and ankylosis, because subchondral sclerosis of the iliac part of the SI joint is a natural aging phenomenon, similar to joint space narrowing and erosions. Nevertheless, for the detection of early erosions and regional ankylosis, CT seems to be the best method[1].

Protocol. CT is obtained by acquisition of semicoronal 3–5 mm slices with a 25° to 30° cranial gantry tilt and bone algorithm image reconstruction. Multidetector CT with a slice thickness of 1.5 mm and a collimation of 1 mm with multiplanar reconstruction (MPR) allows direct imaging in different planes and is therefore an improvement over the limited axial slices, which is especially important for assessment of the obliquely oriented SI joint.

Radiological gradings of CT categories are summarized in Table 1. Normal variants of SI joints are nonuniform joint space narrowing and subchondral sclerosis, especially on the iliac side. CT enables differentiation of osteitis condensans ilii from septic arthritis, minor lesions such as fatigue fissuring or insufficiency fractures, as well as osteoarthritis (intraarticular gas phenomenon)[23].

The main contraindications of CT are metallic artefact depending on slice thickness, type and form of the metal, young age, and gravidity.

Studies comparing radiographs and CT show that CT is more accurate than radiography in the detection of morphological changes, but unable to differentiate active from inactive disease[24,25].

In a prospective study of patients with suspected sacroiliitis, the sensitivity and specificity of MRI for detection of cor-

Table 1. Radiological grading of radiographs and high resolution CT categories.

Radiological Grading of Radiographs	High Resolution CT Categories
0 = Normal	I(A) SIJ > 4 mm
1 = Erosion (uncertain)	I(B) SIJ < 2 mm
2 = Erosion with subchondral sclerosis, early bridging (minimal)	II(A) Contour irregularities
	II(B) Erosion (early iliac, later sacral side)
3 = Pseudodilatation erosion, sclerosis, bridging (moderate)	III(A) Subchondral sclerosis (osteitis)
4 = Ankylosis	III(B) "Spur formation" (enchondral ossification)
	IV(A) Transarticular bony bridges
	IV(B) Ankylosis (synchondrosis)

CT: computerized tomography, SIJ: sacroiliac joint.

tical erosions and subchondral sclerosis when compared to CT were 94.3% and 100%, respectively. Most national guidelines, like those from Austria, do not recommend radiographs or CT for patients with suspected sacroiliitis[26].

MRI [T1 with fat saturation and fast short-tau inversion recovery (STIR)] can replace CT in cases with a strong clinical suspicion of sacroiliitis and equivocal or normal plain radiograph[27].

Scintigraphy

Scintigraphy is a useful technique and screening method to detect bony metabolism, which can be increased in cases with inflammation[1]. The role for imaging of the SI joints in the diagnosis of sacroiliitis is age- and sex-specific, which has led to questions about its sensitivity and specificity[28,29].

Quantitative bone scintigraphy is very sensitive to abnormalities in SI joints, but the findings are not specific enough to consistently diagnose inflammatory sacroiliitis. It is influenced by many nonspecific factors (e.g., hopping on one leg will increase the uptake). Using an improved imaging procedure, Hanly, *et al*[30] were able to demonstrate that only single photon emission CT (SPECT) scanning clearly distinguishes between patients with inflammatory low back pain and controls. Yildiz and colleagues recently confirmed the improved diagnostic capability of SPECT imaging of the SI region, achieving figures of 97% for sensitivity and 90% for specificity. This procedure was better than the use of nanocolloid scintigraphy[31].

Protocol. The standard protocol uses ^{99m}Tc-MDP intravenously injected, with acquisition of 3 sequential phases: arterial perfusion (first minutes), vascular phase (5–10 minutes postinjection), and late phase (2–3 hours postinjection). Bone scintigraphy is routinely carried out 2–3 hours after intravenous administration of ^{99m}Tc. Planar films are used to assess quantitative and qualitative uptake in the SI joints. Regions of interest are drawn in the right and left inferior portions of the SI joints, excluding uninvolved surrounding bone as much as possible.

The static bone phase compares the count in each SI joint with the uptake in the sacrum (SI joint:sacral peak count ratio). Abnormally increased uptake indicates the active inflammation in early stages also, allowing differentiation of other causes of low back pain.

The blood pool phase represents activity from soft tissue inflammation and helps to exclude activity from other surrounding structures, such as ureter and iliacal vessels.

Due to 3-dimensional localization in and around the SI joints, the use of SPECT improves differentiation of the uptake in inflammatory disease[30]. Quantitative analysis uses a horizontal profile over the SI joints, dividing the peak uptake over the SI joints by the peak uptake over the midsacrum. Qualitative analysis compares uptake over the iliac tuberosity (dorsal syndesmosis) to the ventral synovial portion of the joint, as follows — Grade 0: ilium > SI joint, Grade 1: ilium = SI joint, Grade 2: ilium < SI joint, indicative for sacroiliitis.

The use of nonsteroidal antiinflammatory drugs has been shown to reduce the sensitivity of bone scintigraphy in the detection of sacroiliitis. Fifty-seven percent of patients with abnormal SPECT scan had abnormalities on MRI, but only 46% of patients with abnormalities in MRI had SPECT scans indicative of sacroiliitis[29]. Thus the 2 imaging modalities do not replicate the same findings. MRI was more sensitive and SPECT was more specific for detection of sacroiliitis. SPECT provides information on disease activity with inflammatory axial disease, permitting appropriate selection of localized or systemic antiinflammatory therapy.

SPECT bone scanning has been shown to provide evidence of bony inflammation in the absence of radiographic changes, and is a useful screening method in generally activated inflammation and for patients where other imaging techniques are limited[30,32].

Magnetic resonance imaging

At present, MRI can be considered the functional imaging technique used the most in patients with sacroiliitis, because it is the only technique enabling observation of both acute and chronic sacroiliitis[1].

Oostveen, *et al* have shown that MRI of the SI joints can be used to identify sacroiliitis earlier than radiography[33]. The positive predictive value of grade ≥ 2 sacroiliitis on MRI for the development of grade ≥ 2 sacroiliitis on radiograph after 3 years was 60%, sensitivity was 85%, and specificity 47%[33].

Although MRI also provides information on structural changes of the SI joint, its special indication is for detecting inflammatory activity of SpA disease.

In the course of sacroiliitis both acute and chronic changes can occur. MRI is helpful in the evaluation of both inactive and active disease. Contrast administration enables differentiation of lesions with high water content due to inflammatory edema from lesions with reduced water content due to fibrous tissue or sclerosis. The enhancement in those lesions can be explained by inflammatory tissue[33]. Acute inflammatory activity can present with bone marrow edema. Bone marrow edema is thought to represent the earliest manifestation of sacroiliitis, because it has been found that bone marrow edema can exist without cartilaginous abnormalities[30,33].

Chronic signs include erosions, sclerosis, changes of joint width, and fat deposition in the bone marrow. Periarticular fat accumulation has different pathophysiological explanations. Some researchers think that it represents fatty infiltration and inflammatory changes; others interpret it as a sign of degeneration[22].

Sclerosis detected by CT has been shown on MRI to correspond to a mixture of inflammation, fatty marrow changes, and increased osseous tissue or marrow fibrosis[22].

CT enables better assessment of osseous proliferation in the ligamentous portion than MRI, but there is no substantial loss of information by using MRI instead of CT, as reported[22].

Because the radiographic grading from 0 to 4 is essential, a similar grading system for MRI was evaluated, with detailed assessment of a chronicity index and an activity index[33-36].

The MRI chronicity index of sacroiliitis was defined from precontrast images as follows:

Grade 0: normal SI joint.

Grade 1: suspicious; without joint width impairment, mild subchondral sclerosis without blurring of the articular cavity, with/without periarticular fat accumulations, and/or < 2 discrete erosions per slice.

Grade 2: moderate subchondral sclerosis without joint width impairment, with less than one-third blurring of the articular cavity, with/without periarticular fat accumulations, and/or ≥ 2 discrete erosions per slice without confluence.

Grade 3: joint width impairment, pronounced subchondral sclerosis obscuring more than one-third of articular cavity with periarticular fat accumulations, and/or pseudodilatation of articular cavity due to confluent erosions and/or circumscribed joint narrowing due to ankylosis buds of less than one-quarter of the articular cavity.

Grade 4: severe; definitive ankylosis of more than one-quarter of the articular cavity.

The MRI activity index defined from contrast enhanced images was defined as follows:

No inflammatory activity with an enhancement factor < 25%; moderate inflammatory activity with an enhancement factor 25% to 70%; and severe inflammatory activity with an enhancement factor < 70%.

The capability of MRI to distinguish between acute and chronic changes and to estimate the degree of disease activity can be beneficial in monitoring the effects of pharmacological treatment[34,35].

The value of MRI in the diagnosis of early sacroiliitis in relation to clinical findings has been assessed by different studies[33,34,38-40]. According to Braun, *et al*[39] the finding from dynamic MRI in acute sacroiliitis seems to correlate with clinical symptoms and signs of disease activity. Dynamic MRI enables quantification of enhancement with correlation of the degree of inflammatory lower back pain and measurements on a visual analog scale[1]. However, this method is difficult to apply as a clinical routine because it is time-consuming and reproducibility may be poor[22].

Other studies have shown that in early sacroiliitis MRI was able to detect inflammatory activity and destructive changes of the sacroiliac joints, but the changes were not associated with clinical findings[33,37,40].

Protocol. The MRI protocol consists of semicoronal T1, semicoronal T1 fat saturation, semicoronal short-tau inversion recovery (STIR) or TIRM, semiaxial T1 fat saturation, semiaxial T2, and semicoronal and semiaxial T1 fat saturation after administration of contrast.

Semiaxial sequences are important as their anatomy of the ventral and dorsal margins of the cartilaginous portion can only be assessed by this view[22] and good visualization of the ligamentous portion of the SI joint can be obtained. The algorithm suggested by Puhakka, *et al*[22] is semicoronal T1, semicoronal and semiaxial STIR. If those sequences are normal, the examination is complete. Otherwise additional semicoronal T1 fat saturation before and after contrast administration as well as semiaxial postcontrast T1 fat saturation sequences should be obtained.

Muche, *et al*[41] evaluated whether the approach by administration of contrast or STIR can get the same diagnostic sensitivity and specificity, which may be important in clinical practice and from a social-economic point of view. The STIR sequence was found to be less sensitive than the contrast enhanced sequences because inflammation of the joint cavum cannot be well detected. Therefore MRI sequences with contrast applications are considered the gold standard to detect inflammatory changes. Our consensus protocol consists of semicoronal T1, semicoronal STIR/TIRM, semicoronal T1 fat saturation with and without contrast, semiaxial T1 fat saturation with and without contrast, and T2 sequences. Contraindications are metal implants including pacemakers; the limitations are claustrophobia, reported in 10% of patients in traditional MRI scanners and in 1% in newer open-model machines. Furthermore, it has relatively high costs.

The advantages of MRI compared to radiography are higher sensitivity and absence of radiation, both especially important in children, as sacroiliitis is common in juvenile SpA[42,43].

Sonography

Muche, *et al*[41] report that the dorsocaudal parts of the synovial joints and the bone marrow are the most frequently inflamed structures in early disease. The dorsal enthesis, dorsal joint capsule, and the dorsal cavum can be well visualized by ultrasound. As inflammation is predominant in the dorsal part of the synovial joint, this could be the reason for the possible detection of sacroiliac inflammation by ultrasound. Color-

Doppler sonography (CDUS) has been used in sacroiliitis by Arslan, *et al*[44] in a group of 21 patients with active sacroiliitis revealing vascularity around or inside the SI joint in 10 patients (48%).

In our preliminary findings, contrast-enhanced CDUS was shown to improve the detection of active sacroiliitis with a high negative predictive value (NPV) in comparison to MRI (NPV of 97%)[45-47]. This may justify the use of contrast-enhanced CDUS as a first-line imaging modality, because of better availability and cost-effectiveness, which can be important for assessment of sacroiliitis in clinical routine.

SUMMARY

As reported by Calin, many patients with sacroiliitis are misdiagnosed and may be treated inappropriately. During the past decade, detection of sacroiliitis has been improved, and the time to get a diagnosis could be shortened from 10 to 7 years[48]. However, it still takes years to establish the diagnosis. Diagnosis is improved by simple, cheap, readily reproducible screening tests[4] and improved imaging techniques. Earlier diagnosis and assessment of disease activity are still a challenge for clinicians and radiologists as scoring tools are limited in their sensitivity to change[49]. At present the following clinical indications for imaging sacroiliitis can be summarized:

1. To establish the diagnosis of sacroiliitis (especially in AS): MRI should be performed in early disease when the diagnosis is suspected but the radiograph is normal. In later disease, a pelvic radiograph (or preferably CT) can be used to confirm the diagnosis.
2. To determine disease activity: Contrast enhanced MRI is the method of choice in the termination of early, mild, and high active disease.
3. To determine the amount of actual destruction in chronic disease: CT accurately depicts the bony destruction.
4. To document sacroiliitis (according to the European Spondylarthropathy Study Group and the modified New York criteria) and to justify treatment of AS with TNF blockers: pelvic radiograph (or preferably CT). If disease activity assessment is taken into account for followup, MRI is necessary.
5. To exclude septic sacroiliitis; early stages can be assessed by MRI, later stages by CT.
6. To evaluate patients with widespread pain and oligoarticular manifestations: scintigraphy allows the assessment of inflammatory manifestations at different sites and can be used in patients with contraindications to MRI.

Overall, imaging techniques may be differentiated into structural techniques like radiography or CT and functional techniques such as contrast enhanced MRI, color-Doppler sonography/contrast enhanced color-Doppler sonography, or scintigraphy. While structural techniques are capable of detecting bony changes during later stage disease, functional techniques help to assess disease activity during both early and chronic sacroiliitis.

CT effectively displays chronic disease as cortical and subchondral alterations and is superior to MRI in detecting those bony abnormalities in particular at the enthesis and ligamentous portion. CT is fast and readily available, but radiation exposure should limit the use in children and young women.

Scintigraphy is sensitive to inflammatory changes and reveals disease activity, but it lacks specificity and is reserved to cases where imaging of general active inflammation is suspected in patients who cannot go for MRI.

MRI can be considered the most sensitive imaging modality, with high specificity, detecting active inflammatory changes of sacroiliac joints; and this before any changes are visible by CT and radiography. Thus, when available, MRI should be the first choice in suspected early SpA, in women and children, and when imaging more sensitive than conventional radiography is required.

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