

## **Can whole body MRI (WB-MRI) support patients' quest for improved long-term management in juvenile idiopathic arthritis (JIA)?**

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Paediatric rheumatology research should address unmet patient needs, in addition to important questions related to disease pathogenesis, timely diagnosis and adequate management, ultimately aiming for improved patient outcomes and minimisation of long-term irreversible damage, aspects that are particularly relevant for diseases with childhood onset. Evidence-based recommendations and patient-driven research agenda are limited in paediatric rheumatology due to the challenges posed by ethical constraints, complex considerations about children's participation in research and often, lack of developmentally appropriate outcomes.

One of the key challenges in paediatric rheumatology is prediction of the disease course, both in terms of flares, remission and treatment response, as well as long-term outcomes, including physical, psychological and social impact. These unmet needs were recently highlighted in a report from the UK Paediatric Rheumatology Clinical Studies Group (CSG), which we read with interest<sup>1</sup>. This study identified the top 10 research priorities in paediatric

rheumatology, which were primarily suggested by the CSG consumer representatives (patients and parents). Their top-rated priorities were, (i) prediction of the disease course in individual patients and (ii) understanding and predicting the long-term outcomes of paediatric rheumatic diseases<sup>1</sup>.

Addressing these priorities has been particularly challenging in juvenile idiopathic arthritis (JIA), the most common chronic rheumatic disease of childhood (with more than 25,000 young people living with JIA in the UK). Despite significant research efforts in the last decades to identify biomarkers for disease course and long-term outcome prediction<sup>2</sup>, there are no reliable prognostic markers validated in clinical practice.

However, recent advances in imaging technology present an opportunity to address this gap. Developments in both ultrasound (US) and magnetic resonance imaging (MRI) in JIA led to their inclusion in clinical recommendations, as they have been proven superior to clinical examination in JIA<sup>3</sup>. MRI showed enhanced ability to detect both inflammation and damage and treatment response in JIA when compared to US<sup>4</sup>.

One benefit of MRI is its ability to detect inflammation in joints with widely varying anatomy. This is important because JIA is a clinically heterogeneous disease, potentially involving both small and large, superficial and deep joints. Although both MRI and US examination in JIA can show inflammation in the hips, knees, wrists, ankles, fingers and toes, MRI is preferred for assessing the cervical spine, temporo-mandibular joints, knees and sacroiliac joints<sup>3</sup>. Furthermore, MRI-detected joint inflammation in JIA patients in remission is clinically relevant as subclinical synovitis in a joint previously affected was shown to be the best predictor of JIA flare in a multivariate analysis (HR= 2.45; p=0.003)<sup>5</sup>. These data suggest that MRI may be the optimal method for identifying inflammation and guiding management in JIA. As long as radiologists are familiar with the appearances of the growing skeleton, misinterpretation can be avoided and inflammation can be identified with confidence<sup>6</sup>.

Although regional MRI scans provide useful information about the assessed joints, they do not alleviate the uncertainty about the presence of subclinical inflammation in other areas. Therefore, we propose the use of whole-body MRI (WB-MRI) for comprehensive assessment of joints and entheses. This builds on an expanding body of evidence for the value of WB-MRI in the management of inflammatory arthritis in adults<sup>7</sup> and is supported by the international initiative to develop a standardised WB-MRI scoring system in JIA<sup>8</sup>. Moreover, as the indications for the use of whole-body MRI in cancer are growing, access to this technique will become more widely available.

We found that WB-MRI can identify subclinical inflammation at various joint sites in JIA patients aged 15-24, with 43.8% JIA patients having subclinical inflammation in at least one joint on WB-MRI, irrespective of their disease activity<sup>9</sup>. In addition, we found that WB-MRI detected inflammation supported clinicians in their decisions about JIA patient management<sup>10</sup>. Further research is needed to investigate if patients with subclinical inflammation would benefit from treatment escalation and the cost-effectiveness of WB-MRI.

Ultimately, an objective method of assessing and monitoring joint inflammation in JIA would have multiple potential advantages for patients, including the ability to explain patients'

symptoms in terms of joint inflammation, damage or other causes, and improved disease management and potentially treatment compliance.

We propose a roadmap for future investigation of WB-MRI utility for JIA management and outcomes guided by patients' priorities, including testing of the clinical utility of WB-MRI in clinical trials and routine practice settings in relation to relevant clinical outcomes, in parallel with investigation of patients' acceptability of WB-MRI scans and clinicians' opinion about their clinical utility (Figure 1). WB-MRI could potentially answer questions related to prediction of flares in clinically suspected/unsuspected joints in patients with different disease states, guide treatment decisions, such as escalation, continuation or tapering of medication, ultimately providing comprehensive musculoskeletal assessment related to long-term outcomes in JIA relevant for patients' function and quality of life.

Future research into validation of WB-MRI protocols and scoring systems for use across age and various JIA phenotypes, including cross-validation against existing MRI protocols is also warranted before we can support the wider implementation of WB-MRI in the management of JIA.

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