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Quantitative magnetic resonance imaging has potential for assessment of spondyloarthritis; the arguments for its exploration and use

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Response to Editorial: Journal of Rheumatology

We read with interest the recent paper on diffusion-weighted imaging as a means of supporting the diagnosis of ankylosing spondylitis [1], and the corresponding editorial questioning the role of DWI [2]. The paper (1) adds to the growing body of evidence supporting the use of DWI to characterise and quantify inflammation in patients with spondyloarthritis [3,4] The corresponding editorial argues that DWI is of limited clinical use and the main criticisms are summarised as follows. The authors argue that:

1. *Any* sequence can be measured numerically and this is a facility not confined to DWI.
2. The number of steps required for normalising measurements and choosing ROIs depends on review of the initial *qualitative* images and is subjective.
3. The variable diffusion of background marrow poses further challenges for DWI

However, if we look in greater detail at the existing literature on *quantitative* imaging, it is apparent that many of these issues can be addressed, and indeed there are multiple advantages that quantitative techniques offer over standard sequences. Taking the criticisms in the editorial in turn, we make the following comments:

1. In a conventional MR image, the signal intensities are influenced by the composition of tissue but also by hardware-related factors such as the spatial variations in the sensitivity of the receiving coil. This means that the biological information contained in the image is 'confounded' by these hardware factors and is not directly comparable across between scanners or between repeat scans (see [5]). The confounding effect of acquisition parameters is, in general, true of all conventional MR imaging. However, quantitative MRI methods typically acquire a *series* of images, allowing us to fit a model to the acquired data and to calculate an *objective* parameter (e.g. ADC) that

reflects *intrinsic* tissues properties, and is largely independent of these confounding factors [5].

Quantitative imaging is now a huge field [5–7], and much of the research performed within this field is founded on the greater objectivity of quantitative MRI methods. There are multiple organisations dedicated to the oversight of quantitative imaging biomarker (QIB) development [7,8]. A key component of the definition of a QIB is that it should be objectively measured [7]; it is misleading to say that, by drawing regions of interest, a conventional MR image can be quantified in the same way.

2. The number of steps adopted by the authors of the papers appear to us to be performed to facilitate direct comparison of DWI measurement with SPARCC scoring. The methodology for determining regions of interest is somewhat cumbersome and its criticism in the context of potential clinical utility is justified. However, it is often necessary to start with relatively basic techniques during the development of new methods. Furthermore, there are other potential approaches to interpreting quantitative images in a clinically relevant way. ROIs do need not be focal; an alternative approach could be to sample the whole of the SIJ, and then analyse this data using thresholding and histographic analysis [9]. This is less subjective that manually defining regions of interest. In the future, more sophisticated segmentation techniques may enable automatic separation of inflamed areas from normal marrow, removing the subjective element altogether [10].
3. The observation in the published paper that background marrow in patients in the pre-treatment group had higher ADC values than patients with non-radiographic AS or chronic back pain is of interest. Rather than being a challenge, this is a question.

Why is this so, and is this a reproducible finding in larger numbers of patients? One advantage of quantitative methods is that they allow us to ask more direct questions of the underlying physiology. Further, there are already methods in other fields (e.g. lesion segmentation in multiple sclerosis) that allow for variable thresholds in the quantification of pathology, which seem well-suited to address this problem.

A particular advantage of quantitative MRI is that multiple techniques, each reflecting different but known aspects of tissue physiology, such as fat fraction, perfusion and diffusion, can be combined as 'multiparametric' imaging. This enables us to examine different aspects of tissue physiology, the 'virtual imaging biopsy'. This in turn may improve our understanding of pathophysiology and enable us to 'unpick' the biology underpinning therapeutic response in a way that conventional qualitative imaging cannot.

Quantitative imaging is in its infancy. There are many problems remaining including acquiring consistent and comparable data across platforms and sites, defining pathological values and validating these in different disease states. Criticism of its current relevance to clinical imaging of bone marrow is legitimate, and it is still necessary to demonstrate additional benefit when combined with conventional imaging. However, in the longer term, it seems plausible that QMRI will one day be a powerful tool for the assessment of disease activity in inflammatory conditions. Clearly, further exploration of this area is needed.

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