Short tau inversion recovery MRI of Modic changes: a reliability study

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Abstract
Background: Limited reliability data exist for evaluation of spinal edema changes on magnetic resonance imaging (MRI) with short tau inversion recovery (STIR) sequences.
Purpose: To assess the inter-observer reliability for evaluation of STIR signal increase related to Modic changes (MCs) on MRI of the lumbar spine.
Material and Methods: We prospectively included 120 patients imaged to confirm their eligibility for the AIM (Antibiotics In Modic changes) trial. Three experienced radiologists independently evaluated MCs on T1-/T2-weighted fast spin-echo images and subsequently MC-related STIR signal increases. Inter-observer reliability was analyzed at four endplates (L4–S1) by calculating kappa values and means of differences with 95% limits of agreement.
Results: Overall agreement (mean Fleiss’ kappa for all endplates and observers) was very good for presence of STIR signal increase (0.86), and moderate for its categorized height (0.51), anteroposterior extent (0.48), and volume (0.56). For height of region with STIR signal increase measured in % points of vertebral body height, the largest mean of differences was 6.9 and widest range for limits of agreement was 22.3 for all endplates combined. The corresponding numbers were 11.2 ± 34.5 for anteroposterior extent of the STIR signal increase measured in % points of anteroposterior endplate diameter and 0.9 ± 7.6 for its maximum measured intensity on a % point scale (0% = normal vertebral marrow intensity, 100% = cerebrospinal fluid intensity).
Conclusion: Inter-observer reliability was very good for the presence and intensity of MC-related STIR signal increases, and moderate for their size.

Keywords
Skeletal-axial, magnetic resonance imaging, spine, adults, imaging sequences, observer performance

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Introduction
Short tau inversion recovery (STIR) sequences are widely used in magnetic resonance imaging (MRI) to evaluate edematous changes in the skeleton, including the spine. Despite widespread use, limited reliability data exist for spinal evaluations with STIR or other fluid-sensitive fat-suppressed series. Such data were included in articles on spondylarthritids (1–5), fractures (6), Modic changes (MCs) (7), hemangiomas (8), and pedicle screw loosening (9). However, all but one (6) of these reliability studies had only two observers, most (1,3–5,7–9) had small patient samples (n = 25–41), only one (8) included measurements of signal intensities; the spondylarthritids studies were limited to lesion

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detection (1–5). Reliability estimates differed widely in these heterogeneous studies where radiologists and non-radiologists interpreted various fat-suppressed 1.5-T or 3-T series. More comprehensive reliability data are needed for radiologists’ lumbar spine evaluations with STIR.

There has been increasing focus on MCs in recent years. MCs are signal changes in the vertebral bone marrow extending from the endplate and are classified into types I (edema type), II (fatty type), and III (sclerotic type) based on T1-weighted (T1W) and T2-weighted (T2W) series (10–12). STIR series are sensitive to edema and are highly relevant for evaluation of MCs. The association between MCs and pain is inconsistent (13–16), but edema type MCs might be symptomatic (17–19). Mechanical, autoimmune, and infectious explanations for MCs have been proposed (20), and various treatments have been and are being tested (21–34). Reliable evaluation of the STIR findings is required to validate their relevance to symptoms and treatment (35–37).

Clinicians and researchers evaluate MCs with a combination of MRI series. The reliability is mostly well described for evaluations with non-fat-suppressed T1W/T2W sequences (38–43), but not for evaluations with fat-suppressed, fluid-sensitive series (7). The primary aim of this study was to assess the inter-observer reliability for evaluation of STIR signal increase related to MCs on MRI of the lumbar spine. For comparison, we also report the inter-observer reliability for the evaluation of these MCs on T1W/T2W fast spin-echo images.

Material and Methods

This reliability study was based on a study-specific MRI of a consecutive subsample (n = 120; 72 women, 48 men; age range = 25–64 years; mean age = 45 years) with chronic low back pain considered for inclusion in the AIM (Antibiotics In Modic changes) trial (32). Inclusion required presence of type I and/or type II MCs at the level of an MRI-confirmed lumbar disc herniation within the preceding two years. All eligibility criteria are listed in the Appendix (Suppl. Table 1). Patients preliminarily eligible for the trial based on these criteria and findings on an existing clinical MRI (n = 220) underwent the new study-specific MRI to confirm or reject their eligibility. All participants included in the study provided written informed consent. The present report adheres to the guidelines for reporting reliability and agreement studies (44).

Images

The 120 study-specific MRI examinations were performed from 15 June 2015 to 2 September 2016 at five centers in Norway, using identical protocols and 1.5-T scanners (Siemens Magnetom Avanto B19). The present study was based on sagittal T1W and T2W fast spin-echo images (=T1/T2) and sagittal STIR images (Table 1).

Evaluation

Three radiologists, all with >10 years of experience in musculoskeletal MRI, independently evaluated the images. The first observer to open the MRI examination saved a mark on the lowest lumbar disc level. All observers reported this level as L5/S1. First, MCs were rated on T1/T2, blinded to other sequences. Later the observers rated STIR findings and decided whether any increased STIR signal was related to an MC visible on T1/T2. The observers were blinded to clinical outcome but knew that patients were preliminarily eligible for the trial. To align their understanding of procedures and rating criteria, the observers rated and discussed MCs and STIR findings in a pilot study (32 MRIs not included in the main study).

On T1/T2, we defined MCs as signal changes in the vertebral bone marrow extending from the endplate, and based rating criteria for MC type and size on prior work (10,11,38,45) (Table 2). Only T1/T2 findings defined MC types I, II and III, not STIR findings. Not recorded as MCs were: (i) changes separated from the endplate; (ii) roundly shaped fatty changes abutting the endplate with a smaller base than height (more likely focal fatty marrow or hemangiomas); and (iii) changes extending through the endplate (Schmorl’s hernias).

On STIR, we defined MC-related signal increase as visible increase compared to normal vertebral bone marrow, formed and located as an MC and/or located in or abutting a region with MC on T1/T2 (and not located in a likely hemangioma). MC-related STIR signal increase was evaluated for presence, height, anteroposterior (AP) extent, volume, and maximum intensity (Table 2). STIR signal decrease was not evaluated. STIR signal intensity was measured in the region with most intense MC-related STIR signal, in the cerebrospinal fluid (CSF) and in normal vertebral body marrow (Table 2, Fig. 1). The measurements were made in circular regions of interest available in our PACS with size 25 mm² (used for most intense MC-related STIR signal and CSF) and 44 mm² (used for normal vertebral body marrow) (Fig. 1). Care was taken to avoid surrounding structures, e.g. intervertebral discs, nerve roots, central vertebral vein. Intensity of CSF varied between levels and was measured at the
same disc level as the MC-related STIR signal. Maximum intensity of the MC-related STIR signal (“Stir”) in % points on a scale from normal vertebral body intensity (“Body,” 0%) to CSF intensity (“CSF,” 100%) was calculated as \( \frac{\text{Stir} - \text{Body}}{\text{CSF} - \text{Body}} \times 100 \).

**Statistical analyses**

For each endplate L4–S1, we calculated Fleiss’ kappa for all observers and Cohen’s kappa for each observer pair. Kappa was unweighted for dichotomous variables and linearly weighted for ordinal variables. McNemar’s test was applied to compare the prevalence of findings between observers. We computed means of differences between observers with 95% limits of agreement for height and AP extent of findings in % points of vertebral body height and AP extent, and for STIR signal intensity in % points on the scale from normal vertebral body intensity (0%) to CSF intensity (100%). We used sample size weighted means and pooled limits of agreement from all endplates to compute the mean differences between the observers with 95% limits of agreement for all endplates. The 95% limits of agreements represent the limits within which 95% of the differences are expected to occur. We used MedCalc 17.6 (MedCalc Software) to compute means, R 3.5 (R Foundation for Statistical Computing) for kappa and weighted means, and Matlab 9.5 (Mathworks) to derive forest plots.

Only data from L4/L5 and L5/S1 were analyzed, due to <10% prevalence of MCs at higher levels. Kappa is usually not reported for findings with prevalence <10%, as very low prevalence can lead to very low kappa values despite very high actual agreement (46). Kappa was interpreted as: \( k \leq 0.20 = \text{poor} \); 0.21–0.40 = \text{fair} \); 0.41–0.60 = \text{moderate} \); 0.61–0.80 = \text{good} \); and 0.81–1.00 = \text{very good agreement beyond chance} \) (47).

**Sample size**

Assuming a finding has a prevalence of 30%, 85 patients are needed to detect \( (\beta = 0.2, \text{two-sided } \alpha = 0.05) \) an unweighted pairwise kappa value of 0.70 as significantly larger than 0.40 (46). We used three observers and 120 patients to further improve the power and increase the size of subgroups. In general, at least 50 individuals are recommended in reliability studies (48).

**Results**

The observers reported MC-related STIR signal increases regardless of MC type on T1/T2. There were no missing data.

**Categorical STIR variables**

Overall agreement between the three radiologists (mean Fleiss’ kappa) was very good for presence of

| Parameter                  | T1 | T2 | STIR |
|---------------------------|----|----|------|
| TR (ms)                   | 575| 3700| 5530 |
| TE (ms)                   | 11 | 87 | 70 |
| ETL                       | 5 | 17 | 20 |
| Acquisitions (n)          | 2 | 2 | 1 |
| Concatenations (n)        | 2 | 1 | 1 |
| Slices (n)                | 17| 17 | 15 |
| Matrix (frequency × phase)| 384 × 269| 384 × 269| 320 × 324 |
| FOV (mm)                  | 300 × 300| 300 × 300| 300 × 300|
| Slice thickness (mm)      | 4.0| 4.0| 4.0 |
| Interslice gap (mm)       | 0.4| 0.4| 0.4 |
| Voxel size (mm)           | 1.1 × 0.8 × 4.0| 1.1 × 0.8 × 4.0| 1.3 × 0.9 × 4.0 |
| Receiver bandwidth (Hz/px)| 161| 161| 182 |
| Phase encoding direction  | Head to feet| Head to feet| Head to feet |
| Saturation pulses         | None| Anterior, 30 mm| Anterior, 30 mm |
| Acquisition time (min:s)  | 1:48| 1:49| 1:38 |
| Coverage                  | From above Th12 to below S2| From above Th12 to below S2| From above Th12 to below S2 |
| Phase oversampling (%)    | 70 | 70 | 70 |
| TI (ms)                   | - | - | - |
| PAT mode                  | Grappa| Grappa| None |

MRI was performed on 1.5-T Magnetom Avanto scanners (Siemens) with B19 software using integrated spine array coil, but no surface coils.

ETL, echo train length; FOV, field of view; MRI, magnetic resonance imaging; PAT, parallel acquisition technique; STIR, short tau inversion recovery; TE, echo time; TI, inversion time; TR, repetition time.

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MC-related STIR signal increase (0.86), and moderate for its height (0.51), AP extent (0.48), and volume (0.56) (Fig. 2). Kappa values were generally lower at L5/S1 inferior to disc.

The prevalence of STIR signal increase differed maximum 11.6% points between observers (observers A vs. B reported prevalence of 58.3% vs. 46.7% at L5/S1 inferior to disc, \(P < 0.001\)).

Mean pairwise Cohens’ kappa across all categorical STIR variables and levels indicated slightly better agreement between observers A and B (0.62) versus A and C (0.52) and B and C (0.52). Further pairwise STIR results are found in the Appendix (Suppl. Fig. 1, Suppl. Table 2).

### Numerical STIR variables

For height of the region with STIR signal increase in % of vertebral body height, the largest mean of differences between observers was 6.9% points and the widest limits of agreement were ±22.3% points, based on data from all levels (Fig. 3). For AP extent of the increased STIR signal in % of AP endplate diameter, the corresponding numbers were 11.2%
points ±34.5% points. For maximum intensity of the STIR signal in % on the scale from normal vertebral body intensity (0%) to CSF intensity (100%), the largest mean of differences and widest limits of agreement were 0.9% and ±7.6% points, based on data from all levels. Results for individual levels are provided in the Appendix (Suppl. Fig. 2).

Reported % points were in the range of 8–100 (mean = 43) for height, 7–100 (mean = 74) for AP extent, and 6–78 (mean = 32) for intensity of STIR signal increases.

**MC evaluation on T1/T2**

On T1/T2, agreement (mean Fleiss’ kappa) was very good for presence of MCs (0.88) and for presence of
primary or secondary type I MCs (0.81) (Fig. 4). Mean kappa was 0.64 for height, 0.56 for AP extent, and 0.69 for volume of MCs on T1/T2. These values were 0.08–0.13 higher than the corresponding kappa values for dimensions of MC-related STIR signal increases.

The largest difference between observers in prevalence of MCs on T1/T2 was 6.7% points (observers A vs. B reported prevalence 79.2% vs. 72.5% at L5/S1 inferior to disc, \( P = 0.021 \)).

Mean pairwise Cohens’ kappa across all categorical T1/T2 variables and levels indicated similar agreement between observers A and B (0.73), A and C (0.71), and B and C (0.73).

The largest mean of differences (and widest limits of agreement) on T1/T2 were for MC height 0.7 (±17.4) % points and for AP extent of MCs 2.6 (±28.8) % points (Fig. 5). These values were smaller than the corresponding values on STIR. On T1/T2, reported % points were in the range of 5–91 (mean = 39) for height and 8–100 (mean = 78) for AP extent.

Further T1/T2 results are detailed in the Appendix (Suppl. Figs. 3 and 4, Suppl. Table 3).

**Discussion**

To our knowledge, this was the first comprehensive study of the inter-observer reliability for evaluations of STIR signal increases in the vertebral bone marrow. Three radiologists evaluated MC-related high-intensity regions on STIR in 120 patients. Overall inter-observer agreement was very good for the presence of STIR signal increase and moderate for its height, AP extent, and volume. In general, % measured height of the STIR signal differed less
between observers than its % measured AP extent. For its maximum intensity (on a scale of 0–100%), mean of differences was $<1\%$ points and limits of agreement within $+/-.6\%$ points.

Further, we have found only one previous study (on 25 patients) of the reliability for MC evaluations on any fat-suppressed fluid-sensitive series (7). In that study, kappa for inter-observer agreement was 0.74 for presence and 0.80 for categorized height of MC-related signal increase. Our corresponding kappa values were 0.86 and 0.51. In patients with possible vertebral fractures (6), kappa for inter-observer agreement on categorized volume of vertebral bone edema on STIR was 0.58; our value was 0.56. It was not reported in these previous studies whether kappa was weighted or categories were combined, so it is not clear whether their kappa values are comparable to ours. In line with our results for intensity measurements, inter-observer agreement was excellent for measurements of signal intensities in vertebral hemangiomas

STIR/fat-saturated T2 images (intra-class correlations of 0.97–0.99) (8).

The very good agreement on presence of STIR signal increases in our study is reassuring for clinical work and research. However, the moderate agreement on the extent of the high STIR signal is not optimal. Moderate inter-observer agreement is common in spine imaging (36,41,49,50), but it implies lowered accuracy when associations with clinical factors are sought (37). More reliable conclusive MRI findings can be based on different observers' separate evaluations followed by their joint conclusion (51). Furthermore, in order to improve agreement between observers, reasons for disagreement should be identified and addressed.

Reasons for disagreement on extent of STIR signal increases may be diffuse outline/gradual lessening of the signals and inhomogeneous bone marrow signal, especially in S1 (where agreement was slightly poorer) (Fig. 2). The AP extent of the MC-related STIR signal often tapers gradually and may blend into a normal...
thin hyperintense zone beneath the bony endplate (Fig. 1). This can partly explain larger disagreement for AP extent than for height. The generally larger AP extent than height of the STIR signal is not a likely explanation, as differences in % measured AP extent of the signal were similar for small and large extents (data not shown). On T1/T2, better agreement was achieved for MC extent both in our study and between other experienced observers (36,40,49,50). Therefore, disagreement on extent of MC-related STIR signal increase is probably due to genuine difficulties in interpretation.

Our study also added new information regarding the detection of any area with type I MCs on T1/T2. Previous studies have focused on primary MC types (38–41). We found very good agreement on presence of any (primary or secondary) type I MCs. This may be partly because we rated borderline type I versus type II MCs with near isointense T1 signal (no clear edema) as type II. MCs that are isointense on T1 (and hyperintense on T2) fall outside the original definition of MC types, and it is unclear how they were classified in other studies.

The strengths of this study include the use of three observers (all experienced radiologists), a pilot study, a large sample, standardized MRI protocols and rating criteria, and inclusion of measurements. Multiple observers improved the power and the generalizability of results, and including more patients rather than more than three observers is an effective strategy for maximizing power (46). The data on reliability for T1/T2 evaluations of MCs supported the credibility of our STIR results. We also standardized MC-related STIR signal intensities against normal bone marrow and CSF at the same or a close level, since intensity values varied both between and within patients and depended on craniocaudal and AP localization.

There are also limitations to the study. It was restricted to patients with previously reported MCs and disc herniation. We would however expect similar reliability for STIR evaluations in other patients with low back pain. Intra-observer reliability was not examined; it is often better than the inter-observer reliability (41,43,49,50). A single type of 1.5-T MRI scanner was used, and the results may not be transferrable to images with a different quality or to scanners with a different field strength. Lesion volume was not measured; it was categorized by taking into account (summing up) the visually estimated affected area on all images. Although precise measurements on all images is less feasible, reliability data also for measured volume would have been useful. Finally, all observers had >10 years of experience in musculoskeletal MRI and the reliability for less specialized or less experienced radiologists is still unknown.

We propose the following implications of our results. First, radiologists can evaluate STIR signal increases in the lumbar spine based on criteria used in this study. Second, clinicians and radiologists can expect more reliable evaluation of the height versus the AP extent of a region with MC-related STIR signal increase. Third, when relevant, radiologists can grade the volume of STIR signal increases with reasonable inter-observer reliability, without performing very time-consuming measurements. Fourth, one should still attempt to improve the reliability for size evaluations of STIR signal increases in research, e.g. by joint pre-training, semi-automated lesion contouring (37), continuous volume measurements, and basing conclusive findings on multiple observers’ evaluations (51). Fifth, maximum STIR signal intensity relative to normal bone marrow and CSF is an attractive variable in further research, due to its excellent inter-observer reliability. Finally, radiologists can use criteria from this study to improve the evaluation of type I MCs on T1W/T2W fast spin-echo images.

In conclusion, the agreement between experienced radiologists was very good regarding the presence of MC-related STIR signal increase and its maximum intensity, and moderate for its extent and volume. These results provide a basis for validating the relevance of such STIR signal increases for symptoms and treatment results.

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