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Assessment of typical SpA lesions on MRI of the spine: do local readers and central readers agree in the DESIR cohort at baseline?

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Submitted

Abstract

Objective

Comparing local reading (LocR) with central reading (CentR) of typical spondyloarhritis lesions including bone marrow edema (BME) and structural lesions on Magnetic Resonance Imaging of the spine (MRI-spine), in patients with inflammatory back pain (IBP; ≥3 months, <3 years).

Methods

Baseline data of 667 patients, age 18-50 years, from the Devenir des Spondylarthopathies Indifferenciees Recentes DESIR cohort were used. Two trained central readers scored anterior and posterior corner BME, fatty lesions, erosions, and syndesmophytes on MRI-spine. Presences of lesions, based on average scores, were used for CentR. A local radiologist and/or rheumatologist scored MRI-spine on presence/doubt/absence of 'inflammation' and 'structural lesions'. Agreement between central readers and readings was calculated (Cohen's Kappa's; κ).

Results

Agreement between central readers was moderate (BME κ=0.55, fatty lesions κ=0.50) to slight (erosions κ=0.12, syndesmophytes κ=0.19). Agreement between LocR and CentR was κ=0.32 (BME) and κ=0.13 (structural lesions). In 78/160 patients (48.8%) LocR were in doubt while CentR scored BME lesions, for structural lesions this was 17.8% (28/157 patients).

Conclusion

Agreement between 2 central readers for scoring spondyloarhritis-like lesions on MRI-spine was moderate but better compared to LocR and CentR agreement. LocR often doubt about the presence of MRI-spine lesions while central trained readers score lesions.

Introduction

In the field of axial spondyloarthritis (axSpA) the role of magnetic resonance imaging (MRI) in daily practice and studies increased over the past years. Sacroiliitis on MRI (MRI-SI) is part of the Assessment of SpondyloArthritis international Society (ASAS) classification criteria for axSpA[1]. Although spinal MRI-lesions are not part of the criteria, the interest in these lesions is growing. Bone marrow edema (BME) on MRI of the spine (MRI-spine) is increasingly used to monitor the effect of anti-inflammatory therapy in axSpA patients[2–5]. Activity on either MRI-SI or MRI-spine is frequently used to define if patients have a 'positive MRI' used as prognostic factor to treatment response in patients with non-radiographic axSpA[6]. Besides this, spinal inflammation in early disease and structural damage on MRI-spine in later disease seem to be related to functional impairment in AS patients[7].

In clinical trials and cohort studies there are always trained readers providing the scores. This is different for daily practice where a local radiologist (in consensus with a rheumatologist) performs the MRI readings aware of the clinical and biological data. In daily practice and clinical studies, readers are assumed to assess the compatibility of MRI-lesions with axSpA. However it is unknown whether there are discrepancies in assessment between daily practice and central readers, and if readings of specialists in daily practice are adequate without specific training concerning the recognition of typical MRI-lesions associated with axSpA. One study compared local and central readings concerning radiographic sacroiliitis and they found a moderate agreement between central readers (kappa=0.54) and between central vs. local readers (kappa=0.55)[8]. Disagreement between central readers was balanced in two directions while local readers report a large proportion of false positives and a small proportion of false negatives, when central reading was considered as external standard. To our knowledge there are no studies addressing this for MRI-spine readings. Therefore the objective of this study was to compare results of local reading (LocR) to central reading (CentR) as external standard for BME and structural lesions seen on MRI-spine, in patients with inflammatory back pain (IBP) of relative short duration.

Methods

Study population, data collection and classification

Baseline data from patients included in the Devenir des Spondylarthopathies Indifferenciees Recentes (DESIR) cohort was used. Inclusion period was from December 2007 until April 2010 in 25 regional centres in France, where patients aged 18-50 years with IBP according to the Calin or Berlin criteria[9,10], persisting ≥3 months

but <3 years, were included. A detailed description of exclusion criteria can be found elsewhere[11]. The DESIR cohort was conducted in accordance with the Declaration of Helsinki and approved by the local ethical committee and health authorities. Written informed consent was obtained from participating patients before inclusion. Study population and data collection assessment of the DESIR cohort have previously been published[12]. The study was registered on clinicaltrials.gov (ID: #NCT01648907) and the clinical database used for the current study was locked on October 30th 2012.
In this study, patients were classified according to the ASAS classification criteria for axSpA based on the central imaging readings (MRI and radiographs) of the sacroiliac (SI) joints[13].

Imaging

Patients enrolled in the DESIR cohort underwent an MRI-spine performed on a 1T-1.5T scanner with acquired sequences T1-weighted Turbo Spin-Echo (TR500-700/TE10-55) and Short Tau Inversion Recovery (TR4000/TE50-70/TI130-160 (1T);140-170msec (1.5T)), with 4mm slice thickness. MRI-spine was performed in sagittal plane and both sequences were viewed simultaneously. Upper (C2-T10) and lower part of MRI-spine (T8-S1) were conducted separately with an overlap of at least 2 vertebrae. In total 708 patients were enrolled in the DESIR cohort but since one or both sequences were missing in 41 patients, MRI-spine data of 667 patients were available.

Central reading

Two central readers (MdH and JBP), both familiar with scoring MRI-spine, participated in a calibration session before starting the reading. The calibration session was a systematic conducted exercise, executed by two senior radiologists (MR and AF) and two senior rheumatologists (DvdH and MD), who already did such calibration sessions before. During the calibration process, definitions of lesions, examples and pitfalls were discussed. Subsequently, the two readers independently read a training set of 20 MRI-spine, followed by the calculation of agreement based on the presence of ≥2 BME lesions (kappa=0.60) and ≥3 fatty lesions (kappa=0.47) and a consensus meeting where the two readers discussed discrepancies, difficult images and possible arrangements concerning the procedures of scoring. After this meeting, the two readers started to read the baseline images of the DESIR cohort.
The central readers independently scored all MRI-spine images, while blinded for clinical and other imaging data. Anterior and posterior corner BME, fatty lesions, erosions, and syndesmophytes were scored per vertebral unit (VU). In total 23 VUs

were scored with C2-C3 as VU1 and L5-S1 as VU23. Central readers scored all lesions only when considered typical for axSpA. When the readers considered the lesions to be due to other causes, like degenerative changes or Scheuermann disease, lesions were not scored. BME and fatty lesions suggestive of spondylitis were scored when visible on ≥2 consecutive slices. For erosions and syndesmophytes suggestive of spondylitis presence on ≥1 slice was sufficient.
When central readers disagreed on the presence of ≥2 BME, an adjudicator (AF) scored all 23 VUs on inflammation. When central readers disagreed on the presence of ≥3 fatty lesions, the adjudicator provided scores in all 23 VUs on the presence of structural lesions for fatty lesions, erosions and syndesmophytes separately. When there was disagreement on both BME and fatty lesions, the adjudicator provided the scores for all MRI-spine lesions. The cut-off values for BME (≥2) and fatty lesions (≥3) were chosen arbitrarily since, at the time, there was no official definition of a positive MRI-spine.
The central reading (CentR), presence/absence of MRI-lesions, was obtained from the average of both central readers scores or, in case of adjudication, the average of the adjudicator score and central reader closest to this score. Where presence represented an average score of ≥1 and absence an average score of <1 lesion. This was done for BME and structural lesions separately.
In addition, the central readers gave an overall verdict whether MRI-spine fulfilled the ASAS consensus definition of a positive MRI. In this definition a spinal MRI is considered positive when there are ≥3 corner BME, each seen on ≥2 consecutive sagittal slices[14].

Local reading

In each participating centre, a local radiologist or rheumatologist decided on the presence of 'BME' and 'structural lesions' on MRI-spine. The local readers were not trained apart from the usual medical education. The local scoring was different and more global compared to the central scoring. Local readers separately scored 'BME' and 'structural lesions', without further distinction for different types of structural lesions. The verdict options the local readers could choose were 'presence', 'doubt' or 'absence' of lesions separately for cervical, thoracic and lumbar spine. These scores will be referred to as 'local reading' (LocR).

Statistical analysis

Agreement between central readers as well as between LocR and CentR was expressed in Cohen's Kappa's (κ) and percentages positive agreement (PPA). PPA is the number of positive readings scored by both readers/readings divided by all of the positive readings of either readers/readings[15]. The strength of agreement related to κ value was interpreted as suggested by Landis and Koch: 0.00-0.20 corresponds to slight agreement, 0.21-0.40 to fair, 0.41-0,60 to moderate, 0.61-0.80 to substantial and 0.81-1.00 to a (almost) perfect agreement[16]. All statistical analyses were performed with SPSS version 22.0 (SPSS Inc., Chicago, IL, USA).

Results

LocR and CentR of MRI-spine were available in 667 (BME) and 666 (structural lesions) patients. Less than half of the patients (n=306; 45.9%) were male. The mean age at onset back pain was 31.9 years (SD ±8.7). Human leukocyte antigen (HLA)-B27 was positive in 58.9% of the patients. There were 596 patients with an onset of IBP <45 years, in whom the ASAS classification criteria for axSpA could be applied. Based on the central imaging readings (MRI and radiographs) of the sacroiliac joints 430 patients fulfilled the ASAS criteria; 242 patients based on sacroiliitis on imaging (imaging arm) and 188 patients based on HLA-B27 positivity (clinical arm).

Central reading agreement

In 86/667 patients adjudication on BME and in 63/667 patients adjudication on structural lesions was needed. Table 1 shows the agreement between central readers on the presence/absence (≥1) for all spinal MRI-lesions. The agreement for BME (κ=0.55) and fatty lesions (κ=0.50) was moderate and the agreement for erosions (κ=0.12) and syndesmophytes (κ=0.19) was slight only. The disagreement on BME lesions was balanced between the readers: in 54 and 64 patients. However, the distribution in disagreement was unequal concerning structural lesions. Central reader 1 scored many more lesions than central reader 2, especially fatty lesions.

Table 1 also shows the agreement based on a 'positive MRI-spine' according to the ASAS definition (κ =0.58) and this was similar to the agreement of central readers on any BME lesion present.

Table 1: Agreement between central reader pair on BME and structural spinal MRI lesions.

		Central reader 1	
		BME lesion present	BME lesion absent
Central reader 2	BME lesion present	142	54
	BME lesion absent	64	407
	Kappa = 0.58 / Percentage positive agreement = 54.6%		
		Central reader 1	
		Fatty lesion present	Fatty lesion absent
	Fatty lesion present	82	4
	Fatty lesion absent	111	470
	Kappa = 0.50 / Percentage positive agreement = 41.6%		
		Central reader 1	
		Erosion present	Erosion absent
	Erosion present	7	8
	Erosion absent	72	580
	Kappa = 0.12 / Percentage positive agreement = 8.0%		
		Central reader 1	
		Syndesmophyte present	Syndesmophyte absent
	Syndesmophyte present	11	18
	Syndesmophyte absent	51	587
	Kappa = 0.19 / Percentage positive agreement = 13.8%		
Central reader 2		**Central reader 1**	
		MRI-spine +	MRI-spine -
	MRI-spine +	77	58
	MRI-spine -	23	509
	Kappa = 0.58 / Percentage positive agreement = 48.7%		
		Central reader 1	
		Structural lesion present	Structural lesion absent
	Structural lesion present	86	9
	Structural lesion absent	146	426
	Kappa = 0.41 / Percentage positive agreement = 35.7%		

Agreement between LocR and CentR

In 91 patients (13.6%) spinal BME lesions were present according to LocR. In 118 patients (17.7%) there was doubt about the presence of BME lesions. LocR scored structural lesions less frequently: in 50 patients (7.5%) structural lesions were scored 'present' and in 48 patients (7.2%) there was doubt. CentR scored BME lesions in 160 patients (24.0%) and structural lesions in 157 patients (23.6%).

Table 2 shows the agreement between LocR and CentR. Agreement on BME lesions (κ=0.27) was slightly higher than on structural lesions (κ=0.13), but both were lower compared to the agreement between the two central readers. Also when looking at the individual scores of the central readers the agreement with LocR on BME lesions (reader 1 κ=0.32; reader 2 κ=0.25) and structural lesions (reader 1 κ=0.09; reader 2 κ=0.09) was slight (table 2). Table 2 also showed the agreement between LocR and CentR when LocR score 'doubt' would be considered as 'lesion present' or as 'lesion

absent'. When doubtful lesions were considered present the agreement increased, indicating that a lot of the lesions considered doubtful by LocR are scored present by CentR. Of the 160 patients in whom CentR scored BME lesions, 48.8% (n=78) got a doubt score by LocR. LocR doubted about the presence of structural lesions in 17.8% (n=28) of the 157 patients in whom CentR scored structural lesions.
In 492 patients, a radiologist performed the LocR. In 206/205 (BME/structural lesions) patients rheumatologists provided the LocR. There is an overlap of 31 patients in which the LocR (BME and structural lesions) was given by a radiologist and rheumatologist. When LocR was given by a radiologist agreement was higher compared to LocR given by a rheumatologist. For BME lesions there was a big difference in agreement of LocR and CentR between specialists; κ=0.36 for radiologists and κ=0.006 for rheumatologists. This difference was less for structural lesions; κ=0.15 for radiologists and κ=0.12 for rheumatologists (table 3).

Agreement per spinal segment

Cervical BME lesions were present in 16 patients according to LocR and 17 patients according to CentR. There were 33 (LocR) and 57 (CentR) patients with thoracic BME lesions and 55 (LocR) and 55 (CentR) patients with lumbar BME lesions. However, LocR and CentR agreed on the presence of BME lesions in 2 (cervical), 13 (thoracic) and 15 (lumbar) patients. LocR scored the presence of structural lesions in 9 (cervical), 27 (thoracic) and 23 patients (lumbar). CentR scored structural lesions in 19 (cervical), 91 (thoracic) and 67 patients (lumbar). LocR and CentR agreed in only 1 (cervical), 12 (thoracic) and 5 (lumbar) patients on the presence of structural lesions (table 4).
In general the agreement on BME as well as on structural lesions was the lowest in the cervical spine. Agreement between the central readers was moderate (cervical κ=0.45; lumbar κ=0.55) to substantial (thoracic κ=0.64) for BME and fair (cervical κ=0.22) to moderate (thoracic κ=0.51; lumbar κ=0.45) for structural lesions. The agreement between LocR and CentR was lower than between the central readers. κ between LocR and CentR was the lowest in cervical spine, then lumbar spine and though κ was the highest in thoracic spine it was still rather low (table 4).
Only for cervical structural lesions, LocR by rheumatologists had a higher agreement with CentR (κ=0.16) than when LocR was performed by radiologists (κ=0.00). In the rest of the segments agreement between LocR by radiologists and CentR was higher compared to LocR by rheumatologists.

Table 2: Agreement between local (LocR) and central (CentR) reading on the presence/absence of BME and structural spinal MRI lesions

LocR		**CentR**	
		BME lesion present	BME lesion absent
	BME lesion present	33	58
	BME lesion absent	49	409
	Doubt	78	40
	Kappa (leaving out 'doubt' group) = 0.27; PPA = 23.6%		
	Kappa ('doubt' group considered as 'lesion present') = 0.45; PPA = 43.0%		
	Kappa ('doubt' group considered as 'lesion absent) = 0.11; PPA = 15.1%		
		Central reader 1	
		BME lesion present	BME lesion absent
	BME lesion present	47	44
	BME lesion absent	73	385
	Doubt	86	32
	Kappa (leaving out 'doubt' group) = 0.32; PPA = 28.7%		
	Kappa ('doubt' group considered as 'lesion present') = 0.48; PPA = 47.2%		
	Kappa ('doubt' group considered as 'lesion absent) = 0.16; PPA = 18.8%		
		Central reader 2	
		BME lesion present	BME lesion absent
	BME lesion present	40	51
	BME lesion absent	74	384
	Doubt	82	36
	Kappa (leaving out 'doubt' group) = 0.25; PPA = 24.2%		
	Kappa ('doubt' group considered as 'lesion present') = 0.43; PPA = 43.1%		
	Kappa ('doubt' group considered as 'lesion absent) = 0.11; PPA = 16.2%		
		CentR	
		Structural lesion present	Structural lesion absent
	Structural lesion present	21	29
	Structural lesion absent	108	460
	Doubt	28	20
	Kappa (leaving out 'doubt' group) = 0.13; PPA = 13.3%		
	Kappa ('doubt' group considered as 'lesion present') = 0.55; PPA = 23.8%		
	Kappa ('doubt' group considered as 'lesion absent) = 0.10; PPA = 11.3%		
		Central reader 1	
		Structural lesion present	Structural lesion absent
	Structural lesion present	26	24
	Structural lesion absent	172	396
	Doubt	34	14
	Kappa (leaving out 'doubt' group) = 0.09; PPA = 11.7%		
	Kappa ('doubt' group considered as 'lesion present') = 0.20; PPA = 22.2%		
	Kappa ('doubt' group considered as 'lesion absent) = 0.07; PPA = 10.2%		
		Central reader 2	
		Structural lesion present	Structural lesion absent
	Structural lesion present	11	39
	Structural lesion absent	61	507
	Doubt	23	25
	Kappa (leaving out 'doubt' group) = 0.09; PPA = 9.9%		
	Kappa ('doubt' group considered as 'lesion present') = 0.24; PPA = 21.4%		
	Kappa ('doubt' group considered as 'lesion absent) = 0.06; PPA = 8.2%		

Table 3. Agreement between local (LocR) and central (CentR) reading on presence/absence of spinal BME and structural MRI lesions. LocR reported separately when performed by radiologists or rheumatologists.

				CentR	
				Present	Absent
LocR	BME	Radiologist	Present	30	41
			Absent	29	304
			Doubt	58	30
		Kappa (leaving out 'doubt' group) = 0.36; PPA = 30.0%			
		Kappa ('doubt' group considered as 'lesion present') = 0.50; PPA = 46.8%			
		Kappa ('doubt' group considered as 'lesion absent) = 0.17; PPA = 19.0%			
				CentR	
				Present	Absent
		Rheumatologist	Present	4	24
			Absent	20	126
			Doubt	21	11
		Kappa (leaving out 'doubt' group) = 0.006; PPA = 8.3%			
		Kappa ('doubt' group considered as 'lesion present') = 0.30; PPA = 31.3%			
		Kappa ('doubt' group considered as 'lesion absent) = 0.00; PPA = 5.8%			
	Structural			**CentR**	
				Present	Absent
		Radiologist	Present	16	15
			Absent	87	338
			Doubt	21	15
		Kappa (leaving out 'doubt' group) = 0.15; PPA = 13.6%			
		Kappa ('doubt' group considered as 'lesion present') = 0.26; PPA = 24.0%			
		Kappa ('doubt' group considered as 'lesion absent) = 0.12; PPA = 11.5%			
				CentR	
				Present	Absent
		Rheumatologist	Present	6	14
			Absent	26	146
			Doubt	7	6
		Kappa (leaving out 'doubt' group) = 0.12; PPA = 13.0%			
		Kappa ('doubt' group considered as 'lesion present') = 0.23; PPA = 22.0%			
		Kappa ('doubt' group considered as 'lesion absent) = 0.09; PPA = 11.3%			

Discussion

In this study we compared BME and structural lesions scored on MRI-spine by local and central readers in patients included in the DESIR cohort. We found that agreement between central readers is moderate at most but agreement between LocR and CentR was even lower.

Until now the DESIR cohort is unique in having reported data of both local and central assessments of imaging readings. Van der Berg et al. showed a moderate agreement at best (κ=0.55), between LocR and CentR of radiographic sacroiliitis[8]. In another study, van der Berg et al. found a substantial agreement (κ=0.70) between LocR and CentR concerning the presence of sacroiliitis on MRI[17]. In both studies

Table 4. Agreement per spinal segment between LocR and CentR for the presence of inflammatory and structural spinal MRI lesions.

		Inflammatory lesions			Structural lesions		
		Cervical	Thoracic	Lumbar	Cervical	Thoracic	Lumbar
Central reader 1 vs central reader 2	Kappa	0.45	0.64	0.55	0.22	0.51	0.45
	PPA in %	19.0	26.6	24.0	10.9	22.5	20.8
Central reader 1 vs LocR*	Kappa	0.05	0.19	0.26	0.03	0.10	0.02
	PPA in %	3.3	11.3	14.2	2.3	7.6	3.9
Central reader 2 vs LocR*	Kappa	0.14	0.27	0.17	0	0.07	0.03
	PPA in %	7.5	14.2	11.6	0	5.7	3.8
CentR vs LocR*	**Kappa**	**0.10**	**0.23**	**0.20**	**0.05**	**0.15**	**0.06**
	PPA in %	**5.7**	**12.6**	**12.0**	**3.4**	**9.2**	**5.3**
CentR vs LocR* (radiologist)	Kappa	0.12	0.31	0.25	0	0.14	0.07
	PPA in %	6.9	15.4	13.8	0	9.0	5.6
CentR vs LocR* (rheumalogist)	Kappa	0	0.08	0.04	0.16	0.18	0.03
	PPA in %	0	6.7	5.7	8.3	10.8	4.0

*LocR score 'doubt' was not taken into account for calculating kappa
PPA = percentage positive agreement

the agreement between LocR and CentR was similar to the agreement between central readers (κ=0.54 for radiographic sacroiliitis and κ=0.73 for sacroiliitis on MRI).
In this study, the agreement on inflammatory spinal lesions between central readers was similar to the agreement van den Berg et al reported for radiographic sacroiliitis. However, this is as far as similarities go, because we found a much lower agreement between LocR and CentR for spinal inflammatory as well as structural lesions compared to the agreement between LocR and CentR for sacroiliitis on radiographs or MRI[8,17]. More important; in our study agreement between LocR and CentR was much lower compared to agreement between central readers; fair versus moderate for BME and slight versus moderate for structural lesions. Unfortunately LocR did not have the option to differentiate between the different types of structural lesions. Neither did they have the option to specify the quantity of any of the lesions. This limited the possibilities to compare the agreement between LocR and CentR.
In BME lesions, we see that disagreement between CentR and LocR was balanced in two directions, when not taking patients with 'doubt' score into account. But for structural lesions the disagreement was unequally distributed; when CentR would be considered as external standard, LocR showed a large proportion of false negatives and a small proportion of false positives. From our data it seems that LocR underrate MRI spinal lesions. CentR more often score BME and structural spinal lesions and in a majority of these positive cases LocR did not take a decision and used the possibility to express their doubt about the presence of MRI spinal lesions due to axSpA. CentR

did not have the possibility to score 'doubt'. This discrepancy in scoring options for LocR and CentR is an issue. LocR was a general and concise score and CentR a detailed and quantified score. The agreement between LocR and CentR improved when 'doubt' scores were allocated to the 'lesions present' group and decreased when they were considered as 'lesions absent'. Also the PPA dramatically increased when 'doubt' scores were considered 'lesions present'. This indicates that LocR do not score as many spinal lesions as CentR. When looking at the LocR of radiologists and rheumatologists separately we see that there is less agreement with CentR when rheumatologists perform LocR compared to radiologists. Especially when looking at BME, rheumatologists more often doubt about the presence of lesions.

Although we can only guess, it seems that LocR would only score MRI-spine lesions when they were very certain. This phenomenon is facilitated by the option for the LocR to neither score present nor absent. Also, local readers might not have enough confidence on the typical appearance of spinal lesions due to axSpA compared to lesions due to other causes like degenerative disc disease or Scheuermann. If this is the case, it seems that local readers are not skilled enough to judge whether spinal MRI-lesions are typical for axSpA and therefore often revert to the option 'doubt'. This scenario is plausible since it is considered difficult to distinguish between SpA and degenerative lesions[18]. Besides, it might be possible to see typical axSpA and degenerative lesions within one patient. Our data could be in line with and supportive to this explanation, since the lesions that were seen by the LocR were rarely confirmed by the CentR. Finally, it is likely that the local readers had access to clinical and other imaging data like MRI and radiographs of the SI joints. This extra information, which the central readers did not have, could influence the judgement of LocR. Taking this in consideration, it is interesting for future investigations to explore whether spinal lesions due to axSpA are seen on the same location as degenerative lesions.

It has been shown that training does not improve the reliability in judgment of sacroiliitis on radiographic or structural lesions seen on MRI-SI[19,20]. We may speculate that training can improve agreement, since the agreement between (trained) central readers was better as compared to the agreement between central and local readers. However, the agreement between central readers was moderate at best and there is still a lot of room for improvement.

A limitation of this study was the difference in scoring procedure of LocR and CentR. Having the option to score 'doubt' in LocR may caused the low agreement between both readings since LocR often used this scoring option. As it is in several studies concerning MRI readings in axSpA, another limitation was the lack of a gold standard.

In conclusion, we found a moderate agreement between two central readers for scoring inflammatory and structural lesions seen on MRI-spine. This agreement was better compared to the agreement between LocR and CentR, which was only considered fair at most.
So, LocR do not score many lesions compared to CentR and doubt in the majority of cases about the presence of spinal MRI lesions.

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