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Comparison of semi-quantitative and visual assessment of early MRI signal evolution in acute ischaemic stroke

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ABSTRACT

Background: The evaluation of DWI/FLAIR mismatch in ischaemic stroke patients with unknown, time from onset can determine the treatment strategy. This approach is based on, visual assessment and may be subject to insufficient inter-rater agreement.
Objective: To compare the inter-rater agreement of visual evaluation of FLAIR MRI and proposed region of interest (ROI) semiquantitative method in large vessel occlusion (LVO) strokes.
Methods: Five readers have analysed MRIs of 104 patients obtained within six hours of the onset of stroke symptoms resulting from LVO visually and semi-quantitatively. For the semiquantitative analysis, a ROI method was used to obtain relative signal intensity compared to the unaffected side. Cut-off values of 1.15 and 1.10 were tested. The analysis yielded FLAIR-positive (abnormal) and negative (normal) findings. Percentage agreement and Fleiss kappa coefficients were calculated.
Results: The visual agreement of 5/5 readers and $\geq$ 4/5 readers occurred in 31% and 59% of cases respectively. Semi-quantitative evaluation using a cut-off value of 1.15 increased the agreements to 67% and 88% respectively. The agreement of visual evaluation was fair. The semi-quantitative method utilising the cut-off of 1.15 had moderate agreement although it increased the number of FLAIR-negative results compared to the visual evaluation. A low cut-off value of 1.10 didn't improve the agreement significantly.
Conclusion: The inter-rater agreement of visual evaluation of FLAIR in patients with short-duration large vessel occlusion stroke was fair. The high cut-off value of semiquantitative evaluation increased the agreement although it changed the proportion of FLAIR positive and negative results.

1. Introduction

Under current guidelines, intravenous thrombolysis (IVT) can be administered for the treatment of acute ischaemic stroke in patients with an unclear time of onset > 4.5 h or in patients who wake up with a stroke if the size of the lesion on diffusion-weighted imaging (DWI) is smaller than one-third of the territory of the middle cerebral artery and if there is no visible signal change in fluid-attenuated inversion recovery (FLAIR) [1]. The selection of DWI-positive (abnormal) and FLAIR-negative (normal) patients is based on visual evaluation which represents the gold standard [1]. Visual evaluation is known to have a suboptimal inter-rater agreement, especially in the case of subtle signal alteration [2–5] although moderate inter-rater reliability of DWI-FLAIR visual mismatch assessment in a 4.5-hour onset window in patients who went on to have IV thrombolysis was also reported [6]. The purpose of this study was to assess the inter-rater agreement of the standard visual FLAIR evaluation in large vessel occlusion (LVO) strokes, and to test a capability of a modified simple-to-use semi-quantitative method for the

Abbreviations: IVT, intravenous thrombolysis; DWI, diffusion-weighted imaging; FLAIR, fluid-attenuated inversion recovery; LVO, large vessel occlusions; TSE, turbo spin echo; TOF, time-of-flight; ADC, apparent diffusion coefficient; ROI, region of interest; RSI, relative signal intensity; CSF, cerebrospinal fluid.

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assessment of DWI/FLAIR mismatch to improve the inter-rater agreement.

2. Methods

2.1. Study population

We have retrospectively evaluated the MRI scans of ischaemic stroke patients examined at our institution within a seven-year period who had clinical signs of a stroke according to a neurological examination, in whom large vessel occlusion was detected in the anterior circulation that was visible on MR angiography and the time from the onset of symptoms to MRI did not exceed six hours. We have identified 125 eligible brain MRIs. We excluded 21 patients who had simultaneous acute ischaemic changes in the posterior circulation, acute bilateral ischaemic lesions, or substantial motion artefacts. All patients were collected from the database of ischaemic stroke patients who received endovascular treatment in our centre, which provides care for the general adult population. The study profile is shown in Table 1.

2.2. MR imaging

The MRI was performed on two 1.5 T systems (Siemens Symphony and Siemens Avanto) using a head coil. The imaging protocol comprised axial T2 turbo spin echo (TSE), axial T2-weighted FLAIR, echo planar DWI, and 3D time-of-flight (TOF) angiography. In the DWI imaging, gradients were applied (b = 0, 500, 1000 mm^2/s or 0, 1000 mm^2/s) along the three axes and trace images were created. An apparent diffusion coefficient (ADC) map was calculated from the acquired measurements. The acquisition parameters of FLAIR are summarised in detail in Table 2.

2.3. Imaging evaluation

The MRI images were evaluated by five radiologists independently, with their years of experience ranging from one to ten years. All the readers were blinded to clinical data, including the time from the onset of symptoms. Follow-up imaging in most of the patients was available but the readers were instructed not to use it. An institutional picture archiving and communication system viewer was used. First, every reader visually evaluated the presence or absence of signal alteration on DWI. Ambiguous findings had to be classified unequivocally as either negative or positive. The evaluation of DWI was followed by visual evaluation of FLAIR. The patients were grouped according to the visual assessment as FLAIR-negative (lacking signal alteration) or FLAIR-positive (exhibiting a signal change). Any visual FLAIR signal abnormality was enough to make a case positive. The subclassification of FLAIR-positive cases into subtle and obvious was not used.

Table 1
Study profile.

Number of patients with LVO stroke and symptom onset < 6 hrs	125	MRI examinations	
Excluded	21	Motion artefact or poor image quality	3 (2%)
		Acute bilateral lesions:	7 (6%)
		Simultaneous posterior circulation lesions	11 (9%)
Included	104	Known exact time from onset	80 (77%)
		Unknown time from onset under 6 h	24 (23%)

LVO large vessel occlusion.

Table 2
Acquisition parameters.

Scanner Manufacturer	Siemens	
Manufacturer's Model names:	Symphony	Aera
Magnetic field strength	1.5 T	
Type of sequence[a]		
DWI		
TR (ms)	4000	4800
TE (ms)	136	67
Flip Angle	90	180
Number of Excitations	6	1
Acquisition Type	2D	2D
B values (mm2/s)	0, 500, 1000	0, 1000
Slice Thickness (mm)	5.0	5.0
Interspace Gap (mm)	1.5	1.5
Field of View (cm)	23 × 23	23 × 23
Matrix Size	256 × 256	180 × 180
Pixel Size	0.898 × 0.898	1.278 × 1.278
Pixel Bandwidth (Hz)	1345	815
T2 FLAIR		
TR (ms)	8760	8600
TE (ms)	124	106
Inversion Time (ms)	2500	2451
Flip Angle	150	150
Number of Excitations	1	1
Acquisition Type	2D	2D
Slice Thickness (mm)	5.0	5.0
Interspace Gap (mm)	1.5	1.5
Field of View (cm)	24 × 18	23 × 23
Matrix Size	512 × 392	256 × 256
Pixel Size (mm)	0.469 × 0.469	0.898 × 0.898
Pixel Bandwidth (Hz)	130	362

DWI diffusion-weighted imaging, *FLAIR* fluid-attenuated inversion recovery, *TR* repetition time, *TE* echo time.
[a] Axial T2 TSE and TOF MRA were also included in the standard imaging protocol

2.4. Semi-quantitative assessment

After the standard visual evaluation, a semi-quantitative assessment was performed. A single slice showing the most prominent extent of cytotoxic oedema seen on DWI was selected for the analysis. The slice selection was performed by every reader individually. The circular region of interest (ROI) of the largest possible size was placed within the affected cerebral tissue, showing the true diffusion restriction on DWI (Fig. 1).

The ROI covered the region of cytotoxic oedema of both white and grey matter. The ROI was copied and placed in the exact location on the corresponding FLAIR slice manually. Afterwards, the ROI was copied and inserted on the unaffected side of the corresponding location on FLAIR. The distance from the midline was used to help guide the correct position. Average intensities were noted, and the RSI was calculated as the ratio between the average value measured within the affected and the unaffected side. In the event of the presence of a prominent chronic white matter change within the ROI on FLAIR, seen as hyperintensity on FLAIR with no correlate on DWI, the size and/or position of the ROI was adjusted to exclude the chronic lesion. For the sake of simplicity, the positioning of the ROI on the contralateral side was performed manually.

The circular ROI was always drawn several pixels away from the ventricles to reduce the influence of cerebrospinal fluid (CSF) on the average signal intensity. However, if ischaemia of the cortical region was obvious and the inclusion of cortical grey matter would have been unavoidable to obtain the largest possible area of the ROI, then both the affected and unaffected contralateral cortex were intentionally included together with a minor portion of sulcal CSF in the ROI thus indirectly implementing information on sulcal CSF volume.

Relative signal intensity (RSI) was recorded for both FLAIR and DWI, although the RSI of DWI was not utilised further. Patients with normal visual findings on DWI were also included in the study population, but in

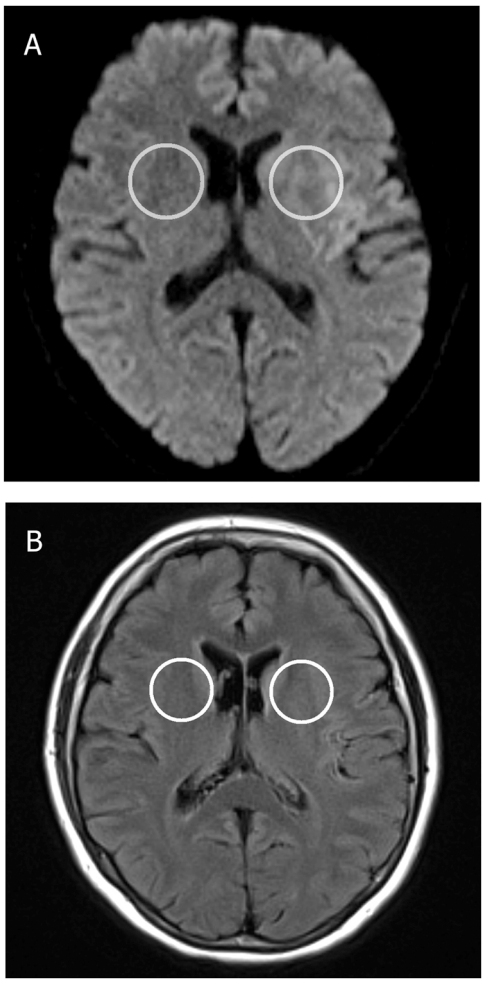

Fig. 1. **a** DWI showing cytotoxic oedema. Region of interest placed within the area of the affected brain tissue and copied to the corresponding contralateral location **b** Corresponding FLAIR image with the same region of interest placed in the same location *DWI*, diffusion-weighted image; *FLAIR*, fluid-attenuated inversion recovery.

this scenario the RSI of FLAIR could not be calculated because of a missing target tissue, and therefore for the purposes of the statistical analysis and calculation of the Fleiss kappa, the RSI = 1 was assigned. The evaluation of DWI and FLAIR was performed by every reader individually, thus yielding five datasets.

2.5. Cut-off values

A cut-off value of FLAIR RSI = 1.15 was applied to categorise the patients as FLAIR-positive or FLAIR-negative. This is the cut-off value used by other authors in previous studies [7,8]. Another cut-off value, FLAIR RSI = 1.10, was tested. This was conducted on purpose after all the MRI data had been collected and it became clear that this cut-off value produces a similar proportion of FLAIR-positive and FLAIR-negative findings to the visual evaluation.

2.6. Statistical analysis

To assess the inter-rater agreement the percentage agreement and Fleiss kappa coefficient were calculated for both the visual and semi-quantitative evaluation.

The correlation among the continuous variables was assessed by means of non-parametric (Spearman) correlation coefficients. The difference in continuous variables among two or more patient groups was assessed by means of a non-parametric Kruskal-Wallis test. The Kruskal-Wallis test is a non-parametric version of the classical ANOVA and it tests whether samples originate from the same distribution. In the case of two groups, it is equivalent to the Mann-Whitney U test. The inter-rater agreement was computed by means of the Fleiss kappa coefficient. This is a statistical measure for assessing the reliability of the agreement between more than two raters who classify items into categories. The measure calculates the degree of agreement in classification over that which would be expected by chance. The statistical analyses were carried out in MATLAB Version 7.5.0.342 (R2007b) and the R software.

3. Results

3.1. Study population

Three out of the 125 patients (2%) with LVO stroke were excluded because of poor image quality or an incomplete protocol. Eleven patients (9%) had coincident acute ischaemic lesions in the posterior circulation and seven (6%) had bilateral lesions. These patients were also excluded, thus producing 104 MR examinations left for the analysis.

The exact time from the onset of symptoms was known in 80 out of 104 patients (77%) (median 118 min, interquartile range 90–148 min). The remaining 24 patients had an unknown time from onset, but it was shorter than six hours. The time distribution is shown in Fig. 2.

3.2. Image analysis

Five datasets (one from each reader) produced altogether 493 abnormal and 27 normal DWI findings. The number of FLAIR-positive (abnormal) and FLAIR-negative (normal) findings out of 493 abnormal DWI readings was calculated using both visual and semi-quantitative assessment. The results are summarised in Table 3. The semi-quantitative evaluation of FLAIR utilising the cut-off value of 1.15 performed by the five readers individually changed the former visual FLAIR status in 87 out of 493 readings compared to the visual approach; specifically, this led to an increase in the number of FLAIR-negative readings from 314 to 401 and a decrease in the number of FLAIR-positive readings from 179 to 92.

3.3. Inter-rater agreement

We further evaluated the agreement of all five readers and of at least

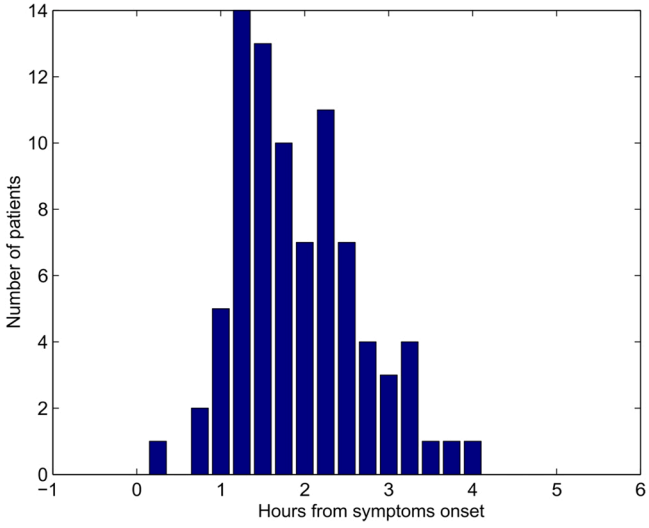

Fig. 2. Time distribution demonstrates time to DWI in patients with known time of stroke onset.

Table 3
Comparison of visual and semi-quantitative evaluation of FLAIR in 104 patients examined within six hrs from onset of stroke showing number of FLAIR-negative and FLAIR-positive results of five readers (A-E)[a].

	FLAIR+		FLAIR-	
Reader	visual	RSI ≥ 1.15	visual	RSI < 1.15
A	58	79	39	18
B	82	86	18	14
C	45	78	55	22
D	70	80	29	19
E	59	78	38	19
SUM	314	401	179	92
change (N)		+ 87		-87

RSI relative signal intensity
[a] The number of patients evaluated by each reader may vary as only patients with a visually detected signal change on DWI were further evaluated by every reader

four readers for both qualitative and semi-quantitative assessment. The percentage agreement was lower in the case of visual evaluation, compared to the semi-quantitative assessment. However, the cut-off value of 1.15 RSI that was used yielded more FLAIR-negative results, thus changing the sensitivity of the test. By using this cut-off value, we obtained 87 additional FLAIR-negative results out of a total of 493 readings. Concerning the five individual readers, this increase ranged between four and 33 FLAIR-negative cases out of 104 patients who were studied. An example where the semi-quantitative method was helpful in improving the agreement demonstrates Fig. 3.

The cut-off value of FLAIR RSI = 1.1 yielded the same number of FLAIR-positive and FLAIR-negative results as in the case of visual evaluation. The Fleiss kappa for both visual and semi-quantitative evaluation was calculated. The Fleiss kappa for the visual assessment was fair, k = 0.30 (95% confidence interval 0.24–0.36), as well as for the semi-quantitative method with the cut-off value of 1.10, k = 0.38 (95% confidence interval 0.32–0.44). The high cut-off value of 1.15 yielded moderate agreement, k = 0.46 (95% confidence interval 0.40–0.52), which was significantly higher than in the case of the visual assessment. Although the agreement for visual FLAIR-negative results for 5/5 readers and ≥ 4/5 was 24% and 45% and for semi-quantitative analysis 61% and 80% respectively, the agreement for FLAIR-positive results was much lower, only 7% for 5/5% and 14% for ≥ 4/5 readers in the case of visual evaluation and 6% for 5/5% and 8% for ≥ 4/5 readers in the case of the semi-quantitative method.

The inter-rater agreement is shown in Table 4 and Fig. 4.

In the group of patients whose FLAIR visual status was assessed identically by at least four readers, the values of FLAIR RSI were further evaluated. The median FLAIR RSI was 1.05 and 1.20 for the visual FLAIR-negative and FLAIR-positive cases, respectively (Fig. 5).

The lowest agreement of visual assessment was typical for signal changes with the FLAIR RSI between 1.09 and 1.13. Such values of FLAIR RSI were measured in 97 readings (20%) out of the total of 493 FLAIR readings.

3.4. Subanalysis of the onset of abnormalities on FLAIR

The FLAIR status was further evaluated in the subgroup of 84 patients with a known time from the onset of symptoms who underwent MRI within 4.5 h from the onset of symptoms. We used visual FLAIR evaluation and semi-quantitative assessment with a FLAIR RSI threshold of 1.15. The results are shown in Tables 5 and 6. In total, only 62.7% of the individual readings had negative (normal) FLAIR using visual evaluation. The semi-quantitative evaluation using the threshold of RSI = 1.15 led to an increase in the number of patients categorised as FLAIR-negative to 81%.

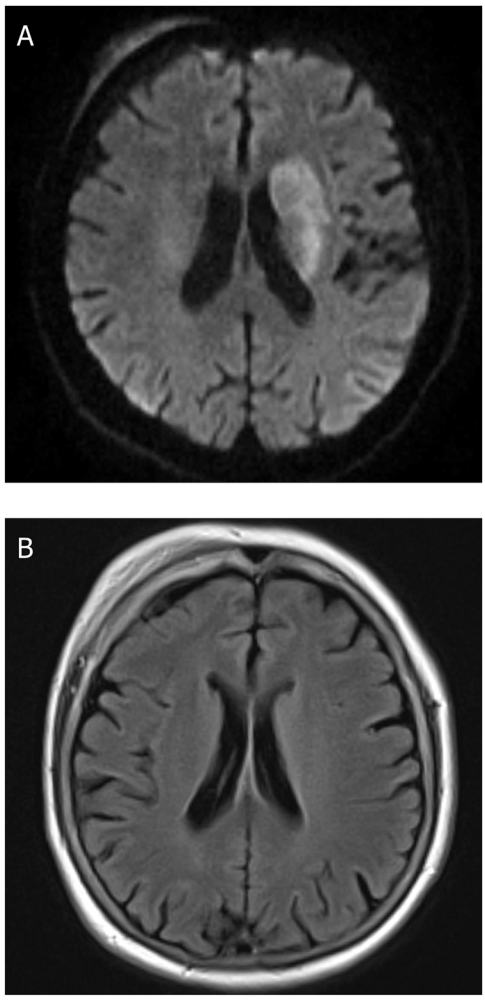

Fig. 3. **a** The figure demonstrates a patient examined 220 min after the onset of the symptoms. DWI is clearly positive, showing increased signal intensity within the basal ganglia on the left. **b** The vague signal alteration visible in a FLAIR image of the same patient produced low inter-rater agreement of the visual evaluation performed by five readers (three FLAIR-positive and two negative results). The application of the semiquantitative method utilising the high cut-off value of 1.15 RSI yielded five FLAIR-negative results, meaning full agreement of the five readers, with the RSI values being 1.11, 1.11, 1.10, 1.08, and 1.05.

Table 4
Comparison of visual and semi-quantitative evaluation of FLAIR in 104 patients examined within six hrs of onset of symptoms showing agreement of five and ≥ four readers.

FLAIR status	Agreement of readers	Visual evaluation	Semi-quantitative evaluation, threshold RSI = 1.15
FLAIR-	[= 5/5]	25 (24%)	63 (61%)
	[≥ 4/5]	47(45%)	83 (80%)
FLAIR+	[= 5/5]	7 (7%)	6 (6%)
	[≥ 4/5]	15 (14%)	8 (8%)
FLAIR+ or FLAIR-	[= 5/5]	32 (31%)	69 (67%)
	[≥ 4/5]	62 (59%)	91 (88%)

FLAIR fluid-attenuated inversion recovery, RSI relative signal intensity.

4. Discussion

We investigated the inter-rater agreement of visual evaluation of the early imaging of LVO stroke patients. It simulates a clinical scenario

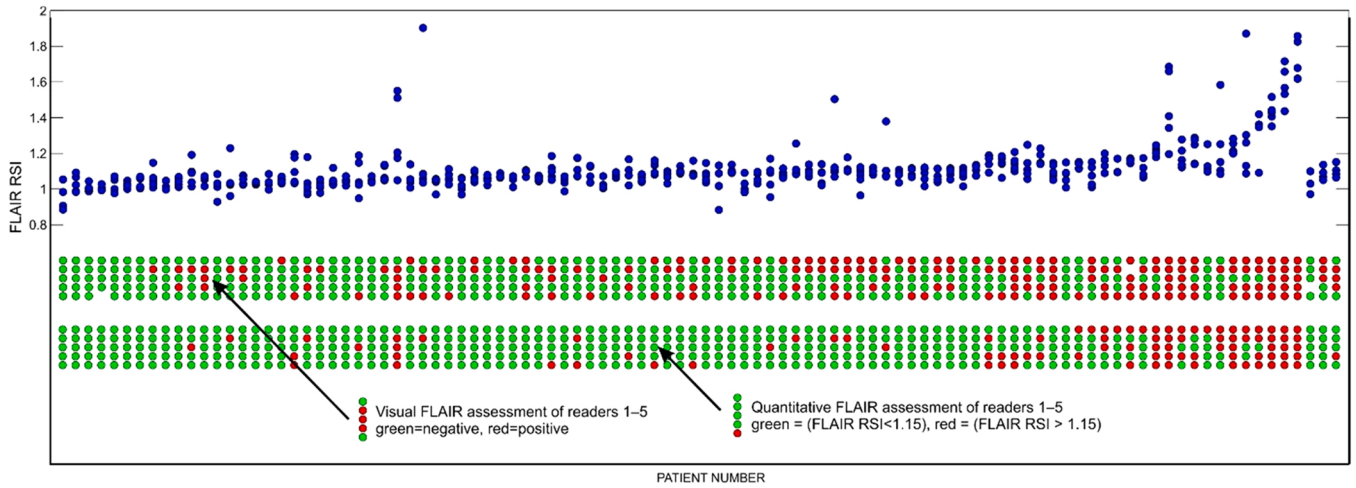

Fig. 4. (Colour) Comparison of FLAIR positives (red) and negatives (green) as seen by five readers with the x-axis showing all consecutive patients. The patients are lined up according to the relative signal intensity measured by reader A (blue dots). The missing visual FLAIR status of certain patients is due to a failure to detect any signal change on diffusion-weighted imaging by the particular reader. *FLAIR*, fluid-attenuated inversion recovery.

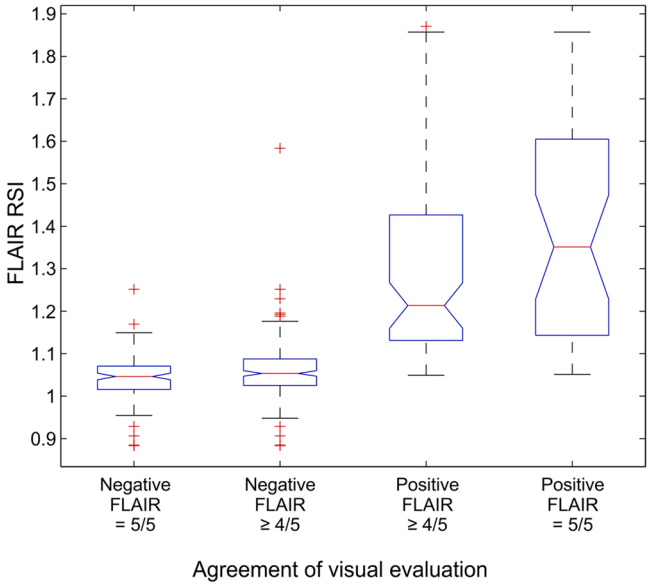

Fig. 5. Box graph showing the relative signal intensities of those patients whose visual assessment was evaluated identically by four and five readers respectively.

Table 5
Semi-quantitative evaluation of the subgroup of 80 patients examined within 4.5 hrs of onset of symptoms, showing FLAIR status[a].

Reader	FLAIR-, RSI threshold = 1.15	FLAIR+ , RSI threshold = 1.15
A	63 (82%)	14 (18%)
B	68 (85%)	12 (15%)
C	62 (78%)	18 (23%)
D	64 (81%)	15 (19%)
E	62 (80%)	16 (20%)
total	319 (81%)	75 (19%)

FLAIR fluid-attenuated inversion recovery, *RSI* relative signal intensity

[a] The number of patients evaluated by each reader may vary as only patients with a visually detected signal change on diffusion-weighted imaging were further evaluated by every reader

Table 6
Visual evaluation of the subgroup of 80 patients examined within 4.5 hrs of onset of symptoms, showing FLAIR status[a].

Reader	Visual FLAIR-	Visual FLAIR+
A	47 (61%)	30 (39%)
B	66 (83%)	14 (18%)
C	35 (44%)	45 (56%)
D	54 (68%)	25 (32%)
E	45 (58%)	33 (42%)
total	247 (63%)	147 (37%)

FLAIR fluid-attenuated inversion recovery

Ethical approval

The study was approved by the Ethics Committee of the University Hospital and Faculty of Medicine and Dentistry of Palacky University Olomouc

The authors confirm that all imaging methods were employed in accordance with national and institutional guidelines and regulations.

[a] The number of patients evaluated by each reader may vary as only patients with a visually detected signal change on diffusion-weighted imaging were further evaluated by every reader

where a patient with an LVO stroke with unknown time from the onset of the symptoms is examined using MRI and a clinician considers the application of IVT prior to mechanical thrombectomy. Although one may expect that the lesions in LVOs would often be present and more easily detected, this was not observed.

The visual evaluation yielded fair inter-rater agreement in LVOs. Despite LVO strokes tending to be large in volume, our expectations of reaching good inter-rater agreement in LVO strokes using visual assessment were not met. We expected that signal alteration would be rather easy to observe even in the case of subtle alteration. This relatively low agreement of visual assessment might be caused by the short time to MRI in the population that was studied, with a median of two hours. Such early signal alteration might be almost imperceptible. As a significant proportion of wake-up strokes might occur soon before the discovery of the symptoms this might be a legitimate concern [9].

We decided to limit stroke patients to LVOs to test the modified ROI method to obtain large ischaemic cores and to test the modification of the usual ROI method. The innovativeness of this model lies in the intentional inclusion of a minor portion of cerebrospinal fluid within the analysed ROI in predominantly cortical lesions (not in the case of deep grey matter lesions), which might have led to the achievement of relatively higher RSI values compared to other studies that strictly avoided the inclusion of cerebrospinal fluid. Both mechanisms (increased signal of cytotoxic oedema and reduced cerebrospinal fluid volume because of

gyral swelling) clearly participate in the increase in the average signal intensity within the ROI on both FLAIR and DWI. Our decision to include sulcal cerebrospinal fluid was motivated by the knowledge that the volume of the fluid on the affected side is often slightly diminished because of incipient gyral swelling, thus increasing the measured values of the RSI and possibly increasing the sensitivity of this approach.

The number of FLAIR-positive and FLAIR-negative findings, as well as the inter-rater agreement in semi-quantitative evaluation, is clearly dependent on the selection of the cut-off value, while the visual assessment is dependent rather on subjective factors. Although the benefit of the semi-quantitative method is that it allows a specific cut-off value to be set, the optimal cut-off value remains unclear with the visual assessment being the gold standard. The inter-rater agreement of the proposed semi-quantitative approach did not outperform the visual evaluation if the low cut-off value of 1.10 (yielding a similar proportion of FLAIR-positive and negative findings as visual assessment) was used. Although it reached higher inter-rater agreement than the visual assessment, it remained fair. According to our observation, this value corresponded to the edge of visual perceptibility. Although the semi-quantitative method may fail to significantly improve agreement if such a low cut-off value is used, we consider it to be objective and that it has the potential to produce reproducible unbiased results, especially in subtle signal change. The high cut-off value of 1.15 improved the agreement significantly but on the other hand it changed the total number of FLAIR-positive and negative results. According to our observation, this cut-off value represents the signal changes which are clearly visible. Still, the method that was applied only improved the agreement in the FLAIR-negative findings, but no improvement was observed in the agreement of the FLAIR-positive results, regardless of whether visual or semi-quantitative analysis was used.

Our decision to test a cut-off value of 1.15 comes from two previous studies where this value was used. Schwamm et al. conducted a prospective safety study of IVT in patients with unwitnessed strokes who were able to receive treatment within 4.5 h of the discovery of their symptoms [8]. They used the threshold of FLAIR RSI < 1.15 to select patients eligible for IVT and reported on the feasibility of such treatment. Although this approach using a cut-off value of 1.15 has been proved to be safe, it has not been studied in any randomised controlled trial yet and it is therefore unclear whether it is superior to visual assessment. The authors of the present study acknowledge that differences exist between our study population and the MR WITNESS study. MR WITNESS included patients with the unwitnessed onset of symptoms and only 23% had LVO, while all patients in the present study had LVO.

The subanalysis of patients presenting within 4.5 h from the onset of the symptoms shows how early FLAIR-positive findings may be found in LVO and opposes the DWI/FLAIR mismatch approach which has been reported to determine that the duration of symptoms is lower than 4.5 h [3,7,10]. Furthermore, patients examined within a time window of 3.0 h from the onset of symptoms are reported to have negative FLAIR with high sensitivity and specificity [11]. On the contrary, according to Ebinger et al., the visibility of FLAIR is not recommended for inferring that the time from the onset of symptoms is higher than 4.5 h [12]. In the subgroup of the present study, patients examined within 4.5 h from the onset of symptoms had normal FLAIR preserved far less often than we expected; in fact, less than two-thirds of the readings had no signal alteration detected using the visual assessment of FLAIR (with an increase to 81% of FLAIR negatives using an RSI cut-off of 1.15). The low number of FLAIR negatives might be caused by the fact that the study population was formed of LVO stroke patients only. We hypothesise that signal alteration visible on FLAIR in the area of the ischaemic core of LVO strokes might develop faster than in non-LVO strokes owing to less effective collateral supply in LVO. Thus DWI-FLAIR mismatch seems problematic and may not be appropriate for identifying patients < 4.5 h from onset. However, one must acknowledge the improved patient outcomes in the wake-up TRIAL.

The limitations of the study lie in the analysis being limited to the symptoms having a duration of six hours or less but on the other hand this simulates a real-life scenario as it is thought that wake-up strokes often start close to awakening [9]. The limitation to six hours also increased the frequency of slight signal alterations, thus negatively influencing the inter-rater agreement. Since the agreement for FLAIR-positivity was only 6% of 5/5 readers and 8% of $\geq 4/5$ for the semi-quantitative analysis and 7% and 15% respectively for the visual evaluation, this underlines the controversial nature of the measure to categorise the patients as either clearly positive or negative. The poor interrater agreement may be partially explained by the uneven proportion of FLAIR-negative and positive results, with the obvious dominance of FLAIR-negative cases. However, we do observe that with the use of semi-quantitative measurements with an RSI threshold of 1.15 the FLAIR status is more homogenous than the visual one.

The fact that we have excluded posterior LVOs as these often present with bilateral ischaemic changes which would limit the application of the proposed semi-quantitative method may be of note. Furthermore, the study was limited to a single centre, which yielded a small dataset. The selection of the ROI method used may be questionable. To employ the semi-quantitative method, we avoided time-consuming manual segmentation of the whole ischaemic tissue and rather preferred the one-plane circular ROI method. The size and shape of the ROI in the semi-quantitative assessment of DWI and FLAIR mismatch has been defined variously by several authors [2,7,11]. According to Song et al., the reader-defined hot spot method gave results that were comparable to the more time-consuming volume segmentation method [7]. In the present study, we decided to test a simplified circular ROI method that is slightly different to the hot spot method, which is aimed at the area of the highest signal. Our circular ROI approach was based on the placement of the ROI of the largest possible size inserted within the affected cerebral tissue. This was fast and simple and did not require the use of high-tech software to perform automated volume segmentation, thus not increasing the cost of such an approach. A limitation of any ROI method, including ours, may be the non-uniform size of the ROI used by different readers, which might lead to a certain variability in the average signal intensity within the ROI. In the case of the inclusion of sulcal fluid, we are aware of a risk of imprecise measurement owing to incorrect oblique axial slices rather than true axial slices, which might have an influence on the amount of sulcal cerebrospinal fluid within ROI. Therefore, true axial slices were required for such evaluation in order to avoid inaccurate RSI measurement. This precise imaging may be sometimes problematic in stroke patients.

In our opinion, the application of a low cut-off value will not outperform a visual assessment in the inter-rater agreement but allows for the setting of a user-defined threshold which is objective and may help readers in the decision-making process, especially if subtle signal alteration is present, until artificial intelligence software is widely available. The aim of our work was not to outperform the automated intelligence or machine learning approaches which are emerging, and which have the potential to become the diagnostic standard [13,14].

5. Conclusion

The inter-rater agreement of visual FLAIR evaluation in patients with short duration large vessel occlusion was unsatisfactory. Semi-quantitative evaluation is an objective method which may help readers evaluate DWI/FLAIR mismatch and yields satisfactory inter-rater agreement if a high cut-off value is used.

CRediT authorship contribution statement

All authors contributed to the conception and design of the study. Material preparation, data collection, and analysis were performed by Jakub Civrny and Tomas Furst. The first draft of the manuscript was written by Jakub Civrny and all authors commented on previous versions of the manuscript. All authors read and approved the final

manuscript.

Ethical approval

The study was approved by the Ethics Committee of the University Hospital and Faculty of Medicine and Dentistry of Palacky University Olomouc. The authors confirm that all imaging methods were employed in accordance with national and institutional guidelines and regulations.

Consent for publication

Not applicable.

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Declaration of Competing Interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

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