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Computer aided diagnosis for ASPECT rating: initial experiences with the Frontier ASPECT Score software

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Abstract

Background: Computer-aided diagnosis is increasingly used in radiology and may support not only unexperienced readers but also senior radiologists. It appears promising, especially in the sometimes challenging detection of early ischemic changes in stroke CT.

Purpose: To compare the new post-processing software prototype Frontier_ASPECTS against two senior radiologists in ASPECTS evaluation.

Material and Methods: Retrospectively, pre-interventional CTs of 100 patients, who underwent endovascular revascularization for acute middle cerebral artery ischemia, were blindly re-analyzed with respect to ASPECTS by two neuroradiologists (separately and in consensus) and by use of Frontier_ASPECTS. In addition to a fully automatic Frontier_ASPECTS reading (Frontier_1), Frontier_ASPECTS readings subsequently manually corrected for old cerebral defects (Frontier_2a), the affected hemisphere (known from CT angiography, Frontier_2b), and both (Frontier_3) were assessed. Statistical analysis was performed by intraclass correlation and Bland–Altman analysis.

Results: Median ASPECTS was 10 for Frontier_3 (range = 5–10), 10 for radiologist_1 (range = 4–10), 9 for radiologist_2 (range = 2–10), and 10 for consensus reading (range = 2–10). All Frontier_ASPECTS variants correlated lowly with consensus reading (Frontier_1, r = 0.281; Frontier_2a, r = 0.357; Frontier_2b, r = 0.333; Frontier_3, r = 0.350; always $P < 0.01$), while both radiologists and consensus reading correlated highly (radiologist_1, r = 0.817; radiologist_2, r = 0.951; always $P < 0.001$). Bland–Altman analysis confirmed a worse agreement between Frontier_3 and consensus reading than between both radiologists and consensus reading.

Conclusion: We found only low agreement between the post-processing software Frontier_ASPECTS and expert consensus reading in ASPECTS evaluation. Notably, performance of Frontier_ASPECTS improved by simple manual corrections but is–at Frontier_ASPECTS' current development status–inferior to the performance of senior radiologists.

Keywords

Computer-aided diagnosis, early ischemic change detection, brain computed tomography, ASPECT score

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Introduction

Computer-aided diagnosis (CAD) has a huge potential in assisting radiological decision-making and is increasingly used in daily practice. Through automatic pattern matching and quantitative image information extraction, CAD software solutions facilitate image interpretation and may support not only unexperienced radiologists but also senior readers. CAD software solutions, such as the currently developed post processing tool syngo.via Frontier ASPECT Score Prototype V1_2_0 (Frontier_ASPECTS; Siemens Healthcare

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GmbH, Erlangen, Germany), appear promising, especially in the sometimes challenging detection of early ischemic changes in brain computed tomography (CT) (1). Frontier_ASPECTS fully automatically analyzes non-contrast brain CTs for early ischemic changes on base of the Alberta Stroke Program Early CT Score (ASPECTS). ASPECTS is a robust 10-point quantitative CT score grading the extent of early ischemic changes within the middle cerebral artery territory and was established to support treatment decision-making in acute stroke treatment (2,3). According to the Frontier_ASPECTS user manual, Frontier_ASPECTS analyzes non-contrast brain CTs in three steps: first, it defines by atlas-based segmentation 10 volumes of interest (VOI) in accordance to the ASPECT score on both sides; second, it measures the mean Hounsfield units (HU) for each VOI (dark voxels are excluded to avoid misinterpretation due to liquor or old infarcts); and third, percentage HU differences between corresponding VOIs are calculated and on their basis the VOIs are classified as ischemic or non-ischemic, and the total ASPECT score is calculated (4). The current study aimed to evaluate the performance of this new post-processing prototype Frontier_ASPECTS in comparison to ASPECTS readings by two senior radiologists.

Material and Methods

Retrospective analysis and use of blinded data were approved by the local ethic committee. (For this type of retrospective study, no formal consent was required.) One hundred consecutive unselected patients who underwent endovascular revascularization for occlusion of the distal internal carotid artery, the middle cerebral artery, or its major branches at our center between 2 January 2015 and 5 November 2017 and who met the inclusion and exclusion criteria were included. Inclusion criteria were: (i) endovascular revascularization at our center; (ii) available non-contrast brain CT plus CT angiography; and (iii) unilateral occlusion of the internal carotid artery and/or middle cerebral artery and/or its major branches. Exclusion criteria were: (i) pre-existing cerebral defects within the current ischemic area which were not reliably distinguishable from acute ischemic changes; and (ii) severe motion or other artifacts impeding CT interpretation. Initial and post-therapeutic (on days 2–14 after thrombectomy) National Institutes of Health Stroke Scale score (NIHSS) were extracted from the electronic medical records.

Computed tomography (CT)

All CT scans were acquired using a Somatom Definition AS+ scanner or a Somatom Definition Flash scanner (Siemens Healthcare GmbH, Erlangen, Germany). Collimation was 128×0.6 mm (AS+) and 40×0.6 mm (Flash). Automated tube voltage selection by CARE kV and automated tube current modulation by X-CARE and CARE Dose 4D were used. For non-contrast brain CT, reference tube voltage was 120 kVP (AS+)/100 kVP (Flash) and reference tube-current-time product was 330 mAs. For CT angiography, the reference tube voltage was 100 kVP, reference tube-current-time product was 140 mAs, and 80 mL contrast media (Ultravist 300, Bayer HealthCare, Leverkusen, Germany) followed by a bolus of 20 mL physiologic salt solution were injected with a flow rate of 4 mL/s. Bolus triggering was performed in the aorta ascendens. Axial non-contrast brain CT images were reconstructed in 5-mm slices using J30 kernel. Axial and coronal CT angiography images were reconstructed in 1-mm slices using I26 kernel.

ASPECTS and Frontier_ASPECTS

Retrospectively, all non-contrast brain CTs were reanalyzed for early ischemic changes (loss of gray-white differentiation, sulcal effacement, parenchymal hypoattenuation, hyperdense artery sign (5,6)) in the middle cerebral artery territory separately by two senior neuroradiologists (JG, SZ) who were blinded to each other, the CT angiography, and the Frontier_ASPECTS results. In doing so, 10 VOIs were defined in accordance with the ASPECT score on both sides by the radiologists and rated as ischemic or non-ischemic (2). Subsequently (with a time interval of four weeks between first and consensus reading, to avoid learning effects), an expert consensus reading of all brain CTs was performed by both radiologists. All brain CTs were then fully automatically analyzed for early ischemic changes by the post-processing tool syngo.via Frontier ASPECT Score Prototype V1_2_0 (Frontier_ASPECTS; Siemens Healthcare GmbH, Erlangen, Germany). Frontier_ASPECTS assigns each VOI to the categories normal/non-ischemic (marked in green, Fig. 1), questionable ischemic/pathologic (marked in yellow), and ischemic (marked in red). As we aimed for a dichotomous variable for the presence of early ischemic changes, and as Frontier_ASPECTS quite often marked VOIs in yellow in either hemisphere, we graded questionable ischemic/yellow VOIs (of Frontier_ASPECTS) as being non-ischemic. In addition to the fully automatic Frontier_ASPECTS reading (Frontier_1), Frontier_ASPECTS readings subsequently manually corrected by the radiologists for old cerebral defects (Frontier_2a, that means that false-positive findings, i.e. VOIs with old cerebral defects which were misclassified by Frontier_ASPECTS as ischemic, were corrected/classified as being not acute ischemic by the radiologists), for the side of middle cerebral artery

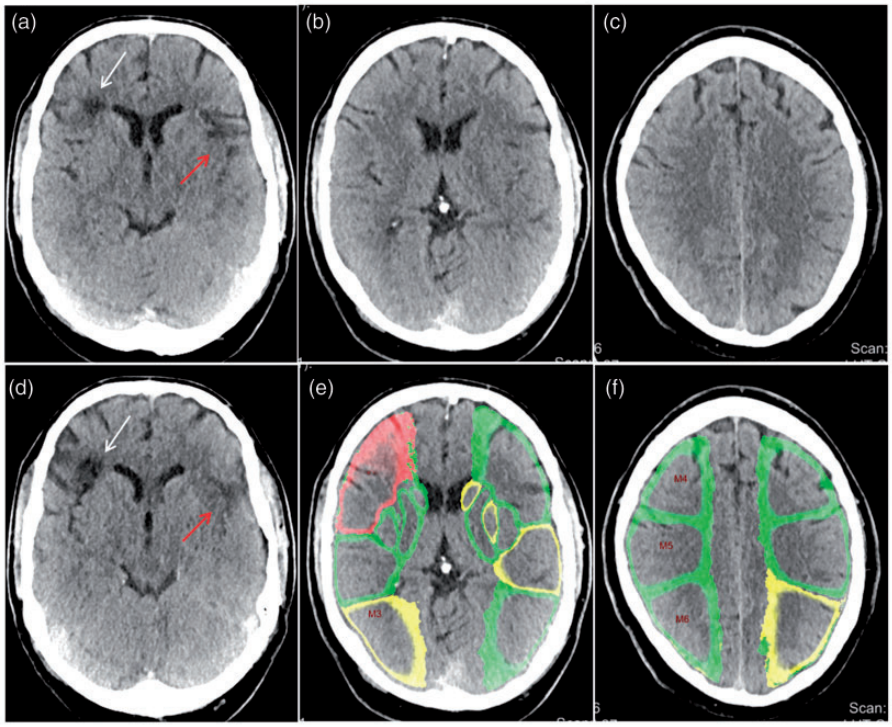

Fig. 1. Different ASPECT scoring by Frontier_ASPECTS and expert consensus reading in a 47-year-old man presenting with acute right hemiparesis due to distal left inner carotid artery occlusion. Frontier_ASPECTS (b, c, e, f) misinterpreted a small old right M1 infarction as acute ischemia (white arrows in (a) and (d); VOI marked red in (e)) and did not detect early ischemic changes in the left putamen, M2 region, and insular ribbon (red arrows in (a) and (d)).

ischemia (Frontier_2b, that means that false-positive Frontier_ASPECTS findings which were located contralateral to the current artery occlusion—known from CT angiography—were corrected/classified as being not acute ischemic by the radiologists), or for both (Frontier_3) were assessed.

Statistical analysis

For statistical analysis SPSS software package (version 24.0, IBM, Armonk, NY, USA) and MedCalc (version 12.3.0.0, MedCalc Software, Mariakerke, Belgium) were used. Testing for normal distribution was performed by D'Agostino–Pearson test. Normally distributed data are presented as mean ± standard deviation. Otherwise medians, interquartile ranges, and ranges are given. Comparison between the four score-based Frontier_ASPECTS variants, both senior radiologists, and the expert consensus reading was performed by intraclass correlation (IC) analysis. Assessment of score-based ASPECTS differences between Frontier_3, both senior radiologists, and the expert consensus reading was done by Bland–Altman analysis. Region-based ASPECTS comparison, in other words inter-rater agreement for all VOIs separately, between Frontier_3, both senior radiologists, and expert consensus reading was performed by IC analysis. A P value < 0.05 was considered statistically significant.

Results

Patients

One hundred patients were included (62 women, 38 men; median age = 74.5 years; interquartile range [IQR] = 11 years; age range = 30–95 years). In 21 of them, no exact time of symptom onset was known. In the remaining 79 patients, median time interval between symptom onset and stroke CT was 91 min (IQR = 39 min; range = 32–836 min). The median NIHSS at admission was 12 (range = 2–21). A total of 21 patients died within 14 days after stroke of stroke consequences or pre-existing severe concomitant diseases. The median post-thrombectomy NIHSS (on days 2–14 after thrombectomy) of the surviving patients was 4 (range = 0–21).

CT imaging and Frontier_ASPECTS

Slight motion artifacts (n = 9), hard-jet artifacts (n = 2), or skewed CT slices (n = 1) were found in a total of 12 brain CTs which were still sufficiently analyzable.

Thirty-two patients presented with pre-existing brain defects (e.g. old infarction, state after hemorrhage, or state after surgery) which did not impede current image reading by the radiologists. A hyperdense artery sign was found in 46 patients. CT angiography detected unilateral occlusion of the internal carotid artery in 31 patients, occlusion of the middle cerebral artery in 55 patients, and occlusion of major branches of the middle cerebral artery (M2 segment) in 14 patients.

All non-contrast brain CTs were post-processed without any problems by Frontier_ASPECTS (Figs. 1 and 2). Median ASPECTS was 9.5 for Frontier_1 (IQR = 0.5; range = 4–10), 10 for Frontier_2a, Frontier_2b, and Frontier_3 (in each case, IQR = 0.5; range = 5–10), 10 for one senior radiologist (IQR = 0.5; range = 4–10), 9 for the other senior radiologist (IQR = 1.5; range = 2–10), and 10 for expert consensus reading (IQR = 1.0; range = 2–10). Score-based IC analysis revealed a low correlation between all Frontier_ASPECTS variants and both the separate neuroradiologists and the expert consensus reading (Table 1). In contrast, both separate senior radiologists score-based ASPECTS readings correlated highly with each other and with consensus reading (Table 1). Consistent with this, Bland–Altman analysis showed worse agreement between Frontier_3 and expert consensus reading (mean ASPECTS difference = –0.9; standard deviation [SD] of mean ASPECTS difference = 1.79) than between both senior radiologists and expert consensus reading (radiologist 1: mean difference = –0.5; SD = 1.10; radiologist 2: mean difference = 0.2; SD = 0.64; Fig. 3). Region-based IC analysis revealed a low correlation between Frontier_3 and both the separate senior radiologists ASPECTS readings and the expert consensus reading (Table 2). Further analysis of the false-positive and false-negative findings of the fully automatic Frontier_ASPECTS reading (Frontier_1) revealed a slightly higher frequency of false-negative findings compared to false-positive findings. The possible

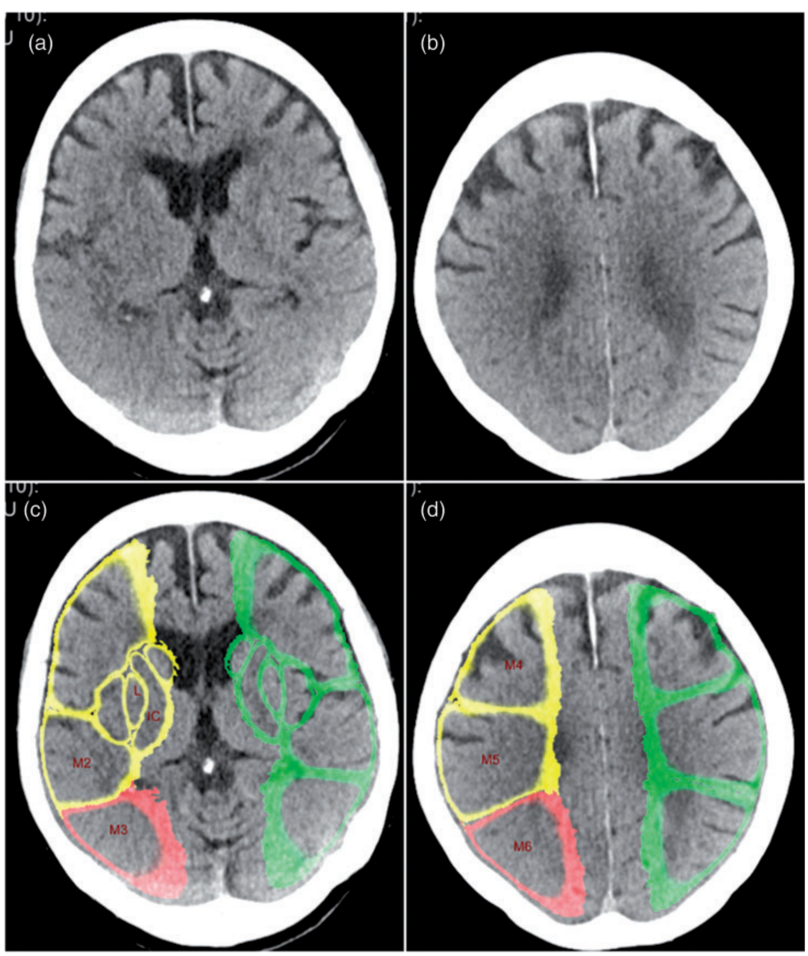

Fig. 2. (a–d) Excellent agreement in early ischemic change detection (in the right M3 and M6 region, marked in red) between Frontier_ASPECTS (c, d) and expert consensus reading in a 78-year-old woman with acute left hemiparesis due to right middle cerebral artery occlusion.

Table 1. Score-based agreement between all Frontier_ASPECTS variants, both senior radiologists, and expert consensus ASPECTS reading.

	Frontier_2a	Frontier_2b	Frontier_3	Reader 1	Reader 2	Consensus reading
Frontier_1	0.686* (0.566–0.777)	0.559* (0.408–0.680)	0.556* (0.405–0.678)	0.263† (0.071–0.436)	0.228‡ (0.034–0.406)	0.281† (0.090–0.452)
Frontier_2a		**0.803*** (0.721–0.863)	**0.825*** (0.751–0.879)	0.414* (0.237–0.564)	0.297† (0.108–0.466)	0.357* (0.174–0.517)
Frontier_2b			**0.980*** (0.970–0.987)	0.342* (0.157–0.504)	0.311† (0.123–0.477)	0.333* (0.147–0.496)
Frontier_3				0.358* (0.175–0.518)	0.313† (0.125–0.479)	0.350* (0.166–0.511)
Reader 1					**0.731*** (0.625–0.811)	**0.817*** (0.739–0.873)
Reader 2						**0.951*** (0.929–0.967)

Values are presented as ICC (95% CI). Figures in bold indicate a high ICC.
*$P < 0.001$.
†$P < 0.01$.
‡$P < 0.05$
ICC, intraclass correlation coefficient; CI, confidence interval.

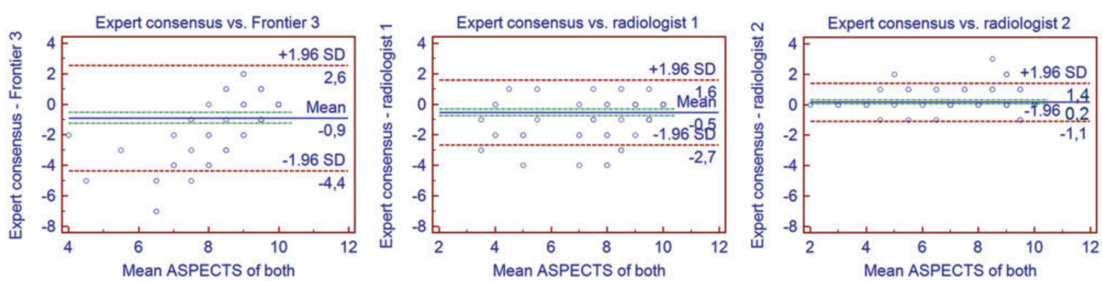

Fig. 3. In the Bland–Altman diagrams, the ASPECTS reading agreement between Frontier_3, both senior radiologists, and the expert consensus reading is illustrated.

Table 2. Region-based agreement between Frontier_3, both senior radiologists, and the expert consensus ASPECTS reading.

	Reader 1	Reader 2	Consensus reading
Frontier_3	0.327* (0.270–0.381)	0.258* (0.199–0.315)	0.287* (0.229–0.343)

Values are presented as ICC (95% CI). Figures in bold indicate a high ICC.
*$P < 0.001$.

reasons for false-positive and false-negative findings are given in Table 3.

Discussion

In this study we found only low agreement in ASPECT scoring in early stroke CT between the new post-processing tool Frontier_ASPECTS and expert consensus reading. Notably, the performance of Frontier_ASPECTS improved after simple manual corrections by the radiologists.

Table 3. Probable causes for false-positive and false-negative findings of the fully automated Frontier_ASPECTS reading (Frontier_1, including double counting).

False-positive findings (n = 31)	n	False-negative findings (n = 37)	n
Incorrect classification due to misinterpretation of old brain defects/atrophic brain regions	17	HU decrease did not reach the threshold (for being classified as ischemic/marked in red)	33
Unclear, partly probably due to misinterpreted leukoencephalopathy	12	Due to a contralateral false-positive finding, the corresponding ipsilateral VOI was classified as normal by Frontier_ASPECTS	6
Due to scanning artifacts	2		

Over the past years, therapy of acute stroke has gradually evolved and has become more aggressive with increased usage of both intravenous thrombolysis and endovascular revascularization (7). Imaging plays an important role not only in initial evaluation of stroke patients but also in appropriate therapy selection. According to the *Imaging Recommendations for Acute Stroke and Transient Ischemic Attack Patients* in potential candidates for endovascular recanalization, the following imaging options are feasible: combination of non-contrast brain CT and digital subtraction angiography; combination of non-contrast brain CT and CT angiography; or magnetic resonance imaging (MRI) including MR angiography (8). As only few centers have 24-h MR availability, the majority of patients currently initially receive a non-contrast brain CT. Here, besides the crucial exclusion of an intracranial hemorrhage, the infarct core visualization is of high relevance. In CT the latter stands for detection of early ischemic changes such as loss of gray-white differentiation, sulcal effacement, parenchymal hypoattenuation, and/or hyperdense artery sign (5,6). The early ischemic change detection was partially standardized by definition of the Alberta Stroke Program Early CT Score (2). Nevertheless, it remains challenging, which is demonstrated by varying inter-observer ASPECTS agreements reported in the literature (9). It is therefore desirable to increase objectivity and robustness of early ischemic change detection. To address this, the new-post processing tool Frontier_ASPECTS has been developed and was tested in daily clinical routine in the current study. Frontier_ASPECTS correctly detected regions with early ischemic changes in many of our patients. In particular, early ischemic changes of the caudate and lentiform nucleus, which are small and normally homogeneous regions, were detected well by Frontier_ASPECTS; however, the Frontier_ASPECTS software had apparently more difficulties in early ischemia change detection in the M1 to M6 region and, for example, in patients with pre-existing brain defects. Brain regions with old infarctions or atrophy were repeatedly misinterpreted by the software as regions with early ischemic changes although, according to the Frontier_ASPECTS user manual, dark voxels are excluded by the Frontier_ASPECTS algorithm (Fig. 1, Table 3). On the other hand, in several cases the density (HU) based Frontier_ASPECTS algorithm failed to detect regions with early ischemic changes, partly due to a contralateral false-positive finding with classification of the corresponding ipsilateral VOIs by Frontier_ASPECTS as normal, partly because the HU decrease did not reach the threshold for the classification of ischemia. Thus, the new Frontier_ASPECTS software prototype appears promising but is, at its current developmental state, inferior to senior neuroradiologists. At present, one cannot exclusively rely on the fully automated Frontier_ASPECTS results. In clinical routine, the Frontier_ASPECTS results must always be checked for plausibility and must be corrected for pre-existing brain defects, atrophy, or the side of vessel occlusion known from CT or MR angiography.

In 2015, Stoel et al. also developed an automated brain CT densitometry software for early ischemia detection (9). In contrast to our results, they reported that the agreement between their automated ASPECTS evaluation and their expert consensus ASPECTS evaluation was as good as the inter-observer agreement between two senior radiologists. This discrepancy between the studies of Stoel et al. and us is difficult to explain, as both ASPECTS software tools base one brain densitometry. One possible explanation is that the study cohort of Stoel et al. was far more homogeneous (consisting of patients with short onset-to-scan time interval and excluding patients with wake-up strokes) than our cohort and that their ASPECTS software was optimized on some patients of their cohort and subsequently evaluated on the residual cohort.

In 2016, Herweh et al. initially tested Brainomix, a fully automated e-ASPECTS software (Brainomix, Oxford, UK, www.brainomix.com) that uses a machine learning classifier trained on a large dataset to voxel-wise differentiate between early or non-acute ischemic changes (10). Investigating 34 stroke patients, they reported a similar performance of e-ASPECTS and of stroke experts. The findings of Herweh et al. were supported by a subsequent multicenter study involving 132 stroke patients in which e-ASPECTS was found non-inferior to ASPECTS reading by senior neuroradiologists (11). Furthermore, Pfaff et al. reported in 220 investigated stroke patients that the e-ASPECTS rating correlated with the functional patient outcome three months after endovascular revascularization and that IC between e-ASPECTS and experienced human raters was high (IC coefficients [ICC] = 0.72–0.76) (12). As we found only a low IC between Frontier_ASPECTS and expert consensus ASPECT scoring, it would be interesting to compare both post-processing tools directly, specifically as the underlying algorithm of both software tools differs with a machine learning classifier approach used by Brainomix and brain densitometry used by Frontier_ASPECTS.

Our study has some limitations. First, the Frontier_ASPECTS prototype was tested only against the readings of two senior radiologists (separately and in consensus). However, as no real gold standard for early ischemic change detection currently exists, expert consensus reading represents the current standard. Second, Frontier_ASPECTS was tested on purpose exclusively in acute stroke patients who had already been selected for thrombectomy. Of course, ASPECTS evaluation is usually meant to support clinicians in patient selection for endovascular recanalization; however, in reanalyzing brain CTs of patients with known acute middle cerebral artery ischemia, the rate of brain regions with early ischemic changes in the current study was not too low for a reasonable comparison. Third, we included both patients with pre-existing brain defects and patients whose brain CTs showed slight artifacts. Both conditions challenge Frontier_ASPECTS but as they are frequent in the clinical routine they were not excluded from the study. Last but not least, only insufficient data on clinical outcome (post-therapeutic NIHSS instead of modified Rankin Scale) were available, as most patients were quickly transferred to rehabilitation centers.

In conclusion, we found only low ASPECTS reading agreement between the post-processing software prototype Frontier_ASPECTS and expert consensus reading. Thus, at its current level of development, the post-processing software prototype Frontier_ASPECTS seems unhelpful for senior radiologists.

Declaration of conflicting interests

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