Improved Reliability of Automated ASPECTS Evaluation Using Iterative Model Reconstruction from Head CT Scans

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ABSTRACT

BACKGROUND AND PURPOSE: Iterative model reconstruction (IMR) has shown to improve computed tomography (CT) image quality compared to hybrid iterative reconstruction (HIR). Alberta Stroke Program Early CT Score (ASPECTS) assessment in early stroke is particularly dependent on high-image quality. Purpose of this study was to investigate the reliability of ASPECTS assessed by humans and software based on HIR and IMR, respectively.

METHODS: Forty-seven consecutive patients with acute anterior circulation large vessel occlusions (LVOs) and successful endovascular thrombectomy were included. ASPECTS was assessed by three neuroradiologists (one attending, two residents) and by automated software in noncontrast axial CT with HIR (iDose4; 5 mm) and IMR (5 and 0.9 mm). Two expert neuroradiologists determined consensus ASPECTS reading using all available image data including MRI. Agreement between four raters (three humans, one software) and consensus were compared using square-weighted kappa (κ).

RESULTS: Human raters achieved moderate to almost perfect agreement ($\kappa = .557$-$.845$) with consensus reading. The attending showed almost perfect agreement for 5 mm HIR ($\kappa_{HIR} = .845$), while residents had mostly substantial agreements without clear trends across reconstructions. Software had substantial to almost perfect agreement with consensus, increasing with IMR 5 and 0.9 mm slice thickness ($\kappa_{HIR} = .751$, $\kappa_{IMR} = .777$, and $\kappa_{IMR0.9} = .814$). Agreements inversely declined for these reconstructions for the attending ($\kappa_{HIR} = .845$, $\kappa_{IMR} = .763$, and $\kappa_{IMR0.9} = .681$).

CONCLUSIONS: Human and software rating showed good reliability of ASPECTS across different CT reconstructions. Human raters performed best with the reconstruction algorithms they had most experience with (HIR for the attending). Automated software benefits from higher resolution with better contrasts in IMR with 0.9 mm slice thickness.

Keywords: Cerebrovascular disease and stroke, computer-assisted image analysis, iterative image reconstruction, middle cerebral artery infarction, multidetector computed tomography.

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Introduction

Endovascular intervention has brought dramatic change to the therapy of acute ischemic stroke. One important aspect concerning the indication for endovascular treatment (EVT) is the evaluation of the degree of cerebral infarct demarcation, which is performed with the Alberta Stroke Program Early Computed Tomography Score (ASPECTS) for large vessel occlusions (LVOs) affecting the branches of the middle cerebral artery.[1] ASPECTS was originally developed to select patients eligible for thrombolytic treatment in hyperacute ischemic stroke.[2] Over the last 7 years, meta-analyses of randomized controlled trials have proven favorable outcome for stroke patients treated with EVT compared to thrombolytic treatment.[3–5] In several of those trials, ASPECTS prior to EVT was used as a criterion to exclude patients who were unlikely to attain clinical benefit from revascularization.[6–8] Thus, in recent guidelines, ASPECTS ≥ 6 is a requirement or criterion to select patients who should receive mechanical thrombectomy.[9,10] However, there are ongoing studies investigating whether patients with larger infarct cores–that is lower ASPECTS–can also benefit from thrombectomy.[11] Specifically, there is evidence that patients with low ASPECTS can benefit from thrombectomy due to a reduction in edema extent.[12] Furthermore, good clinical outcome after EVT in cases with low ASPECTS is associated with good collateral status.[13]

Recently, clinically validated machine learning algorithms became commercially available, which allow automated calculation of ASPECTS. In potential candidates for

thrombectomy, fully automated evaluation of ASPECTS by software more closely matched a consensus reference than human rater assessment.[14]

Over the last decade, iterative reconstruction (IR) algorithms have advanced CT technology and have largely replaced filtered back projection (FBP). IR can be subdivided into hybrid and model-based or fully iterative algorithms.[15] Compared with hybrid IR (HIR), iterative model reconstruction (IMR; a model-based IR [MBIR] algorithm) can further improve the signal-to-noise ratio (SNR), but requires more reconstruction time. Moreover, novel IR approaches have the potential to reduce radiation dose in CT. Specifically, in head CT among children, IMR–the algorithm used in this study–was able to significantly reduce the relative dose and increase image quality compared with FBP.[16] However, to our best knowledge, no prior study has investigated the impact of a MBIR algorithm on ASPECTS reading.

In this study, we aim to investigate the potential of a recently introduced CT image reconstruction technique (IMR) to improve reliability in a frequent clinical use case–that is selection of stroke patients eligible for EVT–that requires high accuracy, reliability, and promptness of evaluation. In order to ensure validity, we only included patients with follow-up MRI, which was considered the gold-standard technique to evaluate final infarct extent. We hypothesize that IMR is able to improve subjective and objective image quality and, thus, reliability of ASPECTS.

Methods

Ethics Approval

The present study was approved by the local institutional review board and was conducted in accordance with the Declaration of Helsinki. The requirement for informed consent was waived by the institutional review board due to the retrospective character of analysis.

Patients

All patients in a prospectively collected registry who underwent EVT in our institution between December 2018 and December 2019 were retrospectively reviewed. Inclusion criteria were proximal middle cerebral artery or distal internal carotid artery occlusion followed by immediate EVT with successful thrombectomy (modified thrombolysis in cerebral infarction [mTICI] 2b or better). Patients who did not have noncontrast CT with HIR and IMR prior to intervention or who did not receive follow-up MRI as part of the routine stroke workup in our institution were excluded (Fig 1). Following this algorithm, 47 patients were included in this study.

CT and MRI Acquisition

All patients were scanned on a 128-row multidetector CT scanner (Ingenuity Core 128; Philips Medical Systems) with 120 kVp tube voltage and 300 mAs current-time product using adaptive tube load. The stroke imaging protocol included noncontrast CT (incremental acquisition), CT angiography (spiral acquisition), and perfusion CT (10 mm, axial). The noncontrast CT was reconstructed using HIR (iDose 4; Philips Medical Systems, Best, The Netherlands) with 5 mm axial slice thickness and IMR (brain routine level 3; Philips Medical Systems, Best, The Netherlands) with 5 and 0.9 mm axial slice thickness, respectively. Follow-up imaging was performed in all patients on a 3-Tesla MRI scanner (Achieva dStream; Philips Medical Systems, Best, The Netherlands) 3-5 days following EVT. The MRI protocol included 3-dimensional fluid attenuated inversion recovery (FLAIR; repetition time [TR] = 4,800 milliseconds; echo time [TE] = 289 milliseconds; inversion time = 1,650 milliseconds) and diffusion tensor imaging (DTI; 15 directions; TR = 9,895 milliseconds; TE = 55 milliseconds; *b*-value = 1,000 seconds/mm^2) sequences.

Human ASPECTS Reading

ASPECTS is a semiquantitative score for early ischemic changes in noncontrast head CT; evaluating 10 predefined regions in the middle cerebral artery territory, it ranges from 0 to 10 points, with higher scores indicating a smaller infarct core.[2] To define reference ASPECTS, two board-certified neuroradiologists (with 10 and 17 years of experience in diagnostic radiology, respectively) independently reviewed all available imaging at the acute stage, including noncontrast CT, CT angiography, CT perfusion, digital subtraction angiography, and follow-up MRI. Expert neuroradiologists were blinded to the results of the automated software (see next section).

Reference ASPECTS was defined in consensus between both expert neuroradiologists by joint review and discussion if scores were diverging. Furthermore, one attending neuroradiologist with 10 years of experience and two residents each with 3 years of experience in ASPECTS rating independently evaluated ASPECTS in all patients for three different reconstruction protocols (HIR with 5 mm slice thickness and IMR with 0.9 and 5 mm slice thickness, respectively). These raters were blinded to any other imaging than noncontrast CT and additional clinical information, except for information on the side of suspected LVO. CT imaging for ASPECTS rating of each reconstruction was presented in random order to allow independent assessment.

Automated ASPECTS Reading

Fully automated ASPECTS rating was performed by RAPID ASPECTS (version 5; iSchemaView, Menlo Park, CA). The software calculates ASPECTS in a series of operations without any user interaction required (see Appendix E1 in Maegerlein et al[14]). Briefly, after normalization (standardization of image size, slice spacing, and removal of head rotation or tilt) nonrigid registration of an atlas outlining the 10 ASPECTS regions is performed. Then, a summary score is calculated based on statistical properties of the underlying voxels in each region and compared to corresponding regions in the opposite brain hemisphere. A random forest classifier uses a priori-derived knowledge to decide for each region if its intensity value distributions are considered affected or unaffected, that is, if a specific region shows demarcation or no demarcation. The software evaluated the same three CT image reconstructions as human raters. The side of automated ASPECTS evaluation was manually corrected in the software interface, if necessary. Of note, changing the side of evaluation did not require time-consuming reprocessing of the CT image; instead, the result was immediately displayed.

Statistical Analysis

Descriptive statistics were calculated as mean and standard deviation (SD) if variables were normally distributed or

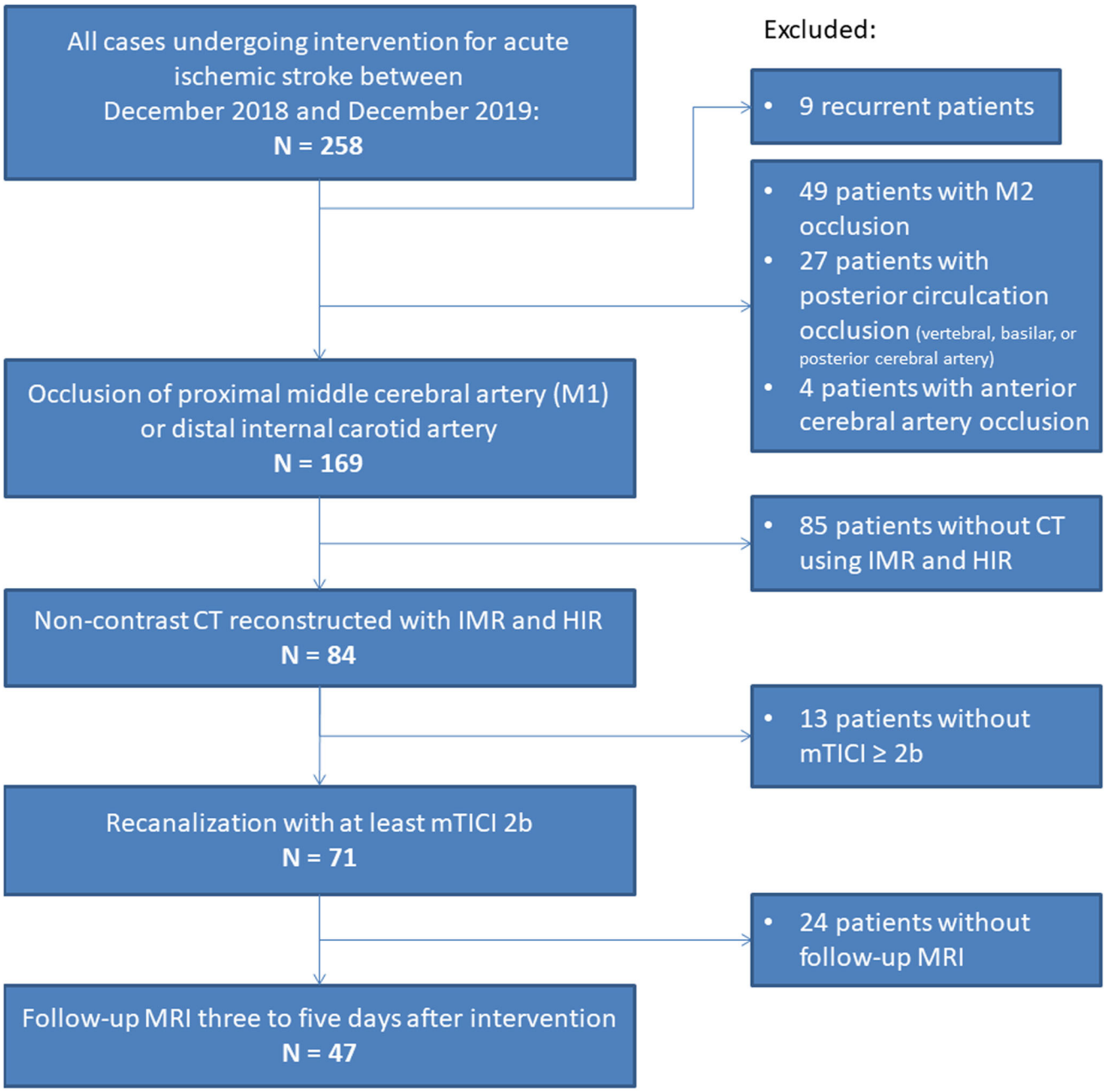

Fig 1. Patient selection algorithm.
Abbreviations: HIR, hybrid iterative reconstruction; IMR, iterative model reconstruction; M1 or M2, middle cerebral artery branch level 1 or branches level 2; mTICI, modified thrombolysis in cerebral infarction; *N*, number.

otherwise as median and interquartile range (IQR). The agreements of ASPECTS for three different CT reconstructions and between three human raters (attending and two residents), one software rater (RAPID), and expert consensus were compared using weighted kappa (κ). The degree of agreement between two raters was calculated using quadratic weights, that is the deviation of individual ratings is proportional to the square. Categories of agreement were defined based on κ values as almost perfect ($\kappa = .81$-1.00), substantial ($\kappa = .61$-$.80$), moderate ($\kappa = .41$-$.60$), and fair ($\kappa = .21$-$.40$).[17]

Weighted κ and 95% confidence intervals were computed in IBM SPSS Statistics (version 26; IBM Corp., Armonk, NY). Statistically significant differences at a level $P < .05$ between κ values were determined based on nonoverlap of 95% confidence intervals.

Results

Forty-seven patients (25 women) were included in this study with a mean age of 72.3 ± 13.4 years (Table 1). All patients were admitted to the hospital for acute ischemic stroke with symptoms of moderate severity (National Institute of Health Stroke Scale = 12 ± 6), and immediately underwent EVT with successful thrombectomy. Additionally, 19 patients were treated with intravenous thrombolysis (recombinant tissue plasminogen activator). The remaining 28 patients did not receive thrombolytic treatment due to contraindications (time

Table 1. Patient Characteristics

Characteristic	Result
Patients, *N*	47
Age, years	72.3 ± 13.4
Female sex, *N* (%)	25 (53%)
NIHSS	12 ± 6
Time from symptom onset to imaging, median (IQR), minutes	83 (58-151)
Treated with intravenous thrombolysis, *N* (%)	19 (40%)
Consensus ASPECTS, median (IQR)	8 (6-9)
$CTDI_{vol}$, mGy	46.5 ± 1.5
DLP, mGy × cm	685.2 ± 57.2

All the data represent mean ± standard deviation unless otherwise indicated
Abbreviations: $CTDI_{vol}$, computed tomography dose index; DLP, dose-length product; IQR, interquartile range; mGy, milliGray; *N*, number; NIHSS, National Institute of Health Stroke Scale.

Table 2. Square-Weighted κ Values and 95% Confidence Intervals for Interobserver Agreement of ASPECTS Between Consensus Reading and Four Raters for Three Different CT Reconstructions

Rater (Years of Experience)	HIR 5 mm, κ (95% CI)	IMR 5 mm, κ (95% CI)	IMR 0.9 mm, κ (95% CI)
Attending (10)	.845 (.758-.933)*	.763 (.661-.865)	.681 (.556-.807)
Resident 1 (3)	.701 (.572-.831)	.69 (.549-.832)	.734 (.616-.852)
Resident 2 (3)	.684 (.547-.820)	.557 (.376-.737)*	.692 (.553-.831)
Software	.751 (.605-.898)	.777 (.637-.916)[a]	.814 (.704-.925)

Abbreviations: 95% CI, 95% confidence interval; HIR, hybrid iterative reconstruction; IMR, iterative model reconstruction; κ, kappa.
[a] Software evaluation failed in one case.
*Statistically significant difference of agreements ($P < .05$).

window exceeded = 18; large infarct core [ASPECTS ≤ 5] = 3; anticoagulant treatment/recent operation = 6; malignoma = 1). Median time from symptom onset to CT imaging was 83 minutes (IQR 58-151 minutes). Radiation dose of noncontrast head CT was measured with a mean volumetric CT dose index ($CTDI_{vol}$) of 46.5 ± 1.5 mGy and dose-length product of 685.2 ± 57.2 mGy*cm. Consensus ASPECTS was skewed toward higher values with a median of 8 (IQR 6-9).

All raters, human and software, showed moderate to almost perfect agreement to consensus ASPECTS with $\kappa > .55$ for any CT reconstruction (Table 2). The attending showed almost perfect agreement with consensus for HIR 5 mm reconstructions ($\kappa_{HIR} = .845$), while IMR 5 and 0.9 mm reconstructions had substantial agreement ($\kappa_{IMR} = .763$ and $\kappa_{IMR0.9} = .681$). One resident (resident 1) presented consistent agreement with consensus across reconstructions and different slice thickness ($\kappa_{HIR} = .701$, $\kappa_{IMR} = .69$, and $\kappa_{IMR0.9} = .734$). The other resident (resident 2) showed more variability with only moderate agreement with consensus for IMR 5 mm reconstructions ($\kappa_{IMR} = .557$). Software evaluation of ASPECTS showed substantial agreement with consensus for 5 mm slice thickness ($\kappa_{HIR} = .751$ and $\kappa_{IMR} = .777$) and excelled for IMR 0.9 mm reconstructions ($\kappa_{IMR0.9} = .814$).

Comparing the agreement between human and software raters revealed that software showed always better numerical agreement with consensus than with any individual human rater for all CT reconstructions (Table 3). Moreover, the attending had almost perfect agreement with resident 1 ($\kappa > .8$) compared to substantial or moderate agreement with resident 2 for all reconstructions. For IMR 0.9 mm, human raters showed always better agreement amongst each other (almost perfect [$\kappa_{IMR0.9} > .8$] except for substantial agreement between attending and resident 2 [$\kappa_{IMR0.9} = .773$]) than with software (all substantial agreement [$\kappa_{IMR0.9} \leq .725$]).

Looking at statistically significant differences in agreements ($P < .05$), there was a significant difference in the agreement between consensus and attending for HIR 5 mm ($\kappa_{HIR} = .845$) and the agreement between consensus and resident 2 for IMR 5 mm ($\kappa_{IMR} = .557$). Furthermore, for IMR 5 mm, the agreement between attending and resident 1 ($\kappa_{IMR} = .838$) differed statistically significant from the agreement between any rater and resident 2 ($\kappa_{IMR} = .509$-$.557$).

Automatic evaluation by software succeeded in all cases, except for one CT with 5 mm IMR. The side of automated ASPECTS evaluation had to be manually corrected in 14 cases (three cases with HIR 5 mm, five cases with IMR 5 mm, and six cases with IMR 0.9 mm slice thickness), but all of these cases had ASPECTS ≥ 8 before or after the correction. Computation of automated ASPECTS was slightly faster for 5 mm slices (approximately 4 minutes and 30 seconds) than for 0.9 mm slices (approximately 5 minutes). Fig 2 shows results of automatic ASPECTS evaluation by software for the three different CT reconstructions in an example case of a 76-year-old man with right-side proximal middle cerebral artery occlusion.

Discussion

This study showed high reliability of ASPECTS compared to consensus reference and assessed by human and software raters in patients undergoing EVT for acute LVO. While the attending neuroradiologist showed almost perfect agreement of consensus with 5 mm HIR (ie, the reconstruction he had the most experience with), the automated software excelled with IMR at a slice thickness of 0.9 mm. The residents were able to assess ASPECTS without any marked exception in reliability across both reconstruction algorithms and with different slice thicknesses.

Of note, this study does not intend to evaluate ASPECTS as a selections criterion for EVT, but rather investigates it as a

Table 3. Cross-Table of Square-Weighted κ Values and 95% Confidence Intervals for Interobserver Agreement of ASPECTS Between Consensus Reading and Four Raters Stratified by CT Reconstruction

	Attending	Resident 1	Resident 2	Software
HIR 5 mm, κ (95% CI)				
Consensus	.845* (.758-.933)	.701 (.572-.831)	.684 (.547-.82)	.751 (.605-.898)
Attending	…	.878 (.814-.943)	.666 (.49-.841)	.691 (.528-.855)
Resident 1	…	…	.667 (.489-.844)	.648 (.5-.796)
Resident 2	…	…	…	.635 (.463-.807)
Software	…	…	…	…
IMR 5 mm κ (95% CI)				
Consensus	.763 (.661-.865)	.690 (.549-.832)	.557 (.376-.737)*	.777 (.637-.916)
Attending	…	.838 (.74-.936)*	.555 (.397-.713)*	.671 (.533-.81)
Resident 1	…	…	.521 (.368-.675)*	.669 (.535-.803)
Resident 2	…	…	…	.509 (.323-.696)*
Software	…	…	…	…
IMR 0.9 mm, κ (95% CI)				
Consensus	.681 (.556-.807)	.734 (.616-.852)	.692 (.553-.831)	.814 (.704-.925)
Attending	…	.841 (.74-.942)	.773 (.651-.896)	.602 (.461-.743)
Resident 1	…	…	.815 (.72-.91)	.725 (.601-.849)
Resident 2	…	…	…	.645 (.458-.833)
Software	…	…	…	…

Abbreviations: 95% CI, 95% confidence interval; HIR, hybrid iterative reconstruction; IMR, iterative model reconstruction; κ, kappa; …, pairwise recurrent κ values are not shown for better readability.
*Statistically significant difference of agreements ($P < .05$).

use case, where high image quality is of major impact. We hypothesized that IMR is able to improve subjective and objective image quality and, thus, reliability. MBIR algorithms (ie, IMR by Philips Healthcare, Veo MBIR by GE Healthcare, and advanced modeled IR [ADMIRE] by Siemens Healthineers) have been designed to improve image quality and reduce radiation dose for CT exams. In this study, image quality was assessed by the performance of ASPECTS rating, both by humans and by an automated algorithm. IMR was introduced into clinical routine in our department 1 year before the study-specific readings were performed. Thus, the expert neuroradiologist with 10 years of experience was trained and gained the most experience with CT reconstructions other than IMR, whereas the residents were equally familiar with both reconstruction algorithms investigated in this study. Therefore, the attending's performance might be explained by the level of experience he had in detecting subtle hypoattenuation in CT images reconstructed with a certain algorithm.[18,19] This is in line with a previous study, wherein a neurology consultant (8 years of experience), who presumably received his training exclusively with FBP, showed the best correlation of ASPECTS rating with expert ground-truth for FBP compared to HIR.[20] Training seems essential to perceive subtle changes of attenuation in noncontrast CT, as summarized in a previous literature review.[18] Presumably, radiologists' training and experience have a higher impact on reliability than subtle improvements in image quality due to different CT reconstruction algorithms.

Correct ASPECTS reading is dependent on correct identification of ASPECTS regions. The score was originally developed based on 10 mm axial scans.[2] It can be difficult for humans to correctly interpolate these regions to 0.9 mm axial slices. Depending on training, this might explain part of the inferior performance with 0.9 mm IMR slices for the attending neuroradiologist compared to 5 mm slice reconstructions. Software for automated ASPECTS evaluation has to normalize images before comparing brain regions (Appendix E1 in Maegerlein et al[14]). Therefore, high-resolution input data consisting of thin axial slices are favorable and reduce interpolation errors during normalization. These technical considerations are likely to explain in part, why automated ASPECTS software performed best with 1 mm axial slices for predicting baseline stroke severity and clinical outcome after 90 days.[21]

Of note, software ASPECTS evaluation succeeded in all cases except for one reconstruction of 5 mm slice thickness using IMR (99% success rate). This constitutes a considerable improvement in software robustness compared to an earlier study (using software version 4.9), which reported 32 failed cases in 226 cases analyzed (86% success rate).[14] Other studies showed good agreement of total ASPECTS between automated software and human readers, but found higher variance in region-specific agreement.[22,23]

To eliminate the human factor, we also assessed how IMR impacts objective image quality using automated software as a quantitative benchmark. Interestingly, the agreement of software rating could be improved by using IMR with a slice thickness of 0.9 mm. It is understood that IMR can further reduce noise levels and improve image contrasts at a given dose level and slice thickness compared to HIR.[15] Reducing slice thickness increases spatial resolution, but decreases the in-plane SNR. Thus, it should become more difficult to perceive subtle hypoattenuations for human readers, but performance can be biased by the aforementioned training and interpolation effects. Software can provide a bias-free benchmark as to what extent differences in CT attenuation are still distinguishable. The SNR in 0.9 mm IMR is obviously sufficient to benefit of higher resolution compared to 5 mm slices.

A limitation of this study is the small sample size and limited number of raters. Therefore, the conclusion that training influences the rating performance may not necessarily be generalizable. Upcoming studies in larger cohorts may confirm our present findings. Furthermore, we did not incorporate dose reductions into the routine CT acquisition protocol, although

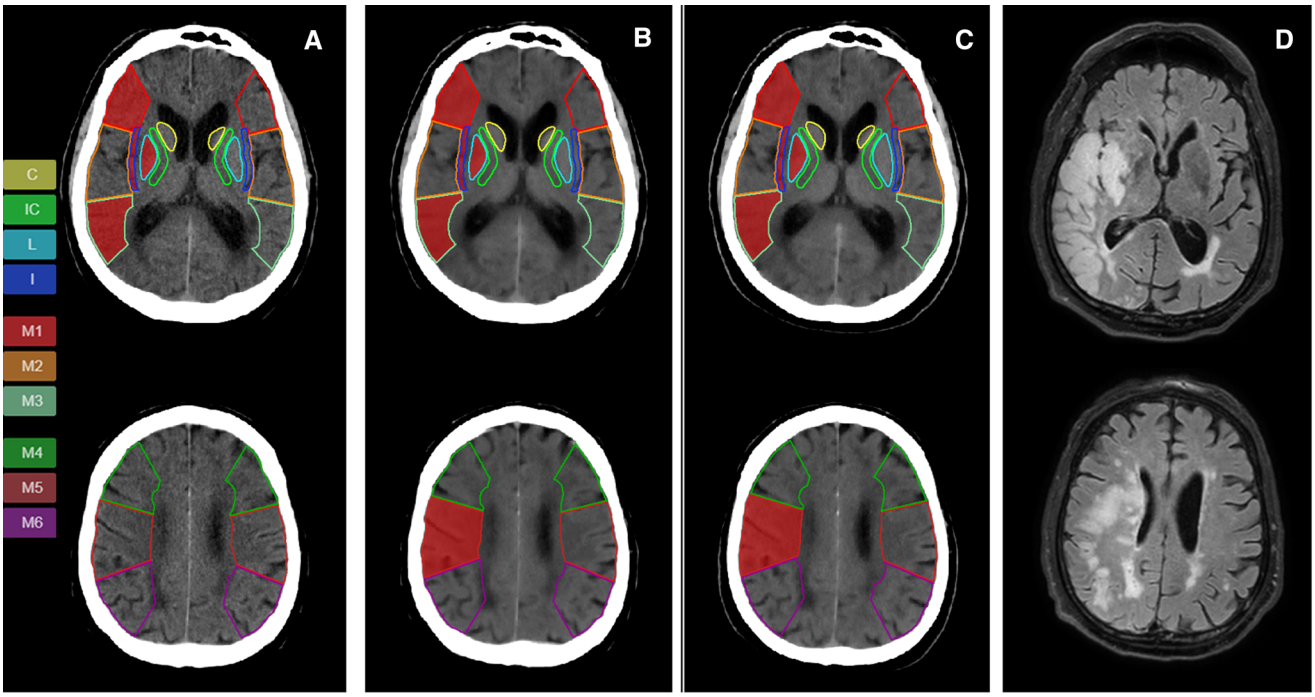

Fig 2. Case of a 76-year-old man with right-side proximal middle cerebral artery occlusion.
Automated ASPECTS was calculated by software (RAPID; iSchemaView, Menlo Park, CA) using axial CT images with HIR 5 mm, IMR 5 mm, and IMR 0.9 mm (A, B, and C). Follow-up MRI was performed after successful endovascular thrombectomy with mTICI = 3 (D). Red overlays are displayed on the ASPECTS regions in axial CT images for which software detected early infarct signs. In brief, the software compares mean Hounsfield units in the region on the side with large vessel occlusion with the same region on the non-occluded side. To compute ASPECTS, 1 point is subtracted from 10 for any signs of early ischemic change in each of 10 defined middle cerebral artery vascular regions. Using 5 mm HIR, automatically calculated ASPECTS was 6, while the attending scored 6, the first resident 5, and the second resident 7 (A). Using 5 mm IMR, automatically calculated ASPECTS was 5, while the attending scored 5, the first resident 4, and the second resident 4 (B). Using 0.9 mm IMR, automatically calculated ASPECTS was 5, while the attending scored 4, the first resident 4, and the second resident 3 (C). Using axial fluid-attenuated inversion recovery MR images, reference ASPECTS of 5 was determined in consensus reading (D). Of note, final infarct demarcation extends clearly to the M2 region that was not identified in prior CT images.
Abbreviations: C, caudate head; I, insula; IC, internal capsule; L, lentiform nucleus; M1, frontal operculum; M2, anterior temporal lobe; M3, posterior temporal lobe; M4, anterior middle cerebral artery territory (MCA); M5, lateral MCA; M6, posterior MCA; mTICI, modified thrombolysis in cerebral infarction.

hybrid and MBIR algorithms have previously shown potential for dose reductions in head CT.[16,24–27] This lack in technically revised data acquisitions is not only due to the retrospective character of this study, but also because of ethical considerations. Correct ASPECTS rating has far-reaching consequences and outweigh radiation protection in the acute emergency setting. Virtual dose reduction can solve this problem, as shown for CT angiography.[28] Unfortunately, simulations of tube current reduction were not feasible for incremental acquisition of head CT as performed in this study. The United States national diagnostic reference level for adult head CT exams is $CTDI_{vol} = 56$ mGy.[29] The applied doses in this study lie well below these levels with a mean $CTDI_{vol} = 46.2 \pm 1.5$ mGy. However, with the results of previous research cited above and of this study, considerable dose reductions seem feasible.

In conclusion, this study suggests that training has a greater influence on agreement of human ASPECTS ratings than improved image contrast as delivered by IMR in standard-dose head CT. Furthermore, software ASPECTS reading can serve as a benchmark for dose reductions in noncontrast head CT. The potential of dose reductions using IMR has been indicated here, but requires further study of actual or virtual dose reductions.

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