Comparison of automated ASPECTS, large vessel occlusion detection and CTP analysis provided by Brainomix and RapidAI in patients with suspected ischaemic stroke

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Objectives: The ischaemic core and penumbra volumes derived from CTP aid the selection of patients with an arterial occlusion for mechanical thrombectomy. Different post-processing software packages may give different CTP outputs, potentially causing variable patient selection for mechanical thrombectomy. The study aims were, firstly, to assess the correlation in CTP outputs from software packages provided by Brainomix and RapidAI. Secondly, the correlation between automated ASPECTS and neuroradiologist-derived ASPECTS and accuracy in detecting large vessel occlusion was assessed. *Materials and Methods:* This retrospective study included patients undergoing CTP for suspected anterior circulation large vessel occlusion. Pearson's correlation coefficient was used for testing the correlation in CTP outputs, ASPECTS/automated ASPECTS, and—in those with complete or near complete occlusion—final infarct volume. Diagnostic statistics were calculated for large vessel occlusion detection. *Results:* Correlation was high for ischaemic core and penumbra volumes (0.862 and 0.832, respectively) but lower for the mismatch ratio (0.477). Agreement in mechanical thrombectomy eligibility was achieved in 85% of cases (46/54). Correlation between ischaemic core and final infarct volume was higher for Brainomix (0.757) than for RapidAI (0.595). The correlation between ASPECTS and automated ASPECTS (0.738 and 0.659) and the accuracy of detecting large vessel occlusion (77% and 71%) was higher for Brainomix than for RapidAI. *Conclusion:* There was high correlation between the CTP output from Brainomix and RapidAI. However, there was a difference in MT eligibility in 15% of cases, which highlights that the decision regarding MT should not be based on imaging parameters alone.

Key Words: Large vessel occlusion—mechanical thrombectomy—CT perfusion—AI

Abbreviations: FIV, final infarct volume; ICC, interclass correlation coefficient; LVO, large vessel occlusion

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Introduction

CT Perfusion (CTP) imaging of the brain provides physiological and hemodynamic information that is not available on unenhanced CT or single-phase CT angiography. CTP can be used to identify patients with penumbral "tissue at risk" within the territory of an occluded vessel who may benefit from recanalization therapy. Furthermore, the ischaemic core volume estimates derived from CTP predict clinical outcomes following acute stroke including long-term disability[1] and haemorrhagic transformation.[2] Therefore, CTP is used to triage patients for mechanical thrombectomy (MT) who fall under 'extended criteria' where the time from symptom onset to presentation is between 6 and 24 hours or unknown.

Post-processing and analysis of CTP data allows the passage of contrast medium through brain tissue to be characterized by parametric maps of the cerebral blood flow (CBF), cerebral blood volume (CBV), mean transit time (MTT) and time to maximum (Tmax). By applying thresholds to these parametric maps, estimates can be made for the volume of severely ischaemic tissue (ischaemic core) and tissue at risk of infarction but potentially salvageable (penumbra). The thresholds for CTP parameters have been derived from multiple randomized controlled trials that included patients with an ICA or M1 middle cerebral artery occlusion and an Alberta stroke programme early CT score (ASPECTS) of greater than 5.[3–5] The volume of the ischaemic core and penumbra were based on a CBF of less than 30% of the contralateral side and a Tmax greater than 6 seconds, respectively. Eligibility for MT required an ischaemic core of less than 70 ml, a mismatch ratio of 1.8, and a mismatch volume of greater than 15 ml. However, the parameters that best estimate core and penumbra volumes are known to vary with clinical and physiological factors (such as grey or white matter involvement[6] and time from vessel occlusion[7]) and the software package used for CTP analysis.[8–10]

The estimates of the ischaemic core and penumbra may differ between software packages due to differences in the selection of arterial input and venous outflow functions, determination of bolus timing, brain segmentation, movement correction, and smoothing algorithms. These differences could cause variable patient selection for MT.

If eligibility criteria are to be consistently applied in hospitals with software packages other than RapidAI, a direct comparison of the output is vital. There have been no prior studies comparing the estimates of the ischaemic core and penumbra volumes derived by software packages from RapidAI and Brainomix. The primary objective of this study was to compare the volume outputs of Brainomix and RapidAI CT automated analysis in a cohort of patients with a suspected large vessel occlusion (LVO) who were potential candidates for MT. Secondary objectives of this study were to assess the accuracy of automated ASPECTS on non-contrast CT (NCCT) and the accuracy in the detection of large vessel occlusion on CTA.

Methods

The study was approved by the Research Ethics Committee.

Cohort

In this single-centre retrospective study, the cohort included all patients with either a suspected or confirmed anterior circulation LVO who underwent a CTP study at Imperial College NHS Healthcare Trust between 1 January 2016 and 31 December 2020. CTP was performed where there was a delayed presentation (generally >6 hours and <24 hours from symptom onset) or when the time of symptom onset was unknown. Patients were identified by searching PACS for all CTP studies that were performed in the context of an acute stroke. Patients were excluded if they underwent a CTP study for reasons other than a suspected or confirmed stroke.

ASPECTS and the presence of a large vessel occlusion were determined for all patients with a NCCT and a CTA, respectively. The CTP ischaemic core and penumbra volumes were only included for patients with a confirmed LVO.

Image analysis

ASPECTS was determined on NCCT and the presence of LVO on CTA by a neuroradiologist with 4 years' experience. ASPECTS was determined as described previously.[11] Images were reviewed with all available clinical and imaging data.

Cases of excessive movement during CTP acquisition were excluded. Cases were excluded from the volumetric analysis where the incorrect Arterial Input Function or Venous Outflow Function were identified.

Software

Access to RapidAI (iSchemaView Inc., Menlo Park, CA, USA) was provided as part of routine clinical care. Brainomix (Brainomix Ltd, Oxford, UK) was accessed via a webserver onto which anonymized DICOM images were uploaded.

Both software packages are fully automated with no requirement for user input. The ischaemic core was defined as the region with a CBF less than 30% of the contralateral side. The penumbra was defined as the region with a Tmax greater than 6 s and not already included in the ischaemic core region. The mismatch ratio was defined as the perfusion deficit (Tmax >6 s) volume divided by the core volume (rCBV <30%).

Scanning protocol

Imaging was acquired on a Siemens Somatom Definition AS 128 Slice Scanner. Scan parameters were: brain coverage of 6 cm, 15 slices, reconstructed image thickness of 10 mm, pitch of 0.55, tube voltage of 120 kV, tube current as per automatic exposure control, matrix dimensions of 512×512; temporal resolution of 1.1 s, and total scan time of 40 s. 60 ml of iohexol solution (Omnipaque 350^{TM}) was injected at 4 ml/s.

Final infarct volume

The final infarct volume (FIV) was calculated using follow-up imaging in patients who had complete or near complete recanalization (modified treatment in cerebral ischaemia [mTICI] score of 2C or 3). Final infarct volume was determined on MRI with diffusion weighted imaging (DWI) within 48 hours. If MRI was unavailable, NCCT performed between 48 hours and 1 week was used. The infarct was segmented by a neuroradiologist (DHM) using ITK-snap.

Statistical analysis

All statistics were calculated using the statsmodels package in Python (version 3.9). Continuous data are presented as a median (IQR) unless otherwise stated and compared using the Mann-Whitney-U test.

Categorical variables were compared using the Fisher's exact test. The Wilcoxon test was used to determine differences in paired volume measurements from each software package. The correlation in ASPECTS and automated ASPECTS was determined using the weighted Cohen's kappa and Pearson's coefficient. The correlation between continuous variables, including ischaemic core, penumbra, and final infarct volumes, was assessed using Pearson's coefficient. To limit the effects of very large numbers, mismatch ratios were censored to a maximum of 10. Agreement in eligibility for MT based on imaging parameters was made using the Cohen's Kappa. The level of agreement was determined by the Kappa value (0.00−0.20 slight agreement, 0.21−0.40 fair agreement, 0.41−0.60 moderate agreement, 0.61−0.80 substantial agreement, 0.81−1.0 almost perfect agreement).[12]

A P value of <0.05 was considered statistically significant.

Results

A total of 90 patients had a CTP study for suspected stroke during the study period, of which 64 (66.7%) had an LVO identified on CTA. There were 62 occlusions within the anterior circulation (ICA or MCA) and 2 were in the basilar artery. Of the 32 patients who were deemed eligible (based on all clinical and imaging criteria) who underwent mechanical thrombectomy, complete or near complete reperfusion was achieved in 12 (37.5%). Clinical and demographic data are shown in Table 1.

Table 1. *Table showing the demographics and clinical detail on patients with a large vessel occlusion.*

Sex (M:F)	30:32
Age	70.5 (58 − 80)
NIHSS	15 (8 − 19)
Hours from symptom onset to imaging[†]	5.8 (2.5 − 9.1)
'Wake up' or unknown onset	21 (34.4%)
LVO	62
ICA	14 (22.6%)
M1 MCA	25 (40.3%)
M2 MCA	23 (37.1%)
Intravenous thrombolysis	15 (24.1%)
Thrombectomy	32 (51.6%)
0	5 (15.6%)
1	2 (6.3%)
2A	3 (9.4%)
2B	10 (31.1%)
2C	6 (18.8%)
3	6 (18.8%)

[†]Excluding 'wake up' strokes where time of onset was unknown.

Automated ASPECTS

In 10/90 (11.1%) and 15/90 (16.7%) cases, there was no automated ASPECTS available for Brainomix and RapidAI, respectively (P=0.389). RapidAI tended to overestimate the size of the infarct giving lower scores (6 [5 − 8]) than Brainomix (7 [6 − 8]) and the neuroradiologist (8 [7 − 9]) (Figure 1). There was good agreement between the neuroradiologist-derived ASPECTS and both automated ASPECTS although agreement was higher for Brainomix (κ=0.448) than for RapidAI (κ=0.365).

Large vessel occlusion

From the total cohort of 90 patients, a CTA was available for 85 patients. The algorithm failed to give an output for 2 cases (2.4%) and 1 case (1.2%) for Brainomix and RapidAI, respectively (P=0.622).

Brainomix had a higher accuracy than RapidAI in the detection of all LVOs (ICA, M1 and M2) considered together (77% vs. 71%, P=0.480) and for M1 LVOs only (94% vs. 83%, P=0.062) (Figure 2), although the differences were not statistically significant. In the detection of M1 LVOs, Brainomix has a higher specificity than RapidAI (97% vs. 77%, P=0.028).

Of the cases with a large vessel occlusion, CTA revealed a severe stenosis (>90%) within the contralateral ICA in 4 (6%) and a tandem occlusion (intracranial and proximal ICA occlusion) in 8 (13%).

CT Perfusion

Brainomix and RapidAI failed to give an output in 5 (7.8%) and 8 (12.5%) cases, respectively (P=0.563). In three cases where RapidAI failed to give an output, the circle of

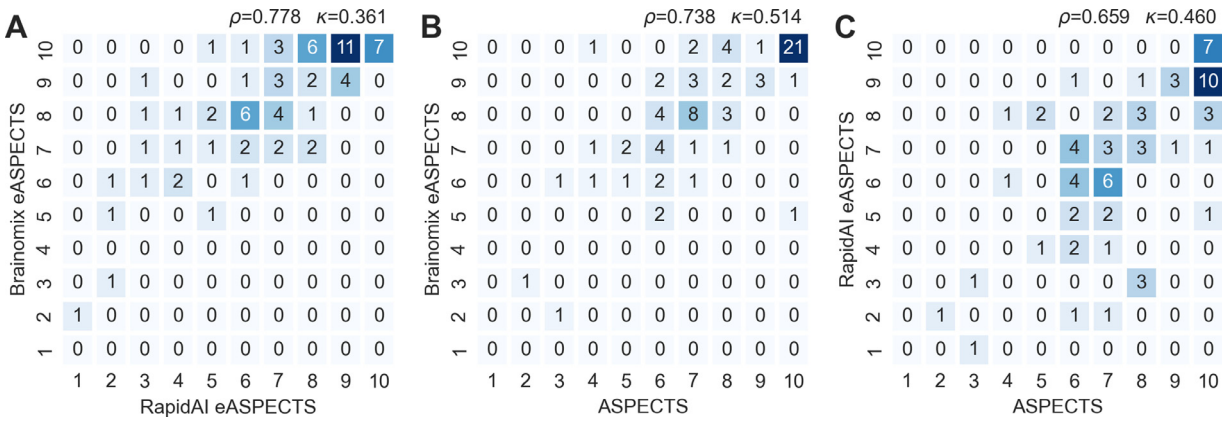

Figure 1. *Heatmap showing comparison of different ASPECTS scores. Equal ASPECTS scores appear along the diagonal. The heatmaps show agreement between Brainomix and RapidAI ASPECTS (A), Brainomix ASPECTS and ASPECTS (B), and RapidAI and ASPECTS (C). While Brainomix ASPECTS and RapidAI ASPECTS were strongly correlated with one another (ρ=0.778), Brainomix had the strongest agreement with ASPECTS (ρ=0.738 versus ρ=0.659). The median RapidAI ASPECTS was lower than Brainomix ASPECTS.*

A

Brainomix		Ground truth: LVO	Ground truth: No LVO	
				PPV
LVO		True positive 42	False positive 1	98%
No LVO		False negative 18	True negative 22	NPV 55%
		Sens. 70%	Spec. 96%	Acc. 77%

B

RapidAI		Ground truth: LVO	Ground truth: No LVO	
				PPV
LVO		True positive 45	False positive 8	85%
No LVO		False negative 16	True negative 15	NPV 48%
		Sens. 74%	Spec. 65%	Acc. 71%

C

Brainomix		Ground truth: M1 LVO	Ground truth: No M1 LVO	
				PPV
M1 LVO		True positive 33	False positive 1	97%
No M1 LVO		False negative 3	True negative 31	NPV 92%
		Sens. 92%	Spec. 97%	Acc. 94%

D

RapidAI		Ground truth: M1 LVO	Ground truth: No M1 LVO	
				PPV
M1 LVO		True positive 33	False positive 8	80%
No M1 LVO		False negative 4	True negative 27	NPV 87%
		Sens. 89%	Spec. 77%	Acc. 83%

Figure 2. *Confusion matrix with diagnostic statistics for Brainomix and RapidAI for LVO of all sizes (ICA, M1 and M2) (A) and for M1 LVO (B). For all LVOs considered together and for M1 occlusions only, Brainomix had a higher accuracy than RapidAI.*

Table 2. *Table showing the volumetric output from the analysis from Brainomix and RapidAI.*

	RapidAI	Brainomix	P value
Core (ml)	22.0 (4.0 – 39.3)	13.0 (5.0 – 24.0)	0.458
Penumbra (ml)	49.0 (27.0 – 79.0)	59.0 (31.0 – 86.5)	0.535
Mismatch Ratio	3.7 (2.2 – 6.7)	5.3 (4.1 – 8.4)	0.005

Willis was not included in the CTP study. In three cases where both Brainomix and RapidAI failed to give an output, there was poor contrast opacification (related to either poor cardiac output or contrast extravasation).

When compared to Brainomix, RapidAI gave a larger median ischaemic core volume (22 ml vs. 13 ml, P=0.458), a smaller penumbra volume (49 ml vs. 59 ml, P=0.535) and a lower mismatch ratio (3.7 vs. 5.3, P=0.005) (Table 2). There was strong positive linear correlation between the volumes derived from each software package (Figure 3). Scatterplots showing the correlation between volumes for ICA, M1 MCA and M2 MCA separately are shown in Supplementary Figure 1, Supplementary Figure 1 and Supplementary Figure 3.

Based solely on CTP parameters, there was agreement in eligibility for MT between software packages in 46 out of the 54 cases where outputs were available (85%) giving a weighted Cohen's Kappa of 0.647 (Figure 4). Table 3 shows CTP parameters of the 8 cases where there was disagreement in MT eligibility between Brainomix and RapidAI.

Final infarct volume

The final infarct volume (FIV) was calculated in a subset of 12 patients where complete or near complete recanalization (mTICI 2C/3) was achieved following MT. FIV was calculated using DWI within 48 hours for 5 patients (42%) and CT for 7 patients (58%). The median infarct volume was 40.5 ml (14.8 – 78.1), which was larger than the ischaemic core estimates from both Brainomix and RapidAI (P<0.001). The correlation with final infarct volume was higher for Brainomix (ρ=0.757) than for RapidAI (ρ=0.595) (Figure 5).

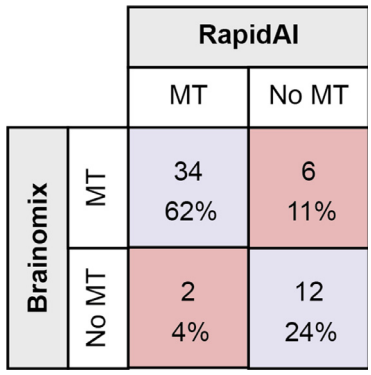

Figure 4. *Confusion matrix showing the association between mechanical thrombectomy eligibility based on CTP parameters derived from Brainomix and RapidAI. Cohen's Kappa was 0.647, indicating a high level of agreement.*

Discussion

CTP is used to select patients with an LVO for MT who present late or at an unknown time after symptoms onset. Multiple vendors offer automated operator-independent analysis of CTP. Used in trials for extended criteria thrombectomy[4], RapidAI is the most established software for the post-processing of CTP in patients with an LVO. For centres using software other than RapidAI, it is important that the outputs of the CTP analysis are comparable so that MT eligibility criteria are applied consistently.

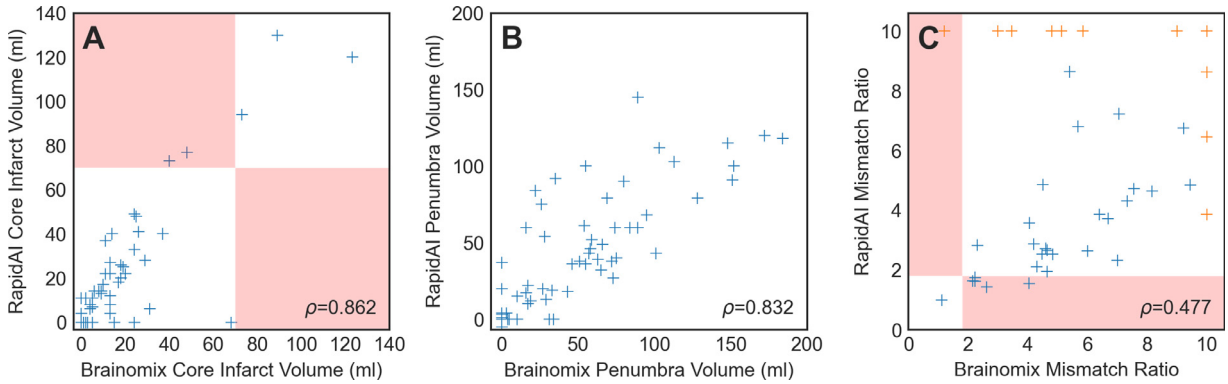

Figure 3. *Scatter plot showing the correlation between the ischaemic core (A), penumbra (B) and mismatch ratio (C) given by Brainomix and RapidAI. There is strong correlation between the ischaemic core and penumbra, which, as expected, is reduced when the ratio between these two values is taken to give a mismatch ratio. Mismatch ratios that were capped at 10 are displayed in orange.*

Table 3. *Table showing the 8 cases where there was disagreement in mechanical thrombectomy eligibility CTP parameters between Brainomix and RapidAI. Values that do not meet criteria are highlighted in bold.*

Age	NIHSS	ASPECTS	M1/M2 LVO	TICI	Brainomix				RapidAI				
					Core	Perfusion deficit†	Penumbra	Mismatch Ratio	MT criteria met	Core	Perfusion deficit†	Penumbra	Mismatch Ratio	MT criteria met
29	-	7	1	-	48	232	184	4.83	+	**77**	195	118	2.53	-
45	22	7	2	-	13	29	16	2.23	+	27	44	17	**1.63**	-
46	17	6	1	-	40	105	65	2.63	+	**73**	105	32	**1.44**	-
56	6	6	2	-	5	24	19	4.8	+	0	12	**12**	∞	-
59	-	6	1	-	24	97	73	4.04	+	49	76	27	**1.55**	-
98	17	8	2	0	2	31	29	15.5	+	0	13	**13**	∞	-
76	11	10	1	2C	0	0	**0**	∞	-	0	37	37	∞	+
80	20	8	1	3	0	0	**0**	∞	-	0	20	20	∞	+

†Perfusion deficit defined as Tmax > 6s.

ASPECTS and LVO

In our patient cohort, the correlation with the neuroradiologist-derived ASPECTS was higher for the Brainomix-derived ASPECTS than for the RapidAI-derived ASPECTS. The precise detail of the algorithms is not disclosed. However, based on visual inspection of the ASPECTS output, we note that the automated segmentation of RapidAI was less accurate than Brainomix, which is likely to contribute to inaccurate automated ASPECTS calculation. This finding is consistent with a prior report of 131 NCCTs that showed a high ICC for Brainomix than for RapidAI (0.871 vs. 0.777).[13]

Brainomix achieved a higher accuracy than RapidAI in detecting LVOs. It should be noted that both software packages still missed LVOs particularly within the terminal ICA and M2 MCA. Therefore, as stated by RapidAI and Brainomix, they should be used as clinical decision support tools to augment, rather than replace, the assessment by a neuroradiologist.

CTP

The main finding in this study is that there is strong correlation between the estimates of the volume of the ischaemic core and penumbra that were derived by Brainomix and RapidAI (ρ=0.862 and ρ=0.832 respectively). Similarly, there is high agreement (85%) in eligibility for MT based on the values derived from each software package with a Cohen's Kappa of 0.65, which indicates 'substantial agreement'. In most cases where there was disagreement, the values straddled the criteria cut-offs.

To our knowledge, this is the first report of a direct comparison in the CTP analysis between Brainomix and RapidAI. A strong correlation between the values derived from different software packages has been reported before. For example, Cai *et al* showed very high agreement with RapidAI and imStroke (YueXi MedicalTech, Nanjing, China) for both core and penumbra estimates (interclass correlation coefficient [ICC] >0.98).[14] Bathla *et al* showed correlation in CTP ischaemic core volume derived from Syngo.via (Siemens Healthineers, Erlangen, Germany) and RapidAI as an ICC of 0.94 and 0.79 in a cohort that did or did not undergo mechanical thrombectomy respectively (a pooled value was not provided). Importantly, the recommendation to proceed to thrombectomy was concordant in 60/62 cases (97%).[15]

Both software packages failed to give an output at a similar rate (7.8—12.5%). In three cases, RapidAI did not give an output due to suboptimal positioning of the imaged slab, which was above the level of the circle of Willis. In a patient group where artefacts caused by movement are common, a balance must be met between giving some clinical information that may be imperfect with the risks of providing erroneous and potentially misleading values. In cases where automated processing has failed,

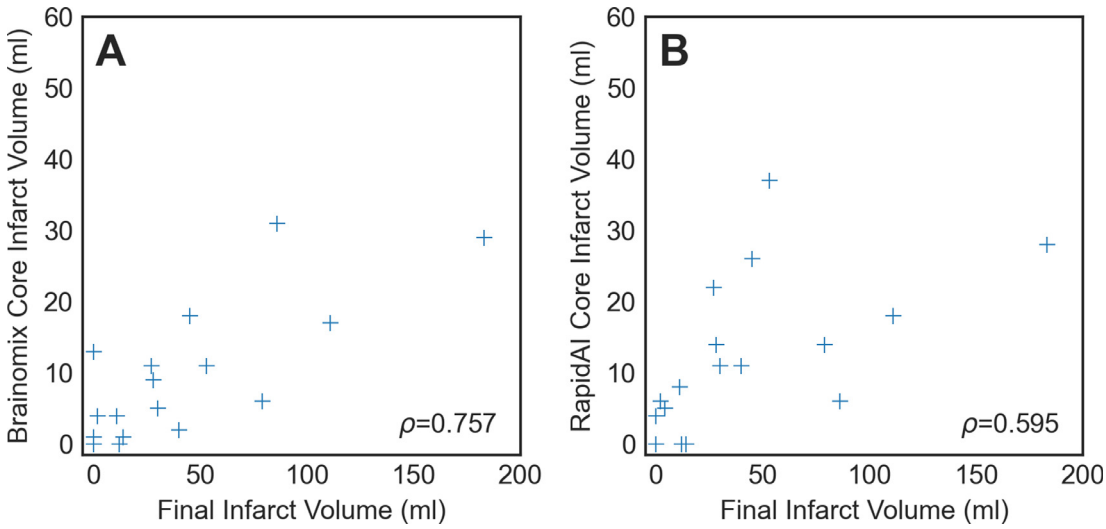

Figure 5. *Scatter plots showing the correlation between the ischaemic core volumes determined using Brainomix (A) and RapidAI (B) with the final infarct volume based on follow-up imaging in patients who had complete or near complete recanalization. The correlation was stronger for Brainomix than for RapidAI (ρ=0.757 versus ρ=0.595).*

the option for 'manual' post-processing could be made available.

Final infarct volume

In a subset of patients where complete reperfusion was achieved, FIV was more strongly correlated with the ischaemic core volumes determined by Brainomix than for RapidAI. However, correlation in both cases was only moderate, highlighting the limitations of using a single CTP parameter to define the ischaemic core. Bouslama *et al* also demonstrated this limitation showing a Pearson's correlation of 0.43 between the CTP derived ischaemic core and the FIV.[16]

While linearly correlated, CTP consistently underestimated the final size of the ischaemic core, which has been demonstrated in prior studies.[17,18] Ischaemic core underestimation may be due to recruitment of collateral flow (thereby improving CBF), incomplete coverage of the infarct within the CTP slab as well as enlargement of the infarct in the interval between CTP imaging and MT.

Limitations

There are some limitations of this study that should be considered. Firstly, there are limitations inherent to single centre retrospective studies. However, a single centre study design offers the advantage of all imaging being performed on the same scanner, eliminating the effects of different hardware, scanning protocols, and image reconstruction, all which have been shown to influence CTP analysis.[19,20] Secondly, the cohort size was modest with relatively few large infarcts. The analysis of the correlation with FIV was further reduced based on the requirement for mTICI of 2C or better. Thirdly, in many cases, FIV was calculated using follow-up NCCT rather than the gold standard of DWI lesion volume on MRI. Finally, the overlap in the volumes provided by Brainomix and RapidAI would ideally have been assessed using a similarity coefficient such as a DICE score. However, this was not possible as the segmentations are not provided by either software package.

Conclusion

There was good correlation between the estimates of the ischaemic core and penumbra volumes that were derived from Brainomix and RapidAI, which gave a high level of agreement in the eligibility for MT based on CTP cut-off criteria. Therefore, Brainomix can be considered an alternative to the more-established RapidAI in the post-processing of CTP in patients with an LVO who are being considered for MT. However, the difference in MT eligibility in 15% of patients highlights that the decision to proceed to MT should not be based solely on imaging parameters.

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Availability of data and material

Not relevant as this was a retrospective database study.

Code availability

Not relevant.

Ethics approval

The study was approved by the Research Ethics Committee.

Informed consent

Not relevant as this was a retrospective database study.

Conflict of interest

The authors have no conflict of interest to declare.

Supplementary materials

Supplementary material associated with this article can be found in the online version at doi:10.1016/j.jstrokecerebrovasdis.2022.106702.

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