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The predictive value of a targeted posterior fossa multimodal stroke protocol for the diagnosis of acute posterior ischemic stroke

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Abstract

Background: There is limited but growing research regarding the accuracy of CTP in diagnosing acute posterior ischemia stroke. We sought to evaluate the diagnostic accuracy of an incremental multimodal CT protocol in acute posterior ischemic stroke.

Methods: Retrospective review of incremental NCCT, CTA-source images and CTP use in 82 consecutive patients with acute posterior ischemic stroke. Readers were blinded to infarct status on follow-up imaging (MRI or CT). Predictive effects of observed diagnostic accuracy and confidence score were quantified with the entropy r^2 value. Sensitivity, specificity, and CI were calculated accounting for multiple reader assessments. Receiver Operating Characteristic analyses, including Area Under the Curve, were conducted for the three modalities. Inter-reader agreement was established with Intraclass Correlation Coefficient.

Results: Follow-up imaging confirmed infarct in 69/82 (84 %) patients. Multimodal protocol with CTP, outperforms CTA-source images and NCCT for correct acute posterior ischemia stroke diagnosis. The Area Under the Curve was 0.741 (95 % CI 0.708–0.773); 0.70 (95 % CI 0.663–0.731, $P = 0.03$) and 0.62 (95 % CI 0.588–0.659, $P < 0.0001$), respectively. Incrementally improved correlation between observed and actual diagnosis ($r^2 = 0.09$, 0.26 and 0.32) and a higher rate of certainty (51.4, 69.3 and 81.7 %) was demonstrated for NCCT, CTA-source images and CTP respectively. Inter-reader agreement for the actual diagnosis was good and improved from 0.68 to 0.83 with incremental multimodal CT use.

Conclusions: CTP enhances confident and correct infarct diagnosis over NCCT and CTA-source images in acute posterior ischemia stroke.

Keywords: Posterior fossa stroke, Ischemia, Infarct, CTP, Acute ischemic stroke, Multimodal CT, Posterior circulation

Background

Acute posterior ischemia stroke accounts for 20 % of ischemic stroke [1] and is most commonly cardioembolic followed by large-artery atherosclerosis [2]. Non contrast CT (NCCT) performs poorly at detecting acute posterior-fossa stroke even utilizing posterior circulation Alberta stroke program early CT score (ASPECTS) [3], largely due to beam hardening artifacts and insufficient contrast resolution. MRI and particularly DWI remains the mainstay of infarct diagnosis but is not yet widely adopted in acute stroke imaging due to its reduced availability, increased cost and scan time. Although the reference standard, DWI demonstrates reduced sensitivity in the context of small and posterior fossa infarction [4]. Both CT angiography (CTA) and CT perfusion (CTP) are previously evaluated in the posterior fossa. CTA-source image (CTA-SI) hypoattenuation is shown to improve detection of posterior fossa infarction and is predictive of clinical outcome [5]. CTP is fast and effective in the emergency evaluation of acute anterior-circulation infarction [6–8] and increases diagnostic certainty for clinical stroke by expert and non-expert readers over CTA-SI [7] and correlates with MRI DWI [9]. Drawbacks of CT include radiation dose and limited spatial coverage with many centres omitting the posterior-fossa by necessity in favour of supratentorial

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coverage. CTP however can be directed to evaluate the posterior fossa according to clinical presentation. Literature regarding the diagnostic performance of posterior-fossa CTP is limited but growing with only three recently published articles [10–12]. Advances in CT such as a table-toggle technique or increase detector number [13], now facilitate more extensive brain coverage with increasing visualization of the posterior fossa. However this extended coverage is not yet widely available. With increasing CTP imaging of the posterior fossa expected, further study of the strengths and limitations of CTP within the context of posterior ischemic stroke is needed. The purpose of this study was therefore to assess the predictive value of each component (NCCT, CTA-SI and CTP) of an incremental CT protocol using targeted posterior fossa CTP for the assessment of posterior ischemic stroke presentation.

Methods

Ethics, consent and permissions
The study was approved by the local institutional research ethics board (Research Ethics Human Research Program, Sunnybrook Health Sciences Centre).

Signed was obtained from each patient or substitute decision maker for study enrollment and publication.

Study design and patients
A retrospective cohort of consecutive acute posterior ischemia stroke patients presenting to a tertiary stroke-center emergency department between 2010 and 2012. Targeted posterior fossa CTP was performed prospectively in patients presenting with signs and symptoms of acute posterior ischemia stroke, diagnosed by an experienced Neurologist (xx, 7 years) within 12 h of symptom onset. Patients were included if their final diagnosis based on clinical and imaging findings was TIA or infarct as arbitrated by the Neurologist. Patients with stroke mimics, fetal posterior cerebral artery on baseline CTA or those with contraindications to iodinated-contrast such as allergy or severe renal impairment (GFR < 20) were excluded. Patients with intracranial stenosis were not excluded from the cohort. Baseline clinical data included gender, age, cardiovascular risk factors, NIHSS (National Institutes of Health Stroke Scale) score, rtPA status and dose.

CT protocol
The CT stroke protocol was performed on a 64-section VCT (GE Healthcare). Aortic-arch to vertex CTA was obtained [7]. CTA source-image (CTA-SI) reformations (4 mm thick, 2-mm gap) were aligned to match the NCCT image. The 40-mm slab biphasic CTP commenced inferior to the frontal horns covering most of the posterior fossa, yet retaining visualization of the bilateral anterior cerebral artery and torcula for ROI placement. First phase was 45 s scan reconstructed at 0.5 s intervals followed by 6 further acquisitions 15 s apart for an additional 90s. CTP parameters are: 80 kVp, 100 mA, 0.5 ml/kg (maximum 50 ml) iodinated contrast agent injected at 4 ml/s with a 3–5 s delay [7]. Effective-doses of individual components are NCCT 1.2mSV, CTA 2.4mSV and CTP 2.5mSV. Lifetime attributable risk of cancer for NCCT at the median age of the studied cohort is 0.01 % [14]. Follow-up was performed at 5–7 days on MRI (57/82; 70 %), unless a readily visible hypodensity involving the affected vascular territory was demonstrated on follow-up NCCT (25/82;30 %). MRI minimally included DWI/ADC maps (TR = 8125 ms/ min TE; 26-cm field of view; 128 × 128 matrix; 5-mm section thickness; no intersection gap) and FLAIR (TR = 8000 ms/ TE = 120 ms/ TI = 200 ms; 22-cm field of view; 320 × 224 matrix; 5-mm section thickness; 1-mm intersection gap).

Image processing
Commercially available software (CTP4; GE Healthcare) was used to calculate CTP maps with color-coding of cerebral blood volume (CBV), cerebral blood flow (CBF) and mean transit time (MTT). Generation of arterial and venous time attenuation curves was based on manual selection of the arterial input function (AIF) within the anterior cerebral artery and the torcula, respectively [7].

Review protocol
Images were reviewed by three readers blinded to imaging outcome; including a neuroradiologist (4 years of experience), a neuroradiology fellow and a neurology fellow (2 years' experience each). The review method simulated the clinical review process, beginning with NCCT, followed by CTA-SI and CTP color maps [7, 15]. Therefore, three DICOM folders were prepared containing NCCT, NCCT + CTA-SI and NCCT + CTA-SI + CTP. In all cases the posterior-circulation ASPECTS [16] regions were specifically reviewed to ensure a systematic approach to scan review and to maximize detection. Images were reviewed independently by the readers in three stages, one for each modality, 2 weeks apart to avoid recall-bias. The readers documented in each step the presence or absence of ischemia/infarction, based on parenchymal hypoattenuation on NCCT (infarct) and CTA-SI (ischemia/infarction) [17], qualitative MTT prolongation and CTP CBF/CBV reduction. We specifically included qualitative CTP because most centers cannot use thresholded parameters in the acute setting. We justified the inclusion of purely ischemic patterns (MTT prolongation/ CBF reduction in the absence of a visible CBV defect) in addition to overt infarction (CBV reduction) because even in the context of TIA (with clinical

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improvement), a perfusion abnormality (signifying ischemia) is associated with an increased probability of DWI/ADC infarction at presentation or follow-up [18, 19]. This approach has been used before in the supratentorium [7] in a recent study of lacunar infarction [15] and posterior fossa CTP [12]. For each posterior fossa ASPECTS location a positive diagnosis required localization to right, left or midline and was scored individually for each modality (total scores 738 for 3 readers). Therefore a positive diagnosis in an incorrect location was considered a false-positive for that location and a false-negative observation for the true infarct location. A six-point level of confidence-score was assigned (1-infarct/ischemia definitely present; 2- probably present; 3-equivocal but suspicious for infarct/ischemia; 4-equivocal but infarct/ischemia presumed absent; 5- infarct/ischemia probably absent; 6- definitely absent). Additionally, readers indicated the affected vascular territory (basilar/perforator, posterior cerebral artery, PICA, AICA, superior cerebellar artery) based on standard vascular anatomy texts. Readers documented their observations separately for each sequence group, without access to prior entries. Final infarct status/ clinical diagnosis was based on DWI/ADC restriction, NCCT hypoattenuation and final clinical diagnosis as assessed by an experienced Neurologist, XX 4 years.

Statistical analysis

Results were expressed as mean ± standard deviation or median + interquartile range (IQR) for quantitative variables and as proportions for categorical findings. Logistic-regression analysis predicted actual from observed stroke diagnosis for the incremental protocol adjusting for confidence scores. OR and 95 % CI were calculated. Actual and observed diagnostic performance was recorded as 0 (absence) and 1 (presence) with l level of confidence score 1 to 6. Combined predictive effects of the observed diagnostic performance and confidence scores in the model were quantified with the entropy r^2 value, where the higher the r^2 value the better the model. Akaike information criterion (AIC) was compared among the three incremental review steps with a lower AIC signifying a better model. Diagnostic accuracy of the incremental protocol was evaluated with Receiver Operating Characteristic (ROC) curve and Area under the Curve (AUC) comparisons [20]. Generalized estimating equations calculated real stroke confirmation from observed diagnosis adjusting for confidence score. A generalized linear model with a binomial distribution was performed using the generalized estimating equation method. Quasilikelihood-information criterion (QIC) was applied to the model fit of the generalized estimating equation with smaller values indicating a better model fit. Because of the correlation resulting from

multiple reader assessments on the same images and the various CT protocols applying to the same subject, the individual sensitivity (Se_i) and specificity (Sp_i) were calculated from the cross table of real stroke diagnosis and observed diagnosis for each sequence [21]. Inter-reader agreement was established with intraclass-correlation coefficient (ICC) [22] to estimate inter-reader concordance for the actual diagnosis. ICC of ≤ 0.20, 0.21–0.40, 0.41–0.60, 0.61–0.80 and 0.81– 1.0 were defined as a poor, fair, moderate, good and very good concordance. A T-test was applied to compare ICC generated using the bootstrap method of 1000 generated and calculated sample sets. Analyses were performed with statistical software package (SAS version 9.3; SAS Institute, Cary, NC). Results were considered significant at $p < 0.05$.

Results

There were 82 patients (43/82; 52 % female) with a mean age of 70 ± 16 years. Baseline demographic characteristics are listed in Table 1. Infarct was confirmed on follow up imaging in 69/82 (84 %) of patients, while the remaining 13 patients were diagnosed with TIA; 35/69 (51 %) were female. Median posterior-circulation ASPECTS was 10 (IQR range 9–10) with 149/5, 904 (2.5 %) positive regions (82 patients × 3 readers × 8 regions [16]). Median NIHSS was 4 (IQR 3–7). No statistically significant difference in age, gender, NIHSS or cardiovascular risk factors was present in patients with confirmed infarct versus patients

Table 1 Baseline Demographic Characteristics of 82 patients with suspected acute posterior ischemic stroke

Female Gender	43 (52)
Cardiovascular risk factors	
Hypertension	28 (34)
Diabetes mellitus	33 (40)
Coronary artery disease	18 (22)
Atrial fibrillation	37 (45)
Smoking	34 (41)
Hypercholesterolemia	15 (18)
Presence of infarct on follow up imaging	69 (84)
Large vessel infarct*	63 (91)
Affected side on follow up imaging	
Right	31 (45)
Left	25 (36)
Midline	5 (7)
Bilateral	8 (12)
Imaging follow up	
MRI	57 (70)
CT	25 (30)

All values represent n (%)
* of 69 patients with confirmed infarct on follow up imaging

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without infarct. Median time from symptom-onset to baseline CT was 115 min (IQR 89–215). Median time to follow-up was 1 day (IQR 0–1). IV rtPA was administered in 23/82 (28 %) with mean dose of 56 ± 21 mg and within a median of 144 min (IQR 134–186). No patients received intra-arterial thrombolysis. Twenty (87 %) of the rtPA-treated patients had confirmed infarct on follow-up imaging. The vascular distribution of posterior ischemic stroke using the incremental CT protocol is summarized on Table 2.

NCCT, CTA and CTP abnormality was present in 43/82 (52.4 %), 44 (53.7 %) and 62 (75.6 %) patients and 56 (13.7 %), 93 (22.7 %) and 117 (29 %) of 410 vascular territories (5 vascular territories × 82 patients) on NCCT, CTA and CTP respectively. The AUC was greater for CTP 0.741 (95 % CI 0.708 - 0.773) compared to CTA-SI 0.70 (95 % CI 0.663–0.731, $P = 0.03$) and NCCT 0.62 (95 % CI 0.588–0.659, $P < 0.0001$), respectively (Fig. 1). Similarly, CTA-SI outperformed NCCT ($P = 0.0001$). For confident diagnosis of infarct absence (Table 3) CTP sensitivity trended 12.6 % higher than CTA-SI ($p = 0.072$) and was significantly higher than NCCT. For confident diagnosis of infarct presence, CTP sensitivity was 15.8 and 30.2 % greater than CTA-SI and NCCT respectively ($p = 0.025$ and $p < 0.0001$) (Figs. 2 and 3). No specificity differences were seen for CTP over CTA-SI although both CTA-SI and CTP showed improvement over NCCT. Table 4 depicts the distribution of the readers' confidence scores for each modality. Significant reduction of equivocal diagnoses is demonstrated between NCCT (68; 9.2 %) and CTA-SI/ CTP (30; 4.1 % for each modality). More confident diagnosis or infarct exclusion was seen with multimodal CT use (NCCT 51.4 %, CTA 69.3 % and CTP 81.7 %) with higher entropy r^2 and lower AIC, confirming better correlation between the observed and actual diagnosis.

Progressive entropy r^2 increase occurred from 0.09 (NCCT), to 0.26 (CTA-SI) and 0.32 (CTP; Table 5). Similarly, the QIC declined from NCCT to CTA-SI and CTP indicating increasingly better fit between the readers' observed diagnosis and confirmed infarcts. Inter-reader agreement for actual diagnosis was good and improved incrementally with multimodal CT use from 0.59 to 0.87 (Table 6). CTP inter-reader agreement was significantly improved over both NCCT and CTA-SI.
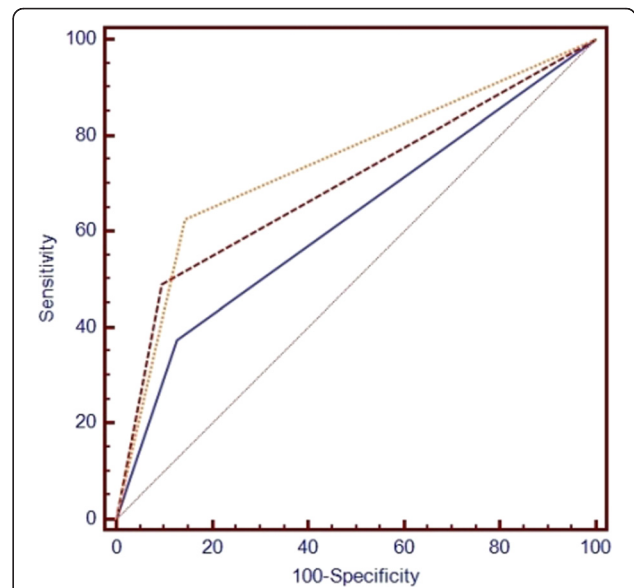
Fig. 1 Receiver Operating Characteristic curves for diagnostic performance of incremental CT protocol for posterior ischemic stroke. The area under the curve of protocol containing targeted posterior fossa CTP (dotted orange line) was greater compared to CTA-SI (dashed brown line, $p = 0.03$) or NCCT (solid blue line $p < 0.0001$)

Discussion

A multimodal CT protocol including targeted posterior-fossa CTP improved acute posterior ischemic stroke diagnosis over NCCT alone or a combination of NCCT/ CTA-SI supporting the addition of CTP to stroke protocols using only NCCT and CTA-SI. This assertion is supported by a recent study showing similar improvement for a multimodal approach in the posterior fossa [11]. Extending on these findings, we demonstrate that multimodal CT demonstrated a greater reader certainty for correct diagnosis, compared to CTA-SI or NCCT with a better inter-reader agreement. Correlation between the observed and actual diagnosis, after adjusting for confidence levels, was 3.75 times greater for CTP than NCCT. Sensitivity of the multimodal protocol for correct diagnosis was increased without significant loss of specificity. The sensitivity for NCCT and CTA-SI is similar to that recently reported in the posterior fossa of 31 % and 33 % but lower on CTP (74 %) while specificity was similar for all modalities (93–98 %). Sensitivity of

Table 2 Vascular distribution of infarct/ischemia at presentation on incremental CT protocol

Vascular territory	Basilar	PCA	PICA	AICA	SCA	Perforator/other
NCCT	0 (0)	10 (0.48)	3 (0.14)	1 (0.05)	3 (0.14)	4 (0.19)
NCCT + CTA-SI	1 (0.17)	2 (0.33)	0 (0)	0 (0)	2 (0.33)	1 (0.17)
NCCT + CTA-SI + CTP	17 (0.18)	39 (0.42)	10 (0.11)	4 (0.04)	12 (0.13)	11 (0.12)

All values represent *n* (%)
PCA posterior cerebral artery, *SCA* superior cerebellar artery, *CTA-SI* CTA-source images

Table 3 Diagnostic performance for acute posterior stroke absence or presence diagnosed with an incremental stroke protocol

	Sensitivity (*Se*)		Specificity (*Sp*)	
	Se % (95 % CI)	*p*-value*	*Sp* % (95 % CI)	*p*-value*
Ischemia/ Infarct absent (Level of confidence score 5 and 6)				
(1) NCCT	41.4 (32.9–50.0)	(1) vs. (2): 0.103	83.7 (80.0–87.4)	(1) vs. (2): < 0.0001
(2) NCCT + CTA-SI	52.3 (43.3–61.2)	(1) vs. (3): 0.0007	95.7 (93.8–97.6)	(1) vs. (3): < 0.0001
(3) NCCT+ CTA-SI + CTP	64.9 (55.7–74.0)	(2) vs. (3): 0.072	92.8 (90.4–95.2)	(2) vs. (3): 0.188
Infarct present (Level of confidence score ≤ 2 vs. > 2)				
(1) NCCT	28.8 (20.6–37.1)	(1) vs. (2): 0.032	91.5 (88.5–94.4)	(1) vs. (2): < 0.0001
(2) NCCT+ CTA-SI	43.2 (33.9–52.6)	(1) vs. (3): < 0.0001	97.7 (96.4–98.9)	(1) vs. (3): 0.002
(3) NCCT+ CTA-SI + CTP	59.0 (49.3–68.7)	(2) vs. (3): 0.025	96.1 (94.2–98.0)	(2) vs. (3): 0.318

NCCT non-contrast CT, *CTA-SI* CTA Source Images, *CTP* CT perfusion
*p-value was obtained by linear regression model of natural log(Se) or log(Sp) for each modality

NCCT in posterior ischemic stroke was expectedly lower than that reported in acute anterior ischemic stroke (28 % vs 52 %) with closer approximation of CTA-SI (43 % vs 58 %) and CTP (59 % vs 70 %) sensitivity. There is a small but growing literature discussing the efficacy of CTP in the diagnosis of acute posterior ischemia stroke [10–12]. In part, this is the result of limited CTP spatial coverage, illustrated by a recent sub-analysis of the BASICS study, where complete CTP coverage of all posterior fossa ASPECTS regions was only available in
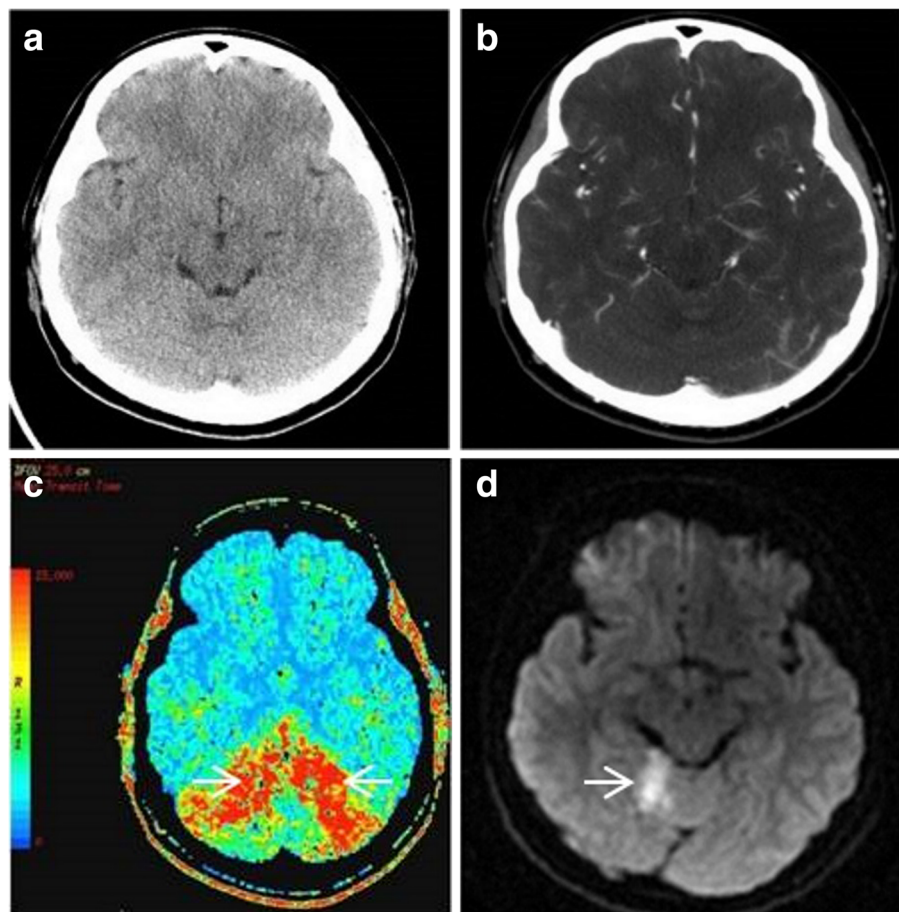
Fig. 2 a NCCT and corresponding (**b**) CTA-SI, (**c**) CTP MTT color maps and (**d**) follow up DWI obtained in 65 year old women presented with posterior ischemic stroke. MTT demonstrates bilateral cerebellar prolongation evolving to right cerebellar hemisphere infarction (arrows). NCCT and CTA-SI are unremarkable

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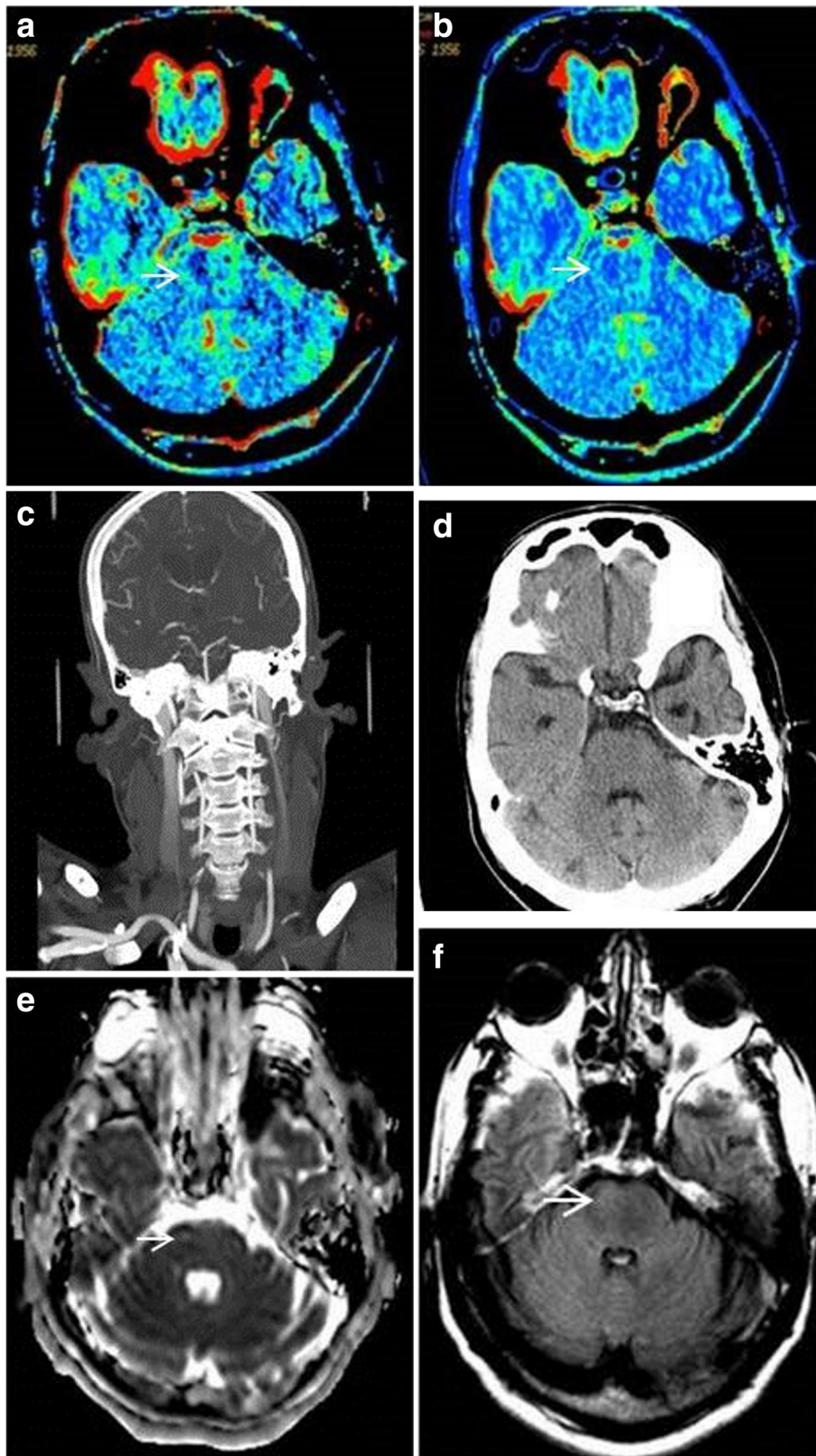
Fig. 3 (See legend on next page.)

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(See figure on previous page.)
Fig. 3 Matched areas of decreased CBF (**a**) and CBV (**b**) in the right pons (arrows) indicating an irreversible infraction in a 72 year old man. CTA (**c**) is negative for arterial filling defects, indicating its lacunar nature. NCCT (**d**) is equivocal. A right hemipontine acute infarction was confirmed on MRI that was obtained 4 days later as shown on DWI/ADC (**e**) and corresponding FLAIR (**f**)

15 % of 27 patients. While this limitation is addressed by the table-toggle technique [10, 13, 23] it is associated with reduced sensitivity for detecting small infarcts [23], offset by greater scan coverage contributing to a higher overall detection rate. As 256-multi-detector-CT scanners become increasingly available, whole-brain coverage will become routine [24, 25]. A prior study, utilizing table-toggle CTP concluded that the performance of infratentorial CTP is comparable to that of supratentorial CTP [10]. In our study we adopted a pragmatic solution to scanning for centres that do not have a table-toggle option or large array detector scanners. Close collaboration with the stroke team enabled us to alter our traditional supratentorial CTP coverage to the posterior fossa. While stroke triage reflects a typical management pathway in major stroke-centres, targeted posterior fossa CTP is unique and allows simultaneous visualization of lower basal ganglia and posterior fossa assisting in diagnosis of posterior ischemic stroke. This imaging approach represents the application of anatomically and clinically directed scanning, maximizing diagnostic benefit over the risk of radiation exposure. Other important differences between the prior study and this should be noted. Previously, only patients with confirmed infarct on follow-up were investigated whereas we included all patients presenting with acute posterior ischemia stroke irrespective of whether the final diagnosis was TIA or infarction. This approach is supported by the importance of DWI abnormality in the context of clinical TIA [26, 27] and studies demonstrating higher recurrent stroke and TIA risk in TIA patients with initial perfusion abnormality [18]. Further, up to 30 % of patients not receiving rtPA because of mild or rapidly improving ischemic stroke have poor functional outcome [28, 29]. These findings are supported by the high number (87 %) of patients included

in the present series that demonstrated infarction. The high proportion of patients with posterior ischemic stroke in the current study is attributable to careful clinical screening and is similar to the 86 % prevalence recently reported in a post hoc analysis of posterior fossa infarcts reported by the DUST investigators [11]. To mitigate against a potential performance bias associated with high infarct presence we required precise lateralization for positive infarct designation. Indeed, only 29 % of the vascular territories assessed were affected. This requirement increases the number of false positive and negative designations if overcalling occurred for a particular modality. Prevalence of CTP and CTA-SI abnormality in the context of known posterior fossa infarct in the BASICS sub-study demonstrated MTT, CBF, CBV and CTA-SI changes in 93, 78, 46 and 78 % of patients respectively [12]. These values are higher than 76 and 54 % for any CTP and CTA-SI abnormality reported in this study. The higher prevalence in BASICS is consistent with recruitment of patients with known basilar occlusion rather than any posterior circulatory vessel occlusion included in the present study.

The present cohort size is approximately double that of the prior single center study and included a 12-h compared to 24-h time to presentation. The CT approach therefore reflects the performance of each modality within a screened cohort, assessed within a clinically meaningful time period with greater potential for successful outcome [30].

CTP adds 30 % to the total effective dose of 6.1 mSv for the CTP protocol. Incremental dose, although small, must confer benefit towards diagnosis because even small radiation doses are important in terms of overall population burden. Conscientious effort should therefore be made to conform to the as low as reasonably

Table 4 Distribution of confidence scores for side-specific presence of infarct/ischemia for each modality (levels 1 and 2 indicate definite and probable presence of ischemia/infarction, levels 5 and 6 indicate definite and probable absence of ischemia/infarction)

Modality	Distribution of each score, *n* (%)					
Confidence Score	1	2	3	4	5	6
NCCT (*n* = 738)	61 (8.3)	47 (6.4)	40 (5.4)	28 (3.8)	244 (33.1)	318 (43.1)
CTA-SI (*n* = 738)	74 (10.0)	34 (4.6)	14 (1.9)	16 (2.2)	162 (22.0)	438 (59.3)
CTP (*n* = 738)	133 (18.0)	18 (2.4)	10 (1.4)	20 (2.7)	87 (11.8)	470 (63.7)

NCCT non-contrast CT, *CTA-SI* CTA Source Images, *CTP* CT perfusion

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Table 5 Logistic regression analysis and generalized estimating equations were used to model the real infarct diagnosis on different observed confidence scores for the corresponding modality

	Logistic regression model			GEEs method		
	r^2	AIC	*p*-value	OR (95 % CI)	QIC	*p*-value
NCCT						
Model fit statistics	0.0856	840.6			840.6	
Observed Confidence Score			< 0.0001	0.67 (0.61–0.74)		< 0.0001
NCCT + CTA-SI						
Model fit statistics	0.2578	686.7			686.7	
Observed Confidence Score			< 0.0001	0.45 (0.39–0.51)		< 0.0001
NCCT + CTA-SI + CTP						
Model fit statistics	0.321	621			620.9	
Observed Confidence Score			< 0.0001	0.47 (0.41–0.52)		< 0.0001

AIC Akaike information criterion, *QIC* quasilikelihood information criterion, *NCCT* non-contrast CT, *CTA-SI* CTA Source Images, *CTP* CT perfusion

achievable (ALARA) principle. A recent study shows that no quantitative CTP parameter differences were demonstrated when CTP dose was reduced by 50 % from 100 mA to 50 mA, however it remains unclear whether performance for infarct detection will remain the same at this reduced dose [31]. Scan obliquity ensures that no significant lens dose exposure occurs unlike CTA which remains the largest single dose contributor. MRI DWI remains the reference standard in acute infarct and provides superior infarct delineation but acute MRI access is limited in many institutions [32]. Therefore, although a recent consensus recommends MRI triage, the decision to treat with IV rtPA is still usually based on NCCT findings [32]. We suggest that CTA and CTP use may improve initial infarct detection over NCCT with the possibility of progressing to MRI where available.

Limitations include the relatively small sample size in comparison to anterior-circulation series. However the present study represents the largest single-center series evaluating pure acute posterior ischemia stroke. In comparison to the DUST study recruiting 88 patients from 14 centers over 4 years we recruited 82 patients in 3 years reflective of a high-volume tertiary institute and arguing against any selection bias. We purposefully utilized multidisciplinary readers of different levels of expertise, reflecting the diversity of everyday practice, where radiology trainees and non-radiologists may be the first to interpret emergency scans before a Neuroradiology staff opinion is sought. The majority of patients received MRI follow-up, with NCCT follow up used only where a radiologically-obvious acute infarct was present. DWI demonstrates high accuracy for stroke detection, but false-negative studies are documented in small and posterior infarcts [4, 33, 34]. It is plausible that a small number of patients may have been misclassified by MRI as negative in the context of a true clinical stroke. Similarly, because any CTP abnormality was considered positive, TIA associated with perfusion deficit, fully recanalized ischemia with residual perfusion defect and intracranial stenosis could all be potentially result in false positive abnormality in the absence of DWI abnormality. The impact of a systematic misclassification error is likely to affect each modality similarly and the effect on modality comparison is presumed negligible.

Conclusions

In conclusion, in centers with limited CTP coverage, targeted posterior fossa CTP in clinically selected patients enhances confident and correct infarct diagnosis and inter-reader reliability.

Table 6 Inter-reader agreement for three readers as reflected by ICC. ICC of 0.61–0.80 and 0.81– 1.0 were defined as good and very good concordance, respectively

Modality	ICC	95 % CI	Interpretation	*p*-value
NCCT	0.6796	0.6034–0.7432	Good	reference
NCCT + CTA-SI	0.7829	0.7312–0.8260	Good	120.4 (< 0.0001)
NCCT + CTA-SI + CTP	0.8337	0.7941–0.8667	Very Good	145.9 (< 0.0001)

ICC intraclass-correlation coefficient, *NCCT* Non-contrast CT, *CTA-SI* CTA Source Images, *CTP* CT perfusion

Competing interests
The authors declare that they have no competing interests.

Authors' contributions
MS - data acquisition, CT interpretation, literature research, data analysis and interpretation, manuscript writing. KB - data acquisition, CT interpretation, manuscript revising. RY - CT interpretation, manuscript revising. LZ - performed the statistical analysis and tables, manuscript revising. SS - participated in the design of the study, manuscript revising. MB - data acquisition, manuscript revising. RA - data acquisition, study design, literature research, data analysis and interpretation, manuscript writing. All authors read and approved the final manuscript.

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