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Comparison of CT perfusion summary maps to early diffusion-weighted images in suspected acute middle cerebral artery stroke☆

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ABSTRACT

Objectives: To assess the accuracy and reliability of one vendor's (*Vital Images, Toshiba Medical, Minnetonka, MN*) automated CT perfusion (CTP) summary maps in identification and volume estimation of infarcted tissue in patients with acute middle cerebral artery (MCA) distribution infarcts.
Subjects and methods: From 1085 CTP examinations over 5.5 years, 43 diffusion-weighted imaging (DWI)-positive patients were included who underwent both CTP and DWI <12 h after symptom onset, with another 43 age-matched patients as controls (DWI-negative). Automated delay-corrected postprocessing software (DC-SVD) generated both infarct "core only" and "core + penumbra" CTP summary maps. Three reviewers independently tabulated Alberta Stroke Program Early CT scores (ASPECTS) of both CTP summary maps and coregistered DWI.
Results: Of 86 included patients, 36 had DWI infarct volumes ≤70 ml, 7 had volumes >70 ml, and 43 were negative; the automated CTP "core only" map correctly classified each as >70 ml or ≤70 ml, while the "core + penumbra" map misclassified 4 as >70 ml. There were strong correlations between DWI volume with both summary map-based volumes: "core only" ($r = 0.93$), and "core + penumbra" ($r = 0.77$) (*both* $p < 0.0001$). Agreement between ASPECTS scores of infarct core on DWI with summary maps was 0.65–0.74 for "core only" map, and 0.61–0.65 for "core + penumbra" (*both* $p < 0.0001$). Using DWI-based ASPECTS scores as the standard, the accuracy of the CTP-based maps were 79.1–86.0% for the "core only" map, and 83.7–88.4% for "core + penumbra."
Conclusion: Automated CTP summary maps appear to be relatively accurate in both the detection of acute MCA distribution infarcts, and the discrimination of volumes using a 70 ml threshold.

1. Introduction

Medical decision strategies in the setting of acute stroke are centered on the feasibility of utilizing thrombolysis to rescue at-risk tissue [1,2]. Currently, patient selection for thrombolytic therapy is heavily dependent on the amount of time since symptom onset. Improved precision of thrombolysis use in the setting of ischemic stroke will require better identification of the existence and scope of the ischemic penumbra [1–3]. Already, the use of diffusion weighted imaging (DWI) in identifying permanently damaged infarcted tissue (i.e. "core") and potentially salvageable penumbra has been well established, and a core volume threshold of 70 ml has been suggested as able to discriminate between outcomes of possible intra-arterial intervention [4–6]. However, MR imaging is not widely and readily available in the acute stroke setting. In the absence of immediate MR imaging, an accurate CT perfusion (CTP) method can help with diagnosis and triaging of stroke patients.

Different CTP map summaries have been suggested for identification of the infarct core and penumbra in stroke patients [7,8]. In addition, significant disparities exist in the results of CTP imaging analysis among different vendors, which has been attributed to differences in a number of factors, including scan

Abbreviations: ACA, anterior cerebral artery; ASPECTS, Alberta Stroke Program Early CT score; CBV, cerebral blood volume; CBF, cerebral blood flow; CTP, CT perfusion; DC-SVD, delay-corrected SVD; DS-SVD, delay-sensitive SVD; DWI, diffusion-weighted imaging; MCA, middle cerebral artery; MTT, mean transit time; PCA, posterior cerebral artery; SVD, singular value decomposition; TTP, time to peak.

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parameters, post-processing steps, and type of deconvolution algorithm [9–11]. Despite such vendor differences, CTP remains a viable imaging modality in the emergency room assessment of acute stroke patients; the validation of CTP summary maps, therefore, remains an alluring prospect [2].

Previous studies have correlated CTP summary map abnormalities with DWI MRI [12,13]. However, many studies have been limited by small patient samples, reliance on delay-sensitive perfusion algorithms, or a significant time delay between CTP and MR imaging [14]. The recent implementation of delay-corrected postprocessing algorithms, such as delay-corrected postprocessing software (DC-SVD), have enabled the generation of CTP maps with less variation and greater accuracy, as compared to non-corrected algorithms (delay sensitive-SVD) [15–17]. Additionally, a delay in the time to acquire CTP and DWI of >12 h makes the analysis susceptible to inaccuracies, due to reperfusion phenomena (a.k.a. "luxury perfusion"), in which both the cerebral blood flow (CBF) and cerebral blood volume (CBV) can return to normal or above-normal levels following infarction [18]. Thus, when comparing the performance of CTP to DWI, it would be optimal to obtain both at <12 h post-symptom onset. Hence, we set out to mitigate such limitations by (1) collecting data from a relatively large patient sample that includes both DWI-positive and DWI-negative patients, (2) implementing a previously substantiated DC-SVD-based vendor algorithm in tandem with coregistered DWI, and (3) excluding subjects that do not have corresponding DWI at <12 h after symptom onset. The goal of this study was to retrospectively compare the performance of one vendor's (*Vital Images*, *a division of Toshiba Medical*, *Minnetonka*, *MN*) CTP summary maps to coregistered DWI in patients with suspected acute middle cerebral artery (MCA) distribution infarcts. The reliability and accuracy of CTP maps was evaluated using the Alberta Stroke Program Early CT score (ASPECTS) and infarct "core" volume, as well as by differentiating small from large infarct cores based on the proposed 70 ml treatment threshold.

2. Methods

2.1. Patient selection

After institutional review board approval, a retrospective review was performed of all acute ischemic stroke patients' imaging who presented between 1/2006 and 7/2011, from which 1085 patients were identified with CTP exams. Patients were initially included (1) if positive for infarct on DWI unilaterally in the MCA distribution <12 h after symptom onset ($n = 70$), or (2) if the patient had a negative MRI at <12 h of symptom onset ($n = 55$). Posterior cerebral artery (PCA) and anterior cerebral artery (ACA) territory infarctions were excluded because data from those patients would not be reliably assessed using ASPECTS scores. Exclusion criteria were: (1) either the CTP or MRI was quite limited or nondiagnostic, due to technical problems (e.g. motion), (2) infarct size <1.5 cm based on axial DWI (as lesions less than this size are generally labeled lacunar infarcts), (3) reperfusion therapy was performed in the interim between CTP and MRI, or (4) >12 h delay between stroke symptom onset and MRI. A total of 43 patients met the criteria for positive MRI findings, and 49 met the criteria for negative findings; of the latter, 6 were excluded to best age-match with the positive examinations. Fig. 1 demonstrates the breakdown of patients in this study, and how the 43 positive and 43 negative stroke patients were selected.

2.2. CTP acquisition

All studies were performed on a 64-slice multidetector scanner (*Brilliance CT*; *Philips Medical Systems*, *Best*, *Netherlands*). As part of a stroke imaging protocol, each patient underwent noncontrast CT followed by CT angiography and CTP. CTP was not performed if an area of hemorrhage was visualized on NECT, which was reviewed by a radiology resident or neuroradiology fellow while the patient was in the scanner, in order to both exclude the presence of hemorrhage as well as to determine the optimum acquisition level for the CTP. CTP consisted of two first-pass acquisitions of 55–60 second dynamic injections/scans (1 image/s), with no delay between the two. Both acquisitions yielded 40 mm of coverage, with four 10 mm-thickness contiguous slices (32 mm × 1.25 mm collimation, 80 kV, 120 mA s). A bolus of 36–40 ml of nonionic contrast (iohexol, Omnipaque 350 mg/ml, GE Healthcare) was administered intravenously for each acquisition, constituting a total of 72–80 ml of IV contrast per each CTP examination. The bottom edge of the levels scanned for each CTP were typically at (1) the bottom edge of the basal ganglia, and (2) the level of top of the lateral ventricles, unless another area had been suspected based on NECT.

2.3. DWI automated volume measurement

DWI scans (5 mm thickness) were coregistered to the CTP examination using a method previously described, with automated rigid coregistration performed on DWI using commercially available software (*Fusion 7D*, *Mirada Solutions*); a neuroradiology staff physician confirmed the quality of fusion (Fig. 2) [18]. The measurement of infarct volume on coregistered DWI was automated by a VITREA workstation (*Vital Images*, *Toshiba Medical*, *Minnetonka*, *MN*). Using this volume, the 43 DWI-positive patients were dichotomized into those with infarct volume >70 ml versus those of ≤70 ml [19,20].

2.4. CTP summary map postprocessing and automated volume measurement

Postprocessing of CTP summary maps was completed using a proprietary vendor algorithm on a VITREA workstation (*Vital Images*, *Toshiba Medical*, *Minnetonka*, *MN*). The workstation's automated postprocessing software relies on a DC-SVD algorithm, as well as on interhemispheric comparison (side-to-side). The MCA territory ("side") with the highest time to peak (TTP) is automatically classified as the lesion side, and the contralateral MCA territory is used as reference for relative parametric values. The algorithm segments CSF and ventricles from the brain parenchyma. Algorithm parameters were set by the vendor, based on preliminary reports of the optimal thresholds [21,22]. The exact thresholds and algorithm for constituting the summary map are proprietary; however, according to the vendor, the primary criteria for determining infarct "core" were, in order of priority: (1) a relative CBV reduction of ≥40% compared to the mean value of the contralateral MCA territory, (2) a TTP elevation ≥7 s as compared to contralateral MCA territory, and (3) a >70% relative mean transit time (MTT) reduction (usually occurring in a near-zero flow state where only noise accounts for measured values) [23]. Penumbra was considered as the cerebral tissue with normal CBV, which had either relative TTP elevation, or MTT prolongation, or relative CBF reduction (>60%). By the vendor's convention, the software automatically tabulates the volume of, and colors the extent of infarct and ischemia, where suspected infarct "core only" is colored as red, ischemic "penumbra" as yellow, and "normal" perfusion as green (Fig. 2). Similar to the DWI volume, patients were categorized into those with a large infarct core (>70 ml) versus a small core (≤70 ml).

2.5. Review of DWI and CTP summary maps

Three staff neuroradiologists with >5 years of experience, who had been blinded to the final results, history of patients, and follow-up images, independently reviewed the DWI scans and CTP