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Optimal sequence timing of CT angiography and perfusion CT in patients with stroke

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ABSTRACT

Objective: Standard stroke CT protocols start with non-enhanced CT followed by perfusion-CT (PCT) and end with CTA. We aimed to evaluate the influence of the sequence of PCT and CTA on quantitative perfusion parameters, venous contrast enhancement and examination time to save critical time in the therapeutic window in stroke patients.

Methods and materials: Stroke CT data sets of 85 patients, 47 patients with CTA before PCT (group A) and 38 with CTA after PCT (group B) were retrospectively analyzed by two experienced neuroradiologists. Parameter maps of cerebral blood flow, cerebral blood volume, time to peak and mean transit time and contrast enhancements (arterial and venous) were compared.

Results: Both readers rated contrast of brain-supplying arteries to be equal in both groups ($p = 0.55$ (intracranial) and $p = 0.73$ (extracranial)) although the extent of venous superimposition of the ICA was rated higher in group B ($p = 0.04$). Quantitative perfusion parameters did not significantly differ between the groups (all $p > 0.18$), while the extent of venous superimposition of the ICA was rated higher in group B ($p = 0.04$). The time to complete the diagnostic CT examination was significantly shorter for group A ($p < 0.01$).

Conclusion: Performing CTA directly after NECT has no significant effect on PCT parameters and avoids venous preloading in CTA, while examination times were significantly shorter.

1. Introduction

Multi-modal stroke imaging has become a diagnostic mainstay in the acute setting [1–6]. It generally includes non-enhanced computed tomography (NECT), perfusion CT (PCT) and CT angiography (CTA) of the supraaortic arteries. NECT is performed to rule-out hemorrhage as well as to detect early signs of cerebral ischemia. While PCT evaluates the hemodynamic relevance of an impaired cerebral blood flow, thereby differentiating between infarction and tissue-at-risk, CTA is able to identify the site and the extent of thrombosis or dissection as well as potential tandem stenoses and arterial collateralization [7–13].

Classically, NECT is performed first followed by PCT with CTA being the last examination. The reasoning behind this sequence of examinations was that a venous preloading could falsify the perfusion parameters to an extent that impairs diagnostic decision making. Recently, this sequence of examinations has been questioned, though [14,15].

As CTA has traditionally been performed after the contrast-load of PCT, it tended to suffer from a venous overlay thereby potentially interfering with the delineation of the supraaortic arteries, e.g. the cavernous segment of the internal carotid artery (ICA). In recent literature some authors used a different scanning sequence, where CTA was performed before PCT [16,17]. In clinical practice it remains unclear what scanning sequence is the best regarding image quality and acquisition time.

As time is brain, the major aim of multimodal stroke imaging is to obtain a correct diagnosis regarding the presence or absence of hemorrhage as well as the site, extent and prognosis of vascular pathologies and cerebral ischemia in the shortest possible time.

The critical time not only includes the imaging per se, but also the time for image interpretation. When analyzing a CTA of the supraaortic arteries, it is more straightforward to identify and delineate the respective vessels and to evaluate potential pathologies when there is little to no overlay by either venous contrast enhancement or bony structures [18,19]. It has been previously shown that thick maximum intensity projections (MIP) after the elimination of bone with either masked bone subtraction, i.e. the subtraction

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of the non-enhanced scan [20], or with dual-energy based bone removal improves the delineation of supraaortic and/or intracranial arteries and reduces the reading time of the CTA [21].

The initial acquisition of CTA directly after NECT and prior to PCT could therefore be advantageous for CTA image interpretation. It may moreover enable an optimal placement of the PCT imaging slab depending on the CT-angiographic results. It would be desirable to avoid contrast preload by the CTA interfering with perfusion parameters. We therefore aimed to evaluate the impact of the sequence of CTA and PCT on the image quality of both modalities as well as on the contrast and delineation of the supraaortic arteries and the calculated perfusion parameters.

2. Materials and methods

Institutional Review Board (IRB) approval was obtained prior to the commencement of the study. The datasets of 85 consecutive patients (46 female and 39 male, mean age: 60.6 ± 15 years; median age: 62.8; range 22–89 years) were retrospectively identified in a database query of our institutional radiology information system. Search criteria were: (1) suspected ischemic stroke; (2) a completed multimodal stroke-CT exam with a standardized protocol as described below, consisting of NECT, CTA of the supraaortic arteries and dynamic PCT of the brain; (3) examination on a modern CT scanner (40- or 64-slice multi detector CT); and (4) complete DICOM data sets of the PCT raw data and 1.0 mm or thinner axial slices of the CTA data. Exclusion criteria were known contraindications for the administration of contrast media, hemorrhage in the non-enhanced CT (NECT), age below 18 years and an incomplete dataset. All patient identifying information was pseudonymized prior to image analysis.

The identified data sets were divided into two groups: group A: "CTA before PCT", in which the CTA scan was performed prior to the PCT scan; and group B: "PCT before CTA", in which the PCT scan was acquired prior to CTA. Group A consisted of 47 patient studies (21 male; 26 female; age: 60.8 ± 14 years; median age: 63.8 years; range 31–89 years). Group B consisted of 38 patient studies (18 male; 20 female; age: 60.4 ± 16 years; median age: 60.7 years; range 21–89 years). 75 examinations were acquired on a Somatom Sensation 64 scanner, 5 on a Somatom Definition and 5 on a Sensation Open Sliding Gantry (all Siemens Healthcare, Forchheim, Germany).

Acquisition parameters were as follows:

- CTA: 120 kV at 220 mAs reference tube current-time product with attenuation-based tube current modulation (CareDose, Siemens Healthcare, Forchheim, Germany), 40 or 64 mm × 0.6 mm collimation, scan start with 4 s delay after bolus-tracking at the level of the ascending aorta, pitch 0.8, caudocranial scan direction. A weight-adapted contrast media and saline chaser injection protocol was applied with 1.1 ml contrast material per kg body weight (Ultravist 370, Bayer Healthcare, Berlin, Germany, i.e. 0.42 g iodine per kg bodyweight) at an injection rate of (0.056 × bodyweight) ml/s followed by 100 ml saline at the identical flow rate. Axial images were reconstructed with a slice thickness of 0.75 or 1.0 mm and an increment of 0.5 or 0.8 mm using a standard CTA reconstruction kernel.
- PCT: 80 kV, 250 mAs, 40 or 64 mm × 0.6 mm collimation, 2.4 or 2.8 cm coverage (2 slices of 1.2 resp. 1.4 cm width) at the level of the basal ganglia, 40 scans every 1.0 s after injection of 14–15 g iodine at 2.0–2.1 g/s followed by a saline flush of 40 ml NaCl at 5 ml/s flow.

All CTA and PCT data were transferred to a multimodality workstation (Syngo MMWP, VA 22, Siemens Healthcare, Forchheim, Germany). The time between CTA and PCT or between PCT and CTA was measured in minutes using the DICOM time stamp of the first image of the corresponding series. Quantitative measurements of the contrast attenuation of the axial CTA "raw" data were performed by manually drawing a region on interest (ROI) at the left and right proximal extracranial ICA and the jugular veins (JV) of both sides. Mean attenuation was calculated in the ICA and JV. MIP reformations in axial, coronal and sagittal orientations were created for CTA reading with a slice thickness and increment of 3/3 mm for the axial images and 5/5 for coronal and sagittal images.

From the PCT datasets, color-coded parameter maps (2 slices of 1.2 or 1.4 cm width) of cerebral blood flow (CBF), cerebral blood volume (CBV), mean transit time (MTT) and time to peak (TPP) were reconstructed using a standard deconvolution model. Quantitative measurements of the contrast enhancement (in Hounsfield units) were performed on the PCT data sets by manually drawing a ROI at the superior sagittal sinus (SSS) and in the white matter of the frontal lobe of an unaffected hemisphere. These measurements were done on the first image of the dynamic perfusion series and at the level of the peak enhancement. The difference of these two values was also calculated. For all four precalculated perfusion parameters a manually drawn ROI measurement was performed at the white matter of the frontal lobe of an unaffected hemisphere to assess quantitative values of CBF, CBF, MTT and TTP.

Two board certified neuroradiologists, who were masked to all clinical data and to the sequence of CTA and PCT acquisition, evaluated the CTA data of all examinations in consensus in a randomized fashion. For each dataset, readers had to fill in a case report form, subjectively assessing contrast enhancement quality of the intracranial and extracranial arteries on a visual analogous scale (VAS with a range from 1 = "excellent" to 5 = "very poor"), venous contamination compromising the view of the extracranial ICA (on a VAS ranging from 1 = "none" to 5 = "extreme contamination") and diagnostic quality of the cavernous segments of the ICA (on a VAS ranging from 1 = "excellent, no venous contamination" to 5 = "very poor, massive overlay due to venous enhancement").

For statistical analysis, all data were collected in a custom designed database using standard software (Access 2003, Microsoft, Redmond, USA). Standard statistical software (SPSS, IBM Inc., Chicago, USA) was used for statistical testing. Levene's test for equality of variances was applied to all criteria of the two groups. The Wilcoxon matched-pairs signed-rank test was applied to test the differences of "venous contamination" of the samples for significance. Student's *t*-test was used to test the other criteria of the samples for significance. A *p*-value of less than 0.05 was considered to indicate statistical significance.

3. Results

There were no significant differences between the groups regarding the age and gender distribution.

When evaluating the CTA parameters, the mean density of the internal jugular vein was significantly higher in group B, i.e. when PCT was performed prior to CTA ($p < 0.01$), while there were no significant differences between the groups regarding the mean density of the ICA ($p = 0.90$). The readers rated both groups to be equal regarding the subjective contrast of the intracranial arteries ($p = 0.55$) as well as the extracranial arteries ($p = 0.73$). However, the extent of venous superimposition of the ICA was rated to be higher ($p = 0.04$) and the diagnostic image quality of the cavernous segments of the ICA to be worse in group B ($p = 0.03$), see Table 1.

Regarding the PCT raw data, the base line attenuation and the attenuation peak in the superior sagittal sinus were significantly higher in group A, i.e. in the group, in which CTA was performed prior to PCT (both $p < 0.01$). However, the delta of the attenuation in