Visualization of large vessel occlusion, clot extent, and collateral supply using volume perfusion flat detector computed tomography in acute stroke patients

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Abstract

Background: Flat detector computed tomography angiography (FDCTA) can be reconstructed from volume perfusion flat detector computed tomography (VP-FDCT). Thus, CTA equivalent stroke imaging might be feasible within the angio suite.

Purpose: To evaluate the diagnostic accuracy of FDCTA in detecting large vessel occlusion (LVO) and collateral supply in acute stroke patients.

Material and Methods: Sixteen patients with LVO of the anterior circulation were analyzed retrospectively. Each patient underwent a multimodal CT stroke protocol, subsequent VP-FDCT, and digital subtraction angiography (DSA) for endovascular stroke therapy. Angiographic images reconstructed secondarily from VP-FDCT were evaluated with regard to visualization of LVO, Collateral Score (CS), Clot Burden Score (CBS), and image quality.

Results: Image quality of FDCTA was sufficient for diagnosis with a strong correlation between CTA and FDCTA (median score: CTA = 4 ± 0.447 ; FDCTA = 4 ± 0.5). Detection of LVO could be achieved with high sensitivity and specificity for FDCTA and CTA (97.9%, 95% confidence interval [CI] = 96.0–99.9; 92.6%, 95% CI = 84.3–100.0 vs. 96.8%, 95% CI = 93.2–100.0; 86.3%, 95% CI = 88.2–95.2). CBS and CS assessment showed no significant difference between FDCTA and CTA for both readers (reader1_{CBS}: $P = 0.751$, reader1_{CS}: $P = 0.718$; reader2_{CBS}: $P = 0.164$; reader2_{CS}: $P = 0.582$) and an excellent interrater agreement (CTA_{CBS}ICC = 0.984, FDCTA_{CBS}ICC = 0.951; CTA_{CS}ICC = 0.754, FDCTA_{CS}ICC = 0.789).

Conclusion: FDCTA, reconstructed from VP-FDCT data, allows reliable detection of ICA or MCA M1 segment occlusion comparable to CTA and may provide information concerning the clot extent with sufficient image quality.

Keywords

Central nervous system, interventional, stroke, flat detector computed tomography

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Introduction

In neuroangiographic imaging, flat detector computed tomography (FDCT) plays an increasing role as it allows the acquisition of computed tomography (CT) such as images within the angio suite (1,2). By a rotational acquisition from an angular range of approximately 200° a three-dimensional (3D) volume can be derived, which can be post-processed and evaluated like multislice CT datasets (3). Thereby, cross-sectional

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imaging of the brain can be performed within the angio suite and intracerebral hemorrhage (ICH) or subarachnoid hemorrhage (SAH) can be sufficiently recognized even though image quality is inferior to CT (2,4).

Moreover, it has been shown that using volume perfusion FDCT (VP-FDCT), parenchymal blood volume (PBV) maps can be generated, which provide an approximation of the cerebral blood volume (CBV), a key parameter of brain perfusion (5,6). In the treatment of patients with acute ischemic stroke (AIS), workflow analysis of the ESCAPE trial showed that imaging-to-reperfusion time is an important predictor of outcome (7). The possibility to perform equivalent diagnostic imaging within the angio suite could shorten imaging-to-reperfusion time and speed up the workflow (8,9). Robust imaging of large vessel occlusion (LVO) and collateral supply out of VP-FDCT datasets, which are comparable to computed tomography angiography (CTA), would help to implement a “one-stop” approach in the work-up of ischemic stroke within the angio suite. However, reliable imaging of the intracranial vasculature, the clot burden, and the collateral supply in AIS is warranted (10–17).

We aimed to compare the diagnostic accuracy of flat detector computed tomography angiography (FDCTA), reconstructed from VP-FDCT, with CTA.

Material and Methods

Patients

Informed consent was gathered by the patients or legal representatives according to local law and regulations. Institutional review board approval was obtained before the commencement of this study and this study was performed in accordance with the ethical standards laid down in the 1964 Declaration of Helsinki and its later amendments.

A total of 16 patients were included retrospectively. Inclusion criteria were NIHSS > 3, symptom onset within the last 6 h and a suspected occlusion of the anterior circulation. In all patients, occlusion of the internal carotid artery (ICA) or the middle cerebral artery (MCA) was suspected. All patients underwent multimodal CT, VP-FDCT, and endovascular treatment (EVT). Baseline characteristics are listed in Table 1.

Multimodal CT

CT was performed using a 128-section scanner (Somatom Definition AS+; Siemens Healthineers, Forchheim, Germany). A multimodal stroke protocol was used in the following order: non-enhanced

Table 1. Baseline characteristics.

Demographic and clinical characteristics	
Gender* (female)	8 (50%)
Age [†] (years)	70 ± 13
Pre-mRS*	0 (0–1)
Hypertension*	15 (93.8%)
Diabetes*	4 (25%)
Hypercholesterolemia*	6 (37.5%)
Atrial fibrillation*	11 (68.8%)
Admission status	
NIHSS [‡]	15 (13–17)
Onset-to-image time (min) [‡]	99.5 (79–231)
I.v. lysis treatment*	13 (81.3%)
General anesthesia before EVT*	10 (62.5%)

*Values are presented as n (%).

[†]Values are presented as mean ± SD.

[‡]Values are presented as median (interquartile range).

mRS, modified Rankin Scale; NIHSS, National Institutes of Health Stroke Scale; I.v., intravenous; EVT, endovascular treatment.

computed tomography (NECT); computed tomography perfusion (CTP); and CTA.

CTA was performed in a caudocranial direction. Coverage in the z-axis was from the aortic arch to the cranial vertex (120 kV, 160 mAs, collimation = 128 × 0.6 mm, rotation time = 0.3 s). A total of 60 mL contrast agent (Imeron[®] 400, Bracco Imaging, Konstanz, Germany) was injected via an 18-gauge cubital-vein-cannula at a rate of 5 mL/s, followed by 50 mL of saline flush. Bolus tracking was performed in the ascending aorta and image acquisition started 4 s after contrast exceeding 100 HU (18).

CTP was performed in caudocranial direction (80 kV, 80 mAs; z-axis coverage = 96 mm; 1 scan every 1.5 s; 67.98-s scan period; 2-s delay after contrast injection). A total of 30 mL contrast agent (Imeron[®] 400, Bracco Imaging, Konstanz, Germany) was injected via an 18-gauge cubital-vein cannula at a rate of 5 mL/s, followed by 50 mL of saline flush.

FDCT/Digital subtraction angiography

Subsequent FDCT was performed at the same angiography systems (Axiom Artis dBA or Axiom Artis Zee Zeego; Siemens Healthineers, Forchheim, Germany) in one session with digital subtraction angiography (DSA).

VP-FDCT (Neuro-PBV IR; Siemens Healthcare, Forchheim, Germany) was performed immediately before EVT. Each acquisition consisted of a mask run, followed by a fill run. Rotation time per run was 8 s (70 kV, 616 × 480 matrix, projection on 30 × 40 cm flat panel size, 200° total angle, 0.5°/frame, 400 frames total, dose per frame 0.36 µGy). Image acquisition was started by using the “bolus watching” method (5).

A total of 60 mL contrast agent (Imeron® 400, Bracco Imaging, Konstanz, Germany) was injected via an 18-gauge cubital-vein cannula at a rate of 5 mL/s, followed by 50 mL of saline flush. For patients' head fixation, a carbon head holder with soft tapes was used.

Post-processing of VP-FDCT and CTA

Post-processing of VP-FDCT images was performed using a dedicated workstation (syngo XWP, Siemens Healthineers, Forchheim, Germany). The mode "native fill," kernel type "HU," and image impression "normal" were used (19).

Angiographic maximum intensity projection (MIP) reconstructions of each VP-FDCT dataset and CTA dataset were generated in transverse and coronal orientation (slice thickness = 1 mm; spacing = 1 mm).

Image analysis

All FDCTA and CTA datasets were evaluated separately and in random order by two independent neuroradiologists (two and five years of experience) blinded to clinical data. Analysis of DSA as reference was performed afterwards in consensus by the same two neuroradiologists.

Visual (qualitative) analysis of both FDCTA and CTA MIP reconstructions was performed in consensus using a 4-point scale, in the style previously described by Hinkmann et al. (20): 1 = poor quality, vasculature not definable, no information; 2 = fair quality, vasculature suboptimal definable, clear loss of information; 3 = good quality, vasculature can be defined without substantial loss of information; and 4 = excellent quality, exact definable vasculature, no loss of information.

The following vascular segments were screened for LVO: distal ICA left/right, segments C6/C7, respectively, according to the Bouthillier classification; proximal M1 left/right; distal M1 left/right; M2-M3 left/right. Vessel occlusion was described using a 2-point scale for FDCTA, CTA, and DSA: 0 = vessel occluded; and 1 = vessel open.

Clot Burden Score (CBS) in FDCTA and CTA datasets was evaluated, as described by Tan et al. (17). Briefly, the CBS describes the extent of thromboembolic occlusion of seven vessel segments of the anterior circulation: the infra- and supraclinoid ICA, the proximal and distal M1 segment, two M2 segments, and the A1 segment of the anterior cerebral artery (ACA). The score applies a scale of 0–10, implying a clot absence by a score of 10 or a multivessel occlusion by a score of 0. If there is a thrombus in the supraclinoid ICA, the proximal M1 segment, or the distal M1 segment, for each a score of 2 is subtracted by 10. If there is a thrombus in the infraclinoid ICA, the ACA, or in the

superior or inferior M2 segment, for each a score of 1 is subtracted by 10. It is irrelevant if the thrombus is completely or partially occlusive. The CBS was evaluated using MIP reconstructions of the FDCTA and CTA datasets. None of our participants presented an occlusion of the ACA or the infraclinoid ICA.

Collateral Score (CS) was surveyed using FDCTA and CTA datasets as described by Tan et al. (17): 0 = no collateral supply of the occluded MCA territory; 1 = collateral supply >0% but ≤50% of the occluded MCA territory; 2 = collateral supply >50% but ≤100% of the occluded MCA territory; and 3 = 100% collateral supply of the occluded MCA territory.

Statistical analysis

For statistical analysis, Spearman correlation was used to correlate LVO between FDCTA, CTA, and DSA. Segment-based sensitivity and specificity of LVO detection was calculated. To compare CBS and CS, a paired t-test was used. A *P* value ≤0.05 was considered as significant.

To assess the interrater agreement of LVO, CBS, and CS, the interrater correlation coefficient (ICC) was used. ICC estimates and their 95% confident intervals (CI) were based on a single rater, absolute-agreement, two-way mixed-effects model (21). Interpretation of average ICC values was as follows: poor ≤0.40; fair = 0.40–0.59; good = 0.60–0.74; and excellent = 0.75–1.00.

All statistical analyses were performed using commercially available software (IBM® SPSS® Statistics Version 19, Chicago, IL, USA).

Results

Qualitative analysis

Overall quality was sufficient to define the vasculature confidently (Table 2). Intracranial vessel anatomy could be identified exactly for 12/16 (75%) CTA datasets (4, range = 3.25–4) and for 10/16 (62.5%) FDCTA

Table 2. Qualitative scoring of FDCTA and CTA.

	Grades of quality			
	1	2	3	4
Modality				
CTA	0 (0)	0 (0)	4 (25)	12 (75)
FDCTA	0 (0)	0 (0)	6 (37.5)	10 (62.5)

Values are presented as n (%)

Analysis was performed by two neuroradiologists in consensus. 1 = poor quality, vasculature not definable, no information; 2 = fair quality, vasculature suboptimal definable, clear loss of information; 3 = good quality, vasculature can be defined without substantial loss of information; 4 = excellent quality, exact definable vasculature, no loss of information.

datasets (4, range = 3–4). No dataset showed suboptimal or missing vessel delineation.

Correlation between CTA and FDCTA was strong ($r = 0.745$; $P = 0.001$).

Large vessel occlusion

A total of 384 vessel segments were scored (128 by FDCTA, 128 by CTA, 128 by DSA). LVO could be detected reliably in all patients.

Analysis of the DSA as reference revealed ICA occlusion in 4/16 patients (2/4 left-sided, 2/4 right-sided). Of these 16 patients, 12 presented with an MCA occlusion. Therefore, the M1 segment was primarily occluded in 10/12 patients (3/10 left-sided, 7/10 right-sided), whereas there was a primarily occlusion of the M2 segment in 2/12 patients (1/2 left-sided, 1/2 right-sided). Overall, 41/128 vessel segment occlusions were scored in the DSA.

Both readers detected occlusions in 38/128 (29.7%) vessel segments when examining CTA datasets.

Reader 1 examined 42/128 (32.8%) vessel segment occlusions when scoring FDCTA datasets, whereas reader 2 scored 34/128 (26.6%) occlusions.

Overall correlation in detecting LVO between CTA and FDCTA was excellent for reader 1 (mean $r = 0.894 \pm 0.07$) and reader 2 (mean $r = 0.767 \pm 0.249$). However, there was no correlation in the right M2/3 segment by reader 2 ($r = 0.289$, $P = 0.278$).

The correlation between FDCTA and DSA was also excellent for reader 1 (mean $r = 0.867 \pm 0.094$) and reader 2 (mean $r = 0.839 \pm 0.447$), with no correlation in detecting vessel occlusion in the right M2/3 segment by reader 2 ($r = 0.447$, $P = 0.082$). For both readers, the mean sensitivity in detecting LVO using CTA was 96.8% (95% CI = 93.2–100.0), the mean specificity was 86.3% (95% CI = 88.2–95.2), the positive predictive value (PPV) was 92.8% (95% CI = 88.2–97.3), and the negative predictive value (NPV) was 95.7% (95% CI = 90.5–100.0). For FDCTA, the mean sensitivity was 97.9% (95% CI = 96.0–99.9), the specificity was 92.6% (95% CI = 84.3–100.0), the PPV was 94.4% (95% CI = 87.3–100.0), and the NPV was 93.8% (95% CI = 87.4–100.0).

Interrater agreement was excellent for both CTA evaluation (mean ICC = 0.93 ± 0.092) and FDCTA assessment (mean ICC = 0.932 ± 0.111).

Clot Burden Score

The median CBS was 6 (mean = 5.0 ± 2.422 , range = 1–8) in CTA measured by reader 1. In FDCTA datasets, the median CBS was 6 (mean = 5.06 ± 2.62 , range = 1–9). Reader 2 evaluated a median CBS of 6 in CTA (mean = 4.75 ± 2.35 , range = 1–8) and FDCTA

(mean = 5.2 ± 2.43 , range = 1–8). There was no significant difference between CTA and FDCTA for both readers (reader 1: $P = 0.751$; reader 2: $P = 0.164$).

Interrater agreement was excellent for both CTA evaluation (ICC = 0.984) and FDCTA assessment (ICC = 0.951).

Collateral Score

Median CS was 1 (mean = 1.56 ± 0.727 , range = 1–3) as assessed in CTA and FDCTA datasets (mean = 1.63 ± 0.619 , range = 1–3) by reader 1. Reader 2 scored a median CS of 1 in CTA (mean = 1.25 ± 0.683 , range = 0–3) and a median of 1 (mean = 1.4 ± 0.986 , range = 0–3) for the FDCTA datasets.

There was no significant difference between CTA and FDCTA for both readers (reader 1: $P = 0.718$; reader 2: $P = 0.582$).

Interrater agreement was excellent in CTA assessment (ICC = 0.754) and FDCTA assessment (ICC = 0.789).

Discussion

In the present study, we demonstrated that detection of LVO and evaluation of collateral status and clot burden is reliably possible when using VP-FDCT. Secondarily reconstructed FDCTA offers an image quality for confident diagnosis of LVO in patients with AIS (Figs. 1 and 2).

Available data revealed that image quality of FDCT is sufficient to exclude ICH (2). In addition, VP-FDCT is a technique providing information on perfusion status highly sensitive in detecting perfusion deficits (6). To our knowledge our study is the first specifically designed to assess image quality and diagnostic accuracy of FDCTA, generated out of VP-FDCT data, compared to CTA in patients with AIS due to LVO.

In our qualitative assessment, FDCTA was sufficient to delineate intracerebral vessel anatomy comparable to CTA. Saake et al. showed that the depiction of cerebral vasculature using FDCTA was significantly superior compared to CTA, a result we could not observe in our trial (22). However, in their study they used a different FDCT program (10s DRH) which is dedicated to image intracranial vasculature. In addition, the performed scan was triggered to the arterial filling. The program we used (Neuro-PBV IR) is primarily designed to measure the CBV, triggered to the “steady state.” Moreover, their sample size was even smaller than ours.

When compared to CT, FDCT is clearly inferior with regards to the assessment of brain parenchyma or signs of early infarction, Alberta Stroke Program Early CT Score (ASPECTS), respectively (23).

Fig. 1. Angiographic MIPs in the axial plain of an 85-year-old male patient before undergoing thrombectomy (2.5-h time-window, NIHSS of 18 at admission). Images from the same planes were reconstructed from VP-FDCT datasets (a–c) and from CTA datasets (d–f). ASPECT score as evaluated on CT images was 9. Both readers scored 6 for the CBS in both modalities and a CS of 1 for CT and 2 for FDCT data. Continuous arrows: occlusion of the distal M1 segment of the MCA. Dashed arrows: filling of the MCA territory via collaterals. Due to the latter phase of contrast, more filling can be delineated with VP-FDCT (c) when compared to CTA (f).

Although it is capable of SAH depiction, the quality of FDCT images is inferior when compared to CT (4). Delineation of small infratentorial SAH is particularly more challenging (9).

However, in line with recent literature presenting FDCTA as a feasible method in imaging intracerebral vasculature, our results showed an excellent correlation between FDCTA and CTA in detecting LVO (23). For the right M2/3 segment, there was no correlation between FDCTA, CTA, and DSA, respectively, when analyzed by reader 2. This might be due to motion artefacts despite a carefully head fixation during the rotational acquisition, as FDCT is sensitive to head motion. On the other hand, a minor experience of the reader might have contributed to this result as well, revealing that training is demanded for this highly specialized method.

Efforts to establish the neuroimaging triage in patients with AIS within the angio suite demand for a sensitive and specific LVO detection. To our knowledge, this is the first study describing similar sensitivity

and specificity of FDCTA and CTA in detecting LVO in AIS, in line with current literature (24). In our trial, FDCTA showed a high level of sensitivity and specificity for the detection of LVO and we could verify the accuracy of FDCTA in ICA or M1 occlusions. However, there are important differences on how FDCTA and CTA are acquired. In CTA, bolus tracking was applied, whereas in VP-FDCT, the bolus watching method was used. For the CBV it is important that there is contrast in the whole brain parenchyma, the so-called “steady state.” This is why the delay between injection and start of the second rotation is in the range of 16–19 s, depending on the opacification of the dural sinus. The acquisition of the CTA images is much quicker, as it is triggered by the opacification of the ascending aorta. In patients with LVO, brain areas depending on collateral supply might show no or only fair contrast enhancement when imaging of the vasculature is performed too early. Although being a static acquisition, VP-FDCT shows a later phase of contrast compared to single-phase CTA. Together with the

Fig. 2. Angiographic MIPs in axial plain of a 74-year-old female patient before undergoing thrombectomy (4-h time-window, NIHSS of 14 at admission). Images from the same planes were reconstructed from VP-FDCT datasets (a–c) and from CTA datasets (d–f). ASPECT score as evaluated on CT images was 4. A CBS of 6 was assessed in both modalities by both readers. A CS of 1 was assessed by both readers for CT and FDCT data. Continuous arrows: occlusion of the carotid-T of the distal ICA. Dashed arrows: in the VP-FDCT datasets, augmented filling of the MCA territory via collaterals can be defined (b, c) when compared to the CTA data (e, f).

rather small patient collective, this might explain the lower sensitivity and specificity values for CTA when compared to FDCTA.

VP-FDCT offers whole brain coverage, which enables the validation of CBS and CS. In contrast to the CBS, the correlation of the CS with CTA data was moderate. As explained before, the later phase of contrast compared to single-phase CTA might explain the different and non-correlating CS and might have misled to an overall slightly higher CS rating in FDCTA (Figs. 1 and 2). As VP-FDCT took place after CTA, this might have an impact on imaging the collateral status. However, we could not observe residual vessel contrast within the mask run datasets. Therefore, we think that this effect is rather negligible in comparison to the different principal of contrast application as described earlier. The later phase of contrast in intracranial vessels when using VP-FDCT might rather be an advantage over single phase CTA. It has already been shown that dynamic imaging, four-dimensional (4D)-CTA with an even higher resolution in time than mCTA, is superior to monophasic CTA in defining CBS and CS, as it offers a more accurate vessel

distinction (18,25). Multiphase CTA (mCTA) is a technique already known for better collateral evaluation compared to single-phase CTA (26,27). Thus, FDCTA might correlate better with mCTA. New, yet prototype-based, 4D-FDCTA could probably improve the delineation of collateral supply and the description of the clot (28). Yang et al. recently reported a comprehensive evaluation of vessel occlusions by using time-resolved FDCTA (29). However, these results are based on not commercially available prototypes, where issues such as C-arm rotational speed, patient safety, and radiation exposure first need to be addressed. This trial, however, is based on data acquired with a product already available and approved. Post-processing is implemented in clinical routine and reconstruction time is comparable to CTA (approximately 3–5 min) but depends on the operators' experience.

Radiation exposure might be comparable with an effective dose of 2.3 mSv for VP-FDCT and 3.6–5 mSv for CTP (30). Due to the rotation angle of 200°, dosimetry of FDCT is not equivalent to CT though and can rather be considered as approximation.

Moreover, in this FDCT approach, information on dynamic perfusion parameters, as offered by CTP, is missing. Static, already available VP-FDCT might not replace multimodal CT. However, as AIS is a dynamic event, especially in outpatients when prolonged imaging-to-groin-puncture time is conceivable, VP-FDCT might be used as an instrument to detect both changes in CBV that describe the infarct core and clot extent (5).

The availability of cross-sectional angiographic images at the site of treatment emphasizes that AIS diagnostic work-up and subsequent EVT is possible within the same room. Time is a crucial parameter and a primary determinant of outcome in patients with AIS due to LVO and thus a fast workflow is warranted (7). FDCT could offer the possibility to perform the whole neuroimaging triage within the angio suite. Patients with suspected LVO would be transferred directly to the angio suite, where hemorrhage would be excluded before invasive DSA. LVO, brain vasculature, and infarct core were visualized immediately before EVT would take place. As a result, imaging-to-groin-puncture time and imaging-to-reperfusion time could be shortened substantially.

Our study has several limitations. First, it is retrospectively designed, which bears the risk of selection bias. Second, possible effects of movement artefacts were not investigated. As patients' heads were fixed, no relevant artefacts were detected. However, our sample size is relatively small and the majority of our patients were under general anesthesia. As FDCT is sensitive to motion artefacts, patients under conscious sedation could show more movement of the head, resulting in an impaired image quality. Third, our study lacks an evaluation of patients with AIS due to LVO of the posterior circulation. As the posterior cranial fossa is a challenging region for imaging a dedicated evaluation is warranted.

In conclusion, our results suggest that FDCTA reconstructed from VP-FDCT allows reliable detection of ICA or MCA M1 segment occlusion and a diagnostic accuracy comparable to CTA. In addition, it may provide information concerning the clot extent and collateral supply.

Declaration of conflicting interests

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