Vessel territory mapping after cerebral revascularization surgery using selective angiographic flat detector perfusion imaging

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The technical feasibility and diagnostic potential of angiographic flat-detector perfusion imaging technique, combining digital subtraction angiography with a flat-detector computed tomography steady-state perfusion imaging, was explored in patients treated with direct or indirect revascularization surgery. This short communication is about an imaging modality with great potential for evaluation, comparison and grading of vascular perfusion territory areas and anatomical location selectively perfused by direct and indirect cerebral bypasses.

Keywords

Angiography; Bypass; Cerebral blood volume; Cerebral revascularization; Cone-beam computed tomography; Perfusion imaging

1. Introduction

Direct and indirect extracranial (EC)-intracranial (IC) revascularization surgery is an important treatment option for specific cerebrovascular conditions. The most accurate diagnostic modality to assess bypass efficacy is yet to be determined. In recent years, an imaging modality combining digital subtraction angiography (DSA) with flat-detector (FD) imaging became available and has proven its value in the practice of interventional neuroradiology [1, 2]. In contrast to conventional perfusion imaging techniques, this examination can be performed not only of the entire brain but also through selective contrast injection in the bypassed artery or ipsilateral external carotid artery. This allows an exact delineation of the bypass supply area and its volume compared to the total brain volume. The clinical significance of this imaging modality for individual patients is somewhat limited. However, application of this technique in the postoperative setting allows more precise evaluation in terms of bypass patency and dynamics, not only in hybrid operating rooms, evaluating freshly constructed bypasses, but also for comparison of different types of bypass (direct vs. indirect,

low vs. high flow) for research purposes or clinical practice in general. This paper illustrates this technique's technical feasibility and diagnostic potential in patients treated by direct or indirect revascularization surgery.

2. Materials and methods

2.1 Imaging experiments

Imaging was carried out on six patients (age range 29-65 years, both sexes) treated with direct or indirect revascularization procedures for moyamoya disease, moyamoya syndrome, refractory hypoperfusion syndrome or as part of complex cerebral aneurysm treatment by our neurovascular team between May 2018 and July 2019. The local ethics committee approved the study protocol (ref. nr. B300201836599). All patients gave written informed consent before inclusion. An overview of patient and bypass characteristics is displayed in Table 1.

2.2 Angiographic imaging and acquisition

Angiographic FD computed-tomography (CT) perfusion imaging was performed on a biplane angiographic system (Artis Zee with Pure® biplane system, Siemens Healthcare GmbH, Forchheim, Germany) at various time intervals after surgery. Image acquisition was made by two rotations of 6 seconds each (one mask run and one contrast fill run), in which 397 frames were obtained in a total scan angle of 200°. A contrast medium mixture of 25 mL contrast agent (Iomeron® 300, Bracco) with 50 mL saline was injected at a rate of 5 mL/s through a 4 French pigtail catheter, positioned at the level of the aortic root. Nine seconds after initiating contrast injection, the fill run was carried out. Selective contrast injection in bypass arteries or external carotid artery in case of burr holes was done by 4 French diagnostic catheters, using 4 mL contrast medium (Iomeron® 300, Bracco) mixed with 16 mL saline, injected at a rate of 2 mL/s injection rate

Table 1. Patient and bypass characteristics.

Patient no	Age (yr)/gender	Diagnosis	Grade*	Initial clinical presentation	Bypass type	Bypass function	Bypass capacity**	Bypass characteristics	Follow-up
1	51/M	MMD	III	Recurrent TIA	Direct	Flow-augmentation	Intermediate	STA-MCA R + L	No recurrent cerebrovascular events
2	58/F	MMS	III	Chronic headache and facial pain R	Indirect	Flow-augmentation	Low	Burr holes R	Pain syndrome stable with medication
3	49/F	MMD	III	Chronic headache R Bilateral iCVA Recurrent TIA	Indirect	Flow-augmentation	Low	Burr holes R + L	Recurrent hemodynamic TIA R ACM
4	65/F	GA	NA	Cerebral aneurysm with headache and vision loss (compression)	Direct	Flow-preservation	High	ECA-MCA L with venous graft	Uncomplicated
5	48/M	MMD	IV	ICH	Direct	Flow-augmentation	Low	STA-MCA L	Spontaneous bypass occlusion No recurrent cerebrovascular events
6	29/M	MMS	IV	Headache	Indirect	Flow-augmentation	Low	Burr holes R + L	Uncomplicated

M = male; F = Female, MMD = moyamoya disease; MMS = moyamoya syndrome; GA = Giant aneurysm; TIA = transient ischemic attack; R = right; L = left; STA = superficial temporal artery; MCA = middle cerebral artery: iCVA = ischemic cerebrovascular accident; ECA = external carotid artery; ICH = intracerebral hemorrhage; NA= not applicable.

*Grading at time of surgery according to Suzuki Grading System.

**Estimated bypass capacity: low ($<$ 50 mL/min); intermediate (50-100 mL/min); high ($>$ 100 mL/min).

with a 2-second delay. Perfusion imaging was performed during steady-state contrast quantity in the brain. Determination of used contrast dilutions, volumes and timings for angiographic perfusion imaging were based on personally communicated research and development experiences of the angiosuite vender, on analysis of the few reported publications about PBV imaging, and on our own experiences in scanning neurovascular patients not related to this study. Concerning the selective injections, the applied contrast dose was based on our own experiences with selective rotational angiography with FD CT, followed by adjustments in dilution after injections in clinical patients with no need for proper PBV measurements, e.g. angiographic CT angiography. During the study period, we observed that lowering the contrast dose to 25% yielded no differences in perfusion results. For both types of injections, we feel there is still room for lowering the contrast dose. However, no modifications were made to our scan protocols, because of risking introduction of non-uniformity between the scanned patients. The additional radiation dose exposure associated with the added FD CT PBV acquisitions was analyzed using the archived dose reports of the angiographic examinations. Brain dose (BD) of individual acquisitions were calculated using the registered dose area products using a Monte-Carlo software tool (PCXMC version 2.0.1.4 Rotation and CT-Expo version 2.4).

2.3 Image processing

After the acquisition, color-coded pooled blood volume (PBV) maps were calculated in units of mL contrast/1000 mL tissue using commercially available syngo DynaPBV Neuro software (Siemens Healthcare GmbH, Forchheim, Germany). Mask runs were available for use as non-enhanced CT scan series. Fill runs were used for rendering FD CT angiography images. Post-processing was executed on a Leonardo workstation to MIP images in para-axial and para-coronal views.

Perfusion volumes were calculated in mL using the syngo 3D Segmentation software. Selective contribution of the bypassed artery or burr holes were computed as percentages of total brain volume. Regional PBV values were quantitatively measured by drawing mirrored ROI on standardized cortical regions using the whole brain perfusion maps described by Struffert et al. [3]. Perfusion imaging data and results of PBV measurements are summarized in Tables 2 and 3. Fig. 1 shows an example of acquired images, including the drawn region of interests (ROI's).

3. Results and discussion

The effectiveness of flow-augmenting cerebral bypass surgery is mainly determined by clinical outcome. Also, radiological perfusion imaging techniques (i.e., Magnetic Resonance Imaging (MRI) perfusion, CT perfusion, and Single Photon Emission CT (SPECT)) have been used to assess and quantify the effects of revascularization on the brains' hemodynamics [4, 5]. Nevertheless, these techniques cannot determine the selective contribution of a bypass artery to brain perfusion.

This paper states that FD CT is an effective method to selectively visualize perfused brain areas of direct and indirect bypasses and obtain volumetric measurements of the bypass
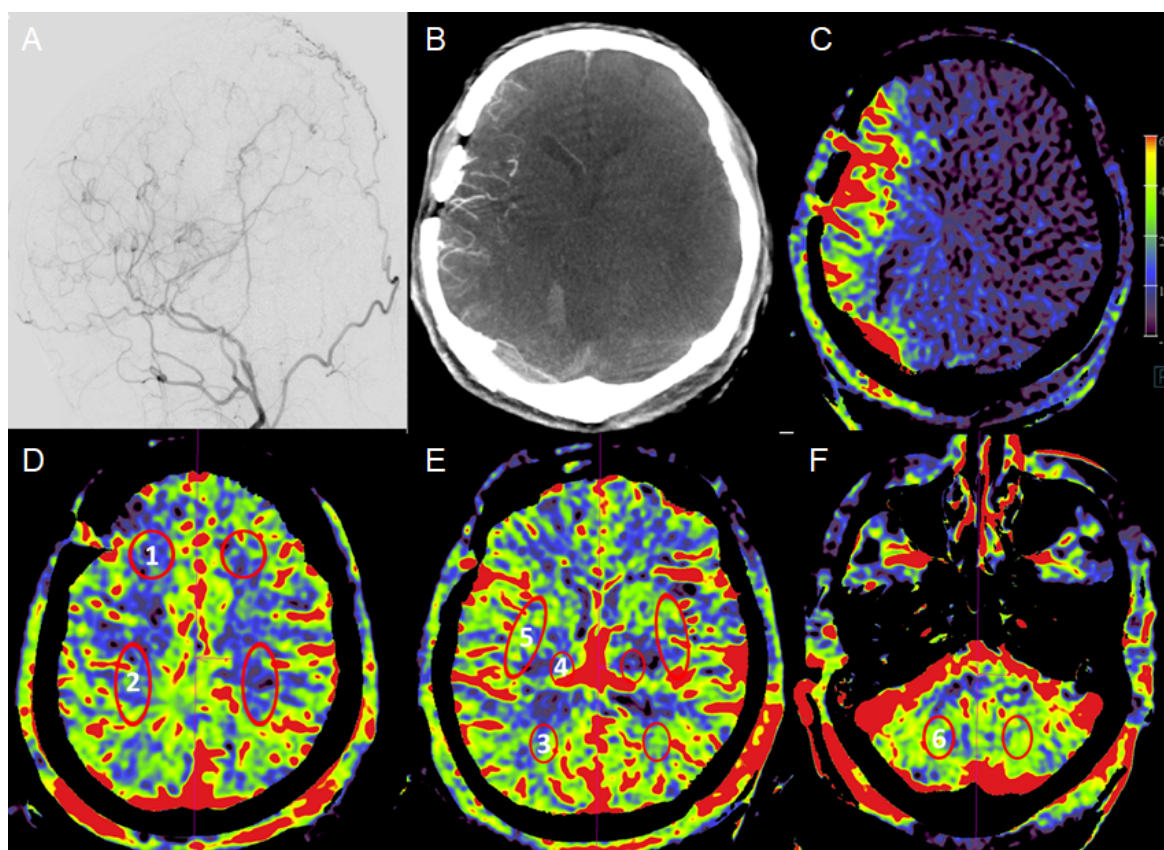
Fig. 1. A-F. Angiographic and PBV images of a 49-year-old female patient with moyamoya disease after bilateral burr hole surgery (Table 1, the patient no. 3). The top row shows lateral DSA projection (A) and axial reformed FD CT angiography image (B) with corresponding PBV image (C), acquired during selective right ECA injection. The bottom row (D-E-F) displays the drawn elliptic ROI's on axial reformed PBV images, acquired during pigtail contrast injection, based on regions defined by Struffert *et al*. [3].

Table 2. Perfusion imaging data.

Patient No.	Surgery-imaging time interval (months)		Total brain volume (mL)	Volume supply area bypass mL (%)	
1	Left	Right	1333	Left	Right
	1/2	1		614 (64%)/533 (40%)	519 (39%)
2	6		1108	119 (11%)	
3	Left	Right	1169	Left	Right
	8	11		79 (7%)	368 (31%)
4	10		1185	329 (28%)	
5	1		1242	0	
6	Left	Right	1470	Left	Right
	5	12		140 (10%)	303 (21%)

mL = milliliter.

supply area. FD CT scans were successfully performed in five out of six patients, with significant motion artifacts present in one patient (patient no. 5). There were no clinical adverse events. The calculated average BD of individual FD CT perfusion scans was lower than the BD of conventional CT perfusion scans in our institution (34.9 mGy and 52.5 mGy, respectively).

We observed that the brain territories perfused by a direct bypass (superficial temporal artery (STA)- middle cerebral artery (MCA) and high flow vein graft bypass) were generally more extensive than the areas supplied by collaterals formed after indirect revascularization surgery. Burr hole revascularization provides well-distributed cortical perfusion. There was still some brain perfusion by leptomeningeal collaterals formed through the craniotomy site in one patient (patient no. 5) with an occluded STA-MCA bypass. Although only one patient (patient no. 4) with a high-flow venous graft bypass has been studied, the perfusion supplied by the venous

Table 3. Parenchymal blood volume values in mL contrast/1000 mL tissue units, mean values, and standard deviations.

Patient No.	ROIs on the left						ROIs on the right					
	1	2	3	4	5	6	1	2	3	4	5	6
1	30.5	20.6	40.7	30.6	29.4	30.7	31.5	31.0	43.1	32.2	35.6	34.2
2	26.3	17.9	25.7	31.0	26.4	34.8	28.1	22.1	33.4	27.6	24.9	34.1
3	27.3	29.1	28.5	23.4	30.9	30.6	22.7	20.7	35.0	26.6	32.4	35.5
4	22.7	20.3	36.2	28.6	30.7	40.1	27.7	21.5	36.5	31.4	29.7	38.6
5	26.6	13.8	26.8	33.0	44.8	21.4	38.4	44.5	20.4	45.3	49.8	25.6
6	34.7	30.7	30.1	28.6	37.0	51.4	27.5	43.1	35.7	34.0	41.6	52.8
Mean	28.0	22.1	31.3	29.2	33.2	34.8	29.3	30.5	34.0	32.9	35.7	36.8
SD	4.1	6.6	5.9	3.3	6.7	10.2	5.3	11.0	7.5	6.7	8.9	8.9

ROI = region of interest. ROIs were placed manually based on regions defined by Struffert et al. [3]: (1) frontal subcortical white matter, (2) parietal subcortical white matter, (3) occipital subcortical white matter, (4) thalamus, (5) lateral basal ganglia, (6) subcortical white matter of cerebellum; SD = standard deviation.

graft in this patient was less than the average STA-MCA bypass observed. We did not expect this and added to our earlier (unpublished) observation that STA-MCA bypass might provide sufficient flow for a proximal MCA branch (i.e., M1 or M2 segments). In the three patients (patient no. 2, 3 and 6) treated with multiple burr hole surgery, the perfused brain volumes by indirect bypass varied extensively from 79 mL (7%) of 1169 mL total brain volume to almost one-third of the brain volume (Table 2).

This study has several limitations. Due to the rarity of patients undergoing surgical cranial revascularization, inclusion of a large number of patients is not easy. Therefore, only six patients were included in our study. However, the principal aim of this study is to highlight the feasibility of the angiographic FD CT perfusion technique. Another remark is that the technique is not superior compared to conventional brain perfusion imaging techniques in terms of performing a full width perfusion imaging. Though, we believe that this technique has clear advantages compared to the other modalities. It provides information about both selective bypass perfusion volumes and (semi-) quantitative perfusion values in the form of PBV values. Important to note is that this imaging modality can be performed in a hybrid operation theatre, enabling on the spot perfusion information of freshly constructed bypasses. It is beyond question that this imaging technique requires further exploration.

A drawback of the FD CT scanning technique lies in its invasiveness and the concomitant (low) risk of thromboembolic complications as with any catheter angiographic examination.

A correct interpretation of the PBV values in our patient group is difficult with the still unknown real significance of absolute PBV values. Struffert et al. [1, 6] reported that cerebral blood volume (CBV) color maps and absolute values obtained with FD CT correlated well with the CBV values and maps acquired with standard CT techniques in pa-

tients with acute symptoms of cerebral ischemia. However, another study in patients with delayed cerebral ischemia comparing FD CT PBV imaging with MRI perfusion showed that PBV is a composite perfusion parameter with both blood flow and blood volume weightings [7]. The uncertainty about the quantitative value of the PBV measurements might partly be dealt with using index ratios of regional PBV values between the two hemispheres. A subsequent issue is to define the anatomical areas and sizes for measuring the PBV values.

This study was conducted in a well demarcated study group, on the initiative of our neurosurgeon, scanned in the best conditions. However, this is not precluding the use of the PBV technique in patients with other neurovascular diseases. For instance, despite potential drawbacks, such as susceptibility for motion artifacts, FD CT perfusion can be of use in an one-stop-shop setting for management of patients with acute ischemic stroke. Precious time from symptom onset to recanalization can be reduced by skipping prior conventional cross-sectional imaging.

4. Conclusions

This paper demonstrates that FD CT is a promising imaging tool to evaluate brain perfusion anatomy after direct and indirect revascularization procedures and grade and compare the vascular contribution of bypass arteries and/or burr holes. This technique's main advantages are that it can be easily implemented in the angiography suite as an add-on tool to conventional angiography and can demonstrate the exact supply areas in 3D of individual bypass or burr hole arteries. The clinical significance of this study for individual patients is rather limited. However, thanks to this technique, postoperative evaluation in terms of bypass patency and dynamics is now possible which enables comparison of different types of bypasses for research purposes. Further research is warranted to explore FD CT perfusion scanning's role in bypass patients in specific and neurovascular patients in general.

Abbreviations

ASL, arterial spin labeling; EC, extracranial; ECA, external carotid arteries; FD, flat-detector; IC, intracranial; PBV, pooled blood volume; STA, superficial temporal artery.

Author contributions

TM performed revascularization procedures. TVDZ executed angiographic imaging and image processing. TVDZ drafted the article. TVDZ, TM and AM participated in data interpretation. AM, LY, MV and TM reviewed the manuscript. All authors contributed to editorial changes in the manuscript. All authors read and approved the final manuscript.

Ethics approval and consent to participate

All procedures performed in studies involving human participants were in accordance with the institutional and/or national research committee's ethical standards and the 1964 Helsinki declaration and its later amendments or comparable

ethical standards. The Central ethical committee board approved this study of Antwerp University Hospital (approval number B300201836599). All subjects signed informed consent.

Acknowledgment

Conflict of interest

The authors declare no conflict of interest.

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