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Title page

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MR vessel-encoded arterial spin labeling with the placement of metallic items to visualize the territorial blood flow after extracranial-intracranial bypass surgery: A proof-of-concept study

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Conflict of interest

None

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<u>Title</u>

MR vessel-encoded arterial spin labeling with the placement of metallic items to visualize the territorial blood flow after extracranial-intracranial bypass surgery: A proof-of-concept study

Abstract

Background: Depiction of bypass blood flow in patients who received extracranial-intracranial (EC–IC) bypass surgery is important for patient care.

Purpose: To develop a vessel encoded arterial spin labeling (VE-ASL) method using surgical staples as a magnetic resonance (MR)-conditional product in patients who received EC–IC bypass surgery.

Methods: Pseudo-continuous labeling was used for VE-ASL acquisition with a 3-tesla MR unit. First, an experimental study was conducted to determine the appropriate number of surgical staples to obtain a spatially sufficient saturation effect. Thereafter, 4 healthy normal volunteers underwent a VE-ASL study to confirm the sufficiency of the saturation effect to the right or left common carotid artery. Finally, VE-ASL scanning was performed in 7 patients after EC–IC bypass surgery to confirm the ability of VE-ASL to visualize the territorial bypass perfusion. All qualitative evaluation was performed by two neuroradiologists using a three-point grading system (2=good, 1=moderate, 0=poor).

Results: A quantity of 200 staples was found to be appropriate for VE-ASL scanning. In healthy volunteers, one neuroradiologist rated the images of all 4 cases as good, while

the other rated 3 cases as good, and 1 case as moderate. For the 7 patients after EC–IC bypass surgery, one neuroradiologist rated all 7 cases as good, and the other rated 6 cases as good and 1 case as moderate.

Conclusion: VE-ASL using surgical staples might be useful for the evaluation of territorial bypass perfusion in patients after EC–IC bypass surgery.

<u>Keywords</u>

CNS; MR-Diffusion/Perfusion; Imaging Sequences

Introduction

Arterial spin labeling (ASL) is widely recognized as a non-invasive technique using magnetic resonance imaging (MRI) to visualize cerebral blood flow. Pseudo-continuous-ASL (pCASL) is currently the most widely used form of ASL because it enables to achieve the acquisition with a low specific absorption rate (SAR) and a high signal-to-noise ratio (SNR) (1). An alternative approach, vessel encoded ASL (VE-ASL), was introduced over the last decade to visualize the territorial blood flow with selective labeling of an individual arterial blood vessel, and its clinical utility for the assessment of various intracranial diseases has been investigated in several studies (2-10). Visualization of the regional perfusion is very important for elucidating the local hemodynamics in patients with steno-occlusive disease or hypervascular disease, or patients following extracranial-intracranial (EC-IC) bypass surgery. However, VE-ASL generally needs specific design of pulse sequence in image acquisition and at present can be performed only by a limited number of advanced MR scanners. In contrast, Hagiwara et al. reported another approach for the acquisition of VE-ASL; they suppressed the vessel signal selectively by placing a metallic item on the subject's neck (11). Although this methodology allows the acquisition of VE-ASL without a specifically tailored pulse sequence, safety concerns remain due to the use of non-medical-grade objects—namely, stainless-steel nuts and bolts. We propose the use of medical grade, MR-conditional products to improve the safety of this modality.

In the present study, we developed a modified VE-ASL methodology using surgical staples as an MR-conditional product for placement on the subject's body surface (12). In addition, to assess the clinical feasibility of this technique, we assessed the VE-ASL images in patients who had undergone extracranial-intracranial bypass surgery to confirm that bypass blood flow was selectively visualized on the VE-ASL images.

Materials and Methods

The study protocol was approved by our institutional review board, and written informed consent was obtained from all participants.

Experimental study

We conducted pCASL perfusion imaging with a 3-tesla MR unit (Discovery 750w

3.0T; GE Healthcare, Chicago, IL). We used a whole-brain three-dimensional spiral fast-spin echo sequence with the following imaging parameters; eight spiral arms of 512 points each, a z-direction phase encoding value of 34, section thickness of 4 mm, TR of 5306 ms, post-labeling delay of 2.525 s, NEX 3, and total acquisition time of 5 min 8 s. An AW Volumeshare5 workstation and a Zio Station2 were used for image processing. For the VE-ASL to generate the susceptibility effect for the suppression of the target vessel, we used surgical staples (Precise Skin Stapler S, 3M, Two Harbors, MN, USA) which is an MR-conditional product, manufactured from nickel-chromium stainless steel (size 6.9×3.6 mm, weight 34.0 mg). For the experimental study, we first measured the range of the magnetic susceptibility effect obtained from the surgical staples during image acquisition when locating them nearby the cylindrical phantom (Fig. 1). Based on the relationship between the number of suture staples and the size of the susceptibility effect, we determined the appropriate number of suture staples to provide a sufficient signal saturation. Next, we assessed the degree of temperature increase around the surgical staples by monitoring a temperature seal attached to the cylindrical phantom.

Pre-clinical assessment in healthy volunteers

Four healthy volunteers (all males; age range: 31–51 yrs) received two types of ASL scanning: conventional ASL and VE-ASL by the placement of surgical staples on their neck surface. The VE-ASL included two acquisitions of the perfusion images with the suppression of the right common carotid artery (i.e., perfusion images of the left carotid and vertebrobasilar arteries) and the left carotid artery (i.e., perfusion images were visually evaluated by two board-certified neuroradiologists in a blinded fashion. Evaluation was performed based on a 3-point grading system, with a score of 2 indicating good (the signal intensity of the target vessel was clearly suppressed), a score of 1 moderate (moderately suppressed), and a score of 0 poor imaging (not or mostly not suppressed).

<u>Clinical assessment in patients who received extracranial-intracranial</u> <u>bypass surgery</u>

From January 2019 to September 2021, 7 consecutive patients (2 males and 5 females; age range: 45–76 yrs) who had undergone EC–IC bypass surgery and consented to additional VE-ASL scanning were included in the current study. All patients were received two types ASL scanning: conventional ASL and VE-ASL using surgical staples. The VE-ASL was performed by placing the surgical staples on the surface of the skin

around the lower auricle to suppress the bypass blood flow only. After the acquisition of two ASL scans, post-processing was performed by subtracting the VE-ASL from conventional ASL to create the perfusion imaging depicting the bypass blood flow only. Visual evaluation was conducted by the two above-mentioned board-certified neuroradiologists using a 3-point grading system, with a score of 2 indicating good (well-depicted bypass blood flow with clear selectiveness), a score of 1 moderate (moderately depicted bypass flow), and a score of 0 poor imaging (poorly depicted bypass flow).

Statistical analysis

In visual evaluation of both healthy volunteers and patients after EC–IC bypass surgery, the kappa (κ)-test was used for the assessment of inter-observer agreement between the two neuroradiologists according to the following scale: 0–0.2, poor agreement; 0.21–0.4, fair agreement; 0.41–0.6, moderate agreement; 0.61–0.8, good agreement; and 0.81–1.0, excellent agreement.

Results

Experimental study

The relationship between the number of surgical staples and the range of magnetic susceptibility artifacts observed on the cylindrical phantom is presented in Fig. 2. The range of magnetic susceptibility effects increased with increasing number of surgical staples until reaching around 200 staples (6,800 mg), and reached a plateau when the number of surgical staples was above 200. From this result, we decided to use a block of 200 surgical staples for the subsequent analysis on human subjects. No medically relevant temperature increase was detected around the surgical staples by the temperature seal attached to the cylindrical phantom.

<u>Pre-clinical assessment in healthy volunteers</u>

All ASL scanning for the four healthy volunteers was successfully performed without any complications. In the visual evaluation in VE-ASL by two neuroradiologists, one rated all of images as score 2 (good: the signal intensity of the target vessel was clearly suppressed), whereas the other rated three cases as score 2, and one case as score 1 (moderate: moderately suppressed). A representative case of VE-ASL images in a healthy volunteer is presented in Fig. 3. The inter-observer agreement between the two neuroradiologists in this visual evaluation was as follows: $\kappa = 0.78$ (good agreement).

Clinical assessment in patients who received extracranial-intracranial

<u>bypass surgery</u>

In the scanning of patients, all acquisitions were successfully performed without any complications, just as for the scanning of the healthy volunteers. In the visual assessment by the two neuroradiologists, one rated all of cases as score 2 (good: well-depicted bypass blood flow with clear selectiveness), whereas the other rated six cases as score 2 and one case as score 1 (moderate: moderately depicted bypass flow) (Table 1). The inter-observer agreement between the two neuroradiologists in this evaluation was as follows: $\kappa = 0.86$ (excellent agreement). A representative clinical case of VE-ASL is presented in Fig. 4.

Discussion

The present study demonstrated a variation on the VE-ASL method using surgical staples as an MR-conditional product, and showed that the bypass blood flow could be

selectively visualized by this method in patients who had undergone EC-IC bypass surgery. For the evaluation of territorial perfusion after EC-IC bypass surgery, digital subtraction angiography (DSA) is considered the gold standard to selectively visualize the bypass blood flow by the catheterization of the specific bypass blood vessel. However, DSA is invasive, and risks both radiation exposure and potential adverse reactions to contrast material (13,14). Unlike DSA, VE-ASL can successfully visualize the territorial perfusion via bypass blood flow noninvasively and within a short scanning time. In addition, the VE-ASL methodology in the current study could be conducted using a conventional ASL sequence design: unlike in the conventional VE-ASL, which requires the design of a complex gradient pulse sequence for the MR unit. Clinically, the evaluation of territorial perfusion via bypass flow is crucial for the detection of bypass failure in patients after EC-IC bypass surgery (15). From this perspective, we believe that the VE-ASL technique introduced in the current study may be useful for the noninvasive post-operative assessment of bypass blood flow in patients after EC-IC bypass surgery.

A previous study investigated the utility of an extrinsic metallic substance to obtain the vessel selectivity in ASL acquisition (11); this previous study utilized stainless-steel nuts and bolts. In contrast, the current study utilized surgical staples, which are an MR-conditional product. Although no complications were reported in either the previous or current study, we believe that the overall safety may be more reliable when using an MR-conditional product as an extrinsic metallic substance. Appropriate number of surgical staples were considered around 200 from the relation between the range of metallic artifact and the number of surgical staples obtained in experimental analysis; our present findings suggest a range of metallic artifact as the block of 200 surgical staples could reach even the common carotid artery which was located at a slightly deep site away from the neck surface, because the depth of the magnetic susceptibility effect was observed to be rather long (~25-30 mm) in the experimental analysis. However, it may be difficult to achieve sufficient saturation in some larger people, typically Europeans or Americans, in order to provide sufficient susceptibility to reach the common carotid artery because of its deeper location away from the body surface. For the clinical use of this technique, the number of surgical staples should thus be optimized based on the specific location of the target vessel and the patient's size. In addition, to make the examination comfortable for the patients, the same amount of material with the alloy of the same composition as the block of 200 surgical staples concealed in gel or a rubberlike polymer would likely be better for placement at the

patient's head or neck surface, rather than placing the block of 200 surgical staples directly.

The VE-ASL method used in the current study depicted the territorial perfusion from bypass blood flow in all but one of the patients. The exception was a patient who was classified as having not clear but moderate selectiveness by one neuroradiologist, and clear selectiveness of the ASL perfusion signal by the other. We speculate that the visibility of the territorial perfusion using VE-ASL might differ somewhat based on characteristics of the target vessel, such as the vessel diameter, the flow velocity, and the angle between the vessel and imaging plane (16). In addition, VE-ASL with the methodology used in the current study was obtained by subtraction of the conventional ASL images from the target vessel-saturated ASL images. Such a post-processing scheme might also affect the complexity of the image interpretation in VE-ASL images. A further optimization study investigating the acquisition conditions, (e.g., the number and location of surgical staples) will be needed before this approach can be applied for the treatment of various other diseases.

The current study has several limitations. First, the number of patients was small.

However, VE-ASL was successfully performed in almost the entire study population. We believe that VE-ASL using the present methodology will prove similarly successful in larger cohorts, although some optimization of the acquisition technique might be needed based on the target disease and vessels. Second, we did not compare the imaging findings of VE-ASL to DSA. Therefore, our technique might require further validation in a future study. Third, we investigated patients only after the bypass surgery, because the main purpose of this study was to assess the territorial bypass flow using VE-ASL. However, the difference in the territorial blood flow between before and after the treatment is of interest, and its investigation also awaits a future study.

In conclusion, VE-ASL for visualization of the territorial perfusion map from bypass blood vessels was successfully performed non-invasively using an MR-conditional product only. This technique can be used as a supportive tool for the assessment of patients following an EC–IC bypass surgery.

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Conflict of interest

None

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Table and Figure captions

No of case	Score by Radiologist A	Score by Radiologist B
1	2	2
2	2	2
3	2	2
4	1	2
5	2	2
6	2	2
7	2	2

Table 1. Result of visual assessment in patients who received EC bypass surgery

Fig. 1. Measurement of magnetic susceptibility effect by surgical staples.

Surgical staples were placed near the cylindrical phantom. The magnetic susceptibility effect obtained by the surgical staples was measured by the length of the negative signal area in the cylindrical phantom (red two-headed arrow).

Fig. 2. Relationship between the range of magnetic susceptibility effects and the number of surgical staples.

The graph shows that the magnetic susceptibility effect increased with increasing number of surgical staples until the number of staples was around 200 (6,800 mg). When the number of surgical staples reached around 200–250, the magnetic

susceptibility effect exhibited a plateau.

Fig. 3. Vessel encoded ASL (VE-ASL) in healthy volunteers.

VE-ASL images with signal suppression to the left common carotid artery are shown. Territorial perfusion corresponding to the left carotid artery was clearly saturated in VE-ASL images.

Fig. 4. Representative VE-ASL imaging in a patient after EC–IC bypass surgery.

VE-ASL imaging was performed in a patient who has undergone left side EC–IC bypass surgery. The STA-MCA bypass route was observed in TOF-MRA (a: arrowhead). In the VE-ASL image overlaying the ASL control image (i.e., anatomical images), left territorial perfusion from the bypass flow was clearly observed (b, c and d).













