

Vessel-selective, non-contrast enhanced, time-resolved MR angiography with vessel-selective arterial spin labeling technique (CINEMA–SELECT) in intracranial arteries

Masanobu Nakamura · Masami Yoneyama ·
Takashi Tabuchi · Atsushi Takemura ·
Makoto Obara · Satoshi Tatsuno · Seishi Sawano

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Abstract We demonstrate the feasibility of the vessel-selective, non-contrast, time-resolved magnetic resonance angiography (MRA) technique, “contrast inherent inflow enhanced multi-phase angiography combining vessel-selective arterial spin labeling technique (CINEMA–SELECT)”. This sequence consists of two major techniques: pulsed star labeling of arterial regions (PULSAR) and Look–Locker sampling. We hypothesize that this technique allows selective labeling of single intracranial arteries, consisting of high-resolution four-dimensional data with a wide coverage of the brain. In this study, a new vessel-selective, time-resolved angiographic technique is demonstrated that can produce individual angiograms non-invasively by labeling the principal arterial vessels proximal to the circle of Willis. Clear vessel delineation is achieved, and the separation of the three vessels is evident in healthy volunteers. This technique could play an important role in the assessment of the structure and hemodynamics of intracranial arteries without the use of contrast agents.

Keywords Vessel selective · Time-resolved MRA · Arterial spin labeling · MRA · PULSAR

Abbreviations

3D	Three-dimensional
3D-T1-TFE	3D T1 turbo field echo
ASL	Arterial spin labeling
AVM	Arteriovenous malformations
BA	Basilar artery
CINEMA	Contrast inherent inflow enhanced multi-phase angiography
CINEMA–FAIR	Contrast inherent inflow enhanced multi-phase angiography combining multiple phases flow-sensitive alternating inversion recovery
CINEMA–SELECT	Contrast inherent inflow enhanced multi-phase angiography combining vessel-selective ASL technique
DSA	Digital subtraction angiography
FA	Flip angle
FAIR	Flow-sensitive alternating inversion recovery
FOV	Field of view
ICAs	Internal carotid arteries
IRB	Institutional review board
MIP	Maximum intensity projection
MRA	Magnetic resonance angiography
MRDSA	Magnetic resonance digital subtraction angiography
MRI	Magnetic resonance imaging
PULSAR	Pulsed star labeling of arterial regions
SENSE	Sensitivity encoding
TE	Echo time
TI	Inversion time
TOF	Time of flight
TR	Repetition time

M. Nakamura (✉) · M. Yoneyama · T. Tabuchi · S. Tatsuno ·
S. Sawano
Yaesu Clinic, 2-1-18 Nihonbashi, Chuou-ku, Tokyo, Japan
e-mail: risen1@mac.com

A. Takemura · M. Obara
Philips Electronics Japan, Tokyo, Japan

1 Introduction

Hemodynamic information is required for the accurate diagnosis, effective treatment, and follow-up examination of numerous diseases, e.g., arteriovenous malformation (AVM), carotid artery stenosis, and moyamoya disease [1, 2]. Clinically, such assessments are generally performed by X-ray digital subtraction angiography (DSA) which provides excellent temporal and spatial resolution, but this is an invasive procedure [3]. X-ray DSA provides high temporal and spatial resolution, but has a number of drawbacks: they are invasive procedures that expose the patient to ionizing radiation, and carry a risk of contrast agent reaction, silent ischemia, or even stroke. A non-invasive alternative, such as one making use of magnetic resonance imaging (MRI), is, therefore, desirable.

In addition to standard time of flight (TOF) [4] and phase-contrast [5] angiographic techniques, MRI is also able to provide angiographic contrast by making use of the principles of arterial spin labeling (ASL) [6–9]. ASL was introduced as an MR technique that enables quantitative measurement and/or MR angiography (MRA) of cerebral blood flow without the need for a contrast agent. Using this approach, we proposed a method for non-contrast volumetric time-resolved MRA by combining flow-sensitive alternating inversion recovery (FAIR) [10] spin labeling with a three-dimensional segmented Look–Locker [11] readout to acquire multiple temporal time frames [12]. This technique requires no catheter insertion or contrast agent and provides useful qualitative information on the morphologic and dynamic filling of intracranial vessels. However, it only allows to visualize all the brain vessels together, and it cannot select specific vessels such as the internal carotid arteries (ICAs), the basilar artery (BA), or the collateral circulation. Vessel-selective information regarding the cerebral vasculature is of interest for a variety of patient groups. For example, in patients with stenocclusive disease, this information reveals the extent of collateral blood flow, which is important for maintaining the viability of the brain tissue when the primary feeding artery is compromised [13].

We have proposed a vessel-selective volumetric non-contrast, time-resolved MRA technique termed contrast inherent inflow enhanced multi-phase angiography combined with a vessel-selective ASL technique (CINEMA–SELECT). This sequence consists of two major techniques: pulsed star labeling of arterial regions (PULSAR) [14] and Look–Locker sampling. The former is a standard ASL technique that can be selective in labeling of the blood in individual vessels. Look–Locker sampling allows monitoring of the temporal dynamics of blood inflow. The combination of the two techniques enables one to sample not only a single image, but also a series of images after

each labeling pulse. Therefore, this method theoretically allows monitoring of the temporal dynamics of blood inflow in specific vessels like the ICAs, the BA, or the collateral circulation. We hypothesize that CINEMA–SELECT allows selective labeling of target intracranial arteries, consisting of high-resolution four-dimensional data with wide coverage of the brain. In this study, the feasibility of this method for intracranial angiography was validated in healthy volunteers.

2 Materials and methods

2.1 Theory and pulse sequence

The CINEMA–SELECT technique combines PULSAR with a three-dimensional (3D) segmented T1-weighted turbo field echo sequence (T1-TFE) (Fig. 1). The PULSAR preparation scheme with the Look–Locker sampling was used for spin labeling in this study. In this sequence, control and labeling pulses are performed at the same location. Each measurement of the sequence is composed of two acquisitions with identical readout. Prior to the T1-TFE readout of the first acquisition, a labeling pulse was applied. For the second acquisition, a control pulse was applied. Upon completion of the two acquisitions, the corresponding temporal phases of the two acquisitions with identical inversion delay were subtracted. Spins moving into the imaging volume (e.g., those from flowing blood) experience only the labeling pulse. Therefore, their signal is retained after the subtraction procedure, and they appear bright. Signal from static tissues cancels out after subtraction of corresponding datasets from two acquisitions with identical inversion time (TI).

2.2 Volunteer study

This study was approved by the local institutional review board, and written informed consent was obtained from all subjects. Healthy volunteers who had no contraindications to MRI and no recent health problems or surgery were recruited. In total, 10 healthy volunteers [8 men, 2 women; mean age: 36.5 years (range 29–42 years)] were included in this study. All experiments were performed on a 3.0-T scanner (Achieva, Philips Healthcare, Best, The Netherlands) with Nova Dual gradients (maximum gradient strength of 80 mT/m, maximum slew rate of 200 T/m/s) and an 8-element head coil.

For each volunteer, a 3D TOF-MRA measurement was performed for comparing the image quality of CINEMA–SELECT and for positioning of the labeling plane with subsequent three—plane maximum—intensity projection (MIP) reconstructions. The sequence parameters of TOF-MRA

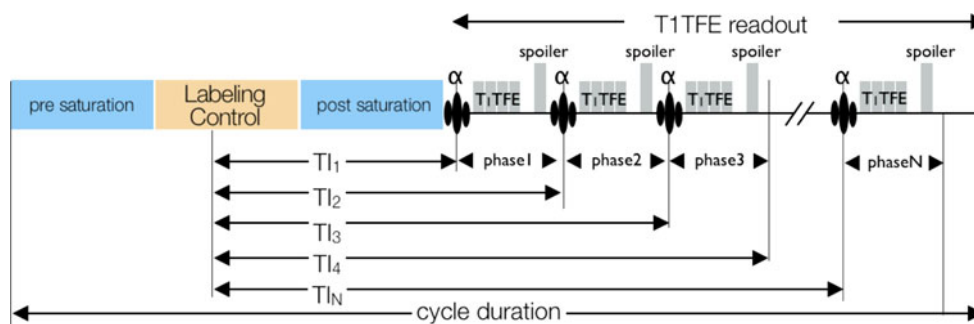


Fig. 1 Pulse diagram of the CINEMA-SELECT sequence. The CINEMA-SELECT technique consists of a PULSAR-based ASL sequence; pre-saturation pulse, labeling/control pulses, and a 90° dephasing pulse. In the first, an optimized four-pulse water excitation technique pre-saturation sequence is applied. Finally, a 90° dephasing pulse is applied with the same geometry as during the pre-saturation sequence to provide a clear starting time of the bolus. A segmented 3D T1-weighted gradient echo sequence (3D-T1-TFE) is acquired

after labeling or control pulses. This cycle will be repeated for the number of shots of the gradient echo sequence. The total label or control experiment duration is controlled by the cycle duration. Look-Locker sampling (i.e., multiple inversion time) was used following each labeling pulse for obtaining time-resolved MRA, enabling visualization of virtual dynamic filling of flowing blood. Upon completion of data acquisitions, corresponding temporal phases of two acquisitions with identical inversion delay are subtracted

were: a field of view (FOV) of $220 \times 200 \text{ mm}^2$, matrix of 400×512 , 3D acquisition with $100 \times 0.65 \text{ mm}$ slices, flip angle (FA) of 17°, repetition time (TR) of 4.5 ms, echo time (TE) of 2.2 ms, sensitivity encoding (SENSE) factor of 2.0, scan duration 6 min.

In this study, a transverse labeling plane was positioned approximately 8 cm below the circle of Willis. Three cycles of the sequence were performed:

1. labeling of left circulation (left ICA);
2. labeling of right circulation (right ICA); and
3. labeling of posterior circulation (vertebral arteries)

Planning of the labeling volume was performed on the basis of three MIPs of the TOF-MRA in a way similar to that of Hendrikse et al. [15]. In short, the size of the labeling slab can be adjusted in one direction and is infinite in the other two directions. For the selective labeling of ICAs, an oblique sagittal labeling slab was chosen based on the axial and coronal MIPs of the circle of Willis. The slab was aligned such that each ICA was labeled independently and signal contribution from the contralateral ICA, as well as the basilar and vertebral arteries, was avoided by lateral angulations of the posterior and proximal parts of the labeling slab. For selective labeling of the posterior vessels, both axial and sagittal MIPs of the circle of Willis were used together with the native TOF images for verification of a minimal amount of contamination by the posterior labeling to both ICAs, which was not always completely avoidable (Fig. 2a).

CINEMA-SELECT imaging was then performed on all volunteers with the following parameters: FOV of $220 \times 200 \text{ mm}^2$, matrix of 224×162 , 3D acquisition with $100 \times 1 \text{ mm}$ slices, resolution of $0.98 \times 1.36 \times 1.00 \text{ mm}^3$, FA of 10°, TR of 4.5 ms, TE of 2.2 ms,

bandwidth of 724 Hz/pixel, number of excitations 1, SENSE factor of 3.0, inversion slab width of 60 mm, temporal resolution/final TI of 220 ms/2115 ms, number of acquired time points 10, total scan time of 3 major vessels (ICAs and posterior vessels) $\times 5 \text{ min} = 15 \text{ min}$. Images of dynamic inflow were obtained with successive acquisitions with labeling delay times of 135, 355, 575, 795, 1015, 1235, 1455, 1675, 1895, and 2115 ms. CINEMA-FAIR was performed for comparing the labeling efficiency in all subjects with the following sequence parameters: FOV of $220 \times 200 \text{ mm}^2$, matrix of 224×162 , 3D acquisition with $100 \times 1 \text{ mm}$ slices, resolution of $0.98 \times 1.36 \times 1.00 \text{ mm}^3$, FA of 10°, TR of 4.5 ms, TE of 2.2 ms, bandwidth of 733 Hz/pixel, number of excitations 1, SENSE factor of 3.0, scan time of 5 min, temporal resolution/final TI of 200 ms/2115 ms. Labeling delay times were performed the same as for CINEMA-SELECT.

2.3 Image analysis volunteer study: signal intensity of the stationary tissue and blood stream

We used the contrast-to-noise ratio (CNR) to determine the temporal change of the blood and stationary tissue. The signal intensity of stationary tissues (gray matter and white matter in this case) and flowing blood (ICA territory and posterior territory) were measured from images of the volunteer subjects. Circular-shaped regions of interest (ROIs) were placed on the subtraction images of labeling and control images in the white matter, gray matter, and at six different locations (both middle cerebral arteries, anterior cerebral arteries, and posterior cerebral arteries). Each sampling was performed at the location shown in Fig. 2a, by use of free DICOM software (OsiriX Medical Imaging Software, OsiriX, Atlanta, GA, USA). The CNR between

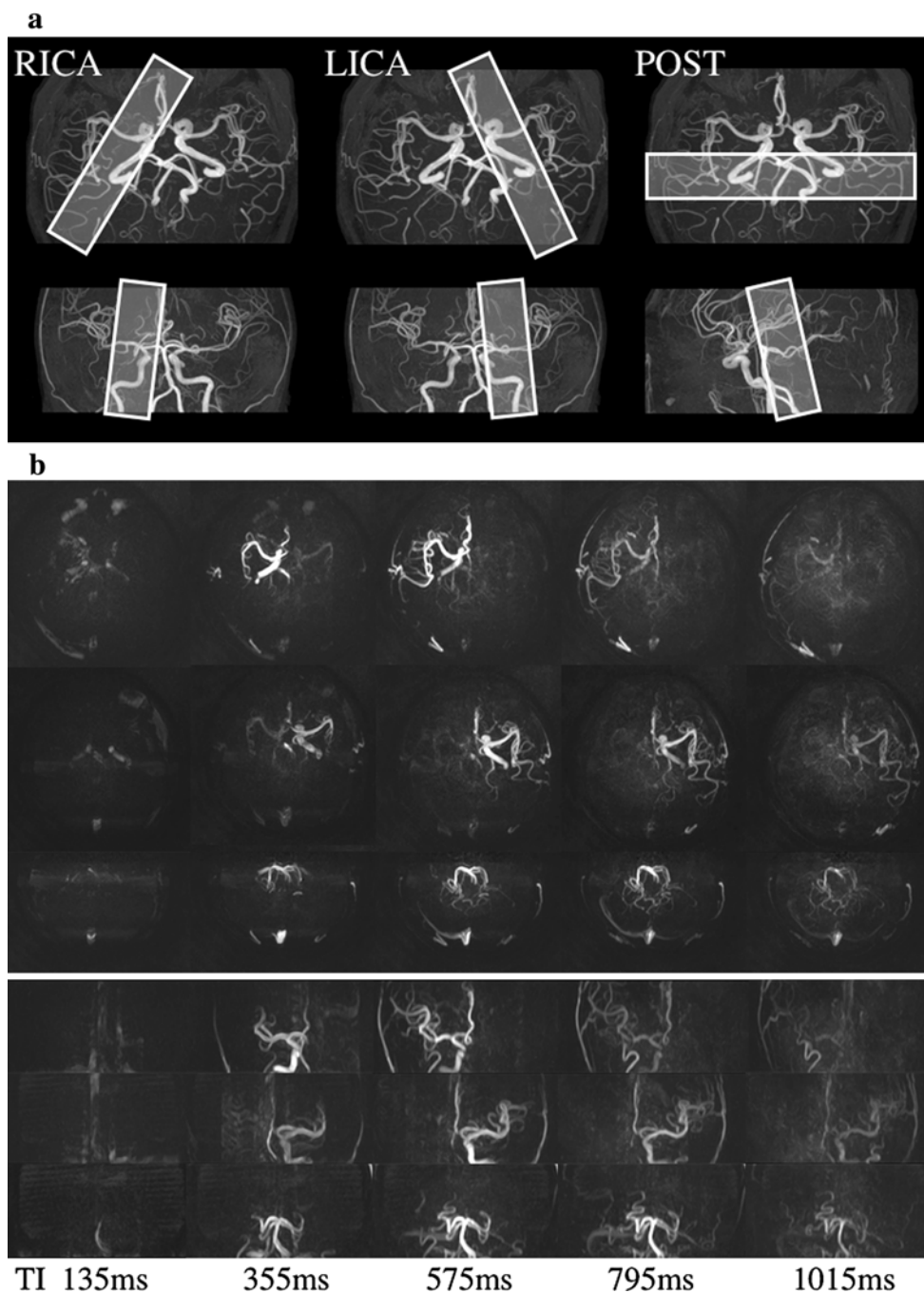


Fig. 2 **a** Planning of the respective labeling of the left ICA, right ICA, and posterior circulation on the MIPs of the circle of Willis of a healthy volunteer. See text for planning instructions. **b** Corresponding CINEMA-SELECT image of all three vessel territories of one

volunteer. Note that all images shown are MIPs of subtracted 3D images as a function of TI. Dynamic filling of blood into vessels is depicted in all temporal phases

the artery and stationary tissues was calculated as follows: $CNR = (SI_{artery} - SI_{tissues}) / SD_{background}$, where $SI_{tissues}$ is the mean signal intensity measured in a region of interest in the adjacent soft tissue. Stationary tissue should be effectively suppressed, and flowing blood should be well visualized.

2.4 Image analysis volunteer study: the signal intensity of flowing blood of CINEMA-SELECT compared to CINEMA-FAIR

In this experiment, we investigated how the labeling efficiency depends on the arrival time of labeled blood. The

labeling efficiency was determined by the CNR of the peak time and arrival time to peak signal. The arrival time to the peak signal was determined on the subtraction of labeling and control images at three different locations of the right middle cerebral arteries (M1, horizontal part; M2, insular part; M3, cortical part). Each sampling point was performed in a position 5 mm from the origin of the M1 portion to the M3 portion, as shown in Fig. 4a. The CNR analyses were performed in different sections of the anterior, middle and posterior cerebral arteries (ACA, MCA, PCA). The CNR of the peak time was calculated as follows: $CNR = (SI_{artery} - SI_{tissues})/SD_{background}$, where $SI_{tissues}$ is the mean signal intensity measured in a region of interest in the adjacent soft tissue.

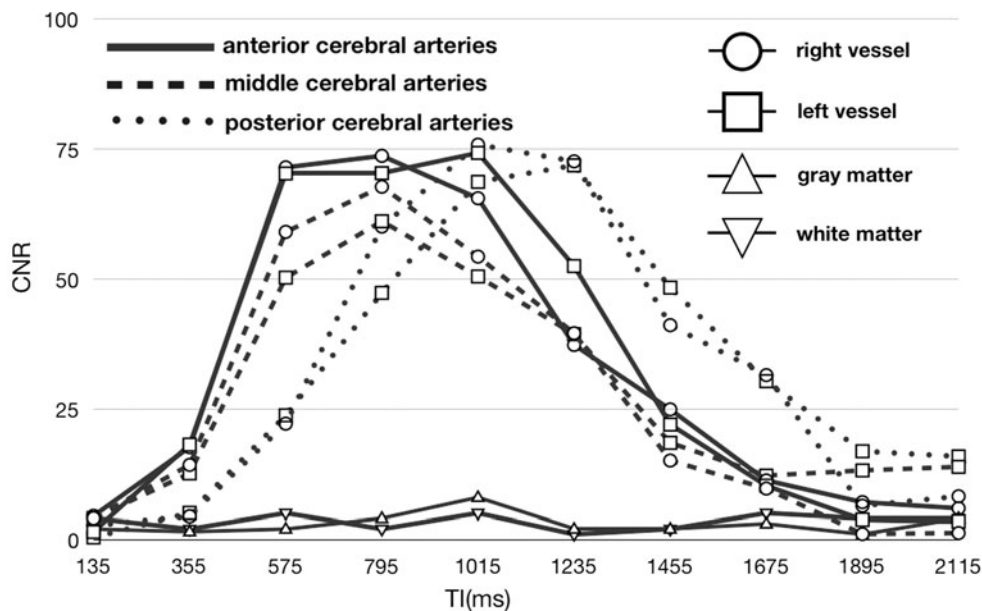
Each measured value was averaged among the 10 volunteers. We checked if its arrival time to the peak signal and the CNR between the artery and adjacent soft tissue were similar to that of the CINEMA-FAIR. Signal intensity changes along the different points of the segment from proximal to distal were analyzed if the peak signal intensity

and time did not show any discrepancy compared to that of the natural flowing phenomenon.

2.5 Image analysis volunteer study: image quality of CINEMA-SELECT compared to TOF-MRA in terms of detailed anatomy

The image quality of CINEMA-SELECT was compared to that of clinical TOF-MRA in terms of the depiction of detailed anatomy. The MIP image of CINEMA-SELECT showing the vascular structures best among the multiple phases was selected and compared to the MIP images of TOF-MRA by two board-certified radiologists (S.T and S.S with 25 and 22 years of experience in MRI, respectively), independently. The depiction of the detailed anatomy was assessed at three different locations of the normal cranial arteries (ICAs, middle cerebral arteries, anterior cerebral arteries, posterior cerebral arteries, basilar arteries, and vertebral arteries) by use of a five-point grading scale (1, CINEMA-SELECT definitely inferior to TOF-MRA; 2,

Fig. 3 CNR as a function of TI at the white matter, gray matter, and six different locations (data are means ± standard deviations). Note that background signals from static tissues are completely suppressed by subtracting of two acquisitions despite signal recovery over time in each cycle duration



TI(ms)	LACA	RACA	LMCA	RMCA	LPCA	RPCA	WM	GM
135	4.02±1.5	1.4±0.5	4.4±1.5	4.0±1.5	2.6±1.0	0.3±0.0	2.5±1.2	4.7±1.5
355	14.2±8.1	18.1±2.3	17.6±3.2	12.5±5.6	4.3±1.4	5.0±1.1	1.5±1.1	2.4±1.5
575	58.9±10.2	70.2±15.6	71.3±12.8	50.2±8.4	22.1±4.3	23.7±1.8	2.5±1.2	5.7±1.0
795	67.6±15.1	70.2±10.5	73.6±13.5	61.0±11.6	60.0±4.7	47.2±10.2	4.2±1.2	2.8±1.6
1015	54.2±18.6	74.1±8.6	65.4±8.5	50.4±8.9	75.7±9.9	68.6±8.3	8.0±2.0	5.3±2.0
1235	39.5±20.8	52.4±11.4	37.2±6.8	39.3±9.6	72.5±13.6	71.7±9.8	2.8±1.3	1.8±1.0
1455	15.0±6.0	21.9±4.6	24.8±6.1	18.4±9.1	41.0±11.2	48.2±2.6	2.4±1.1	2.7±1.3
1675	9.6±2.8	10.2±2.0	11.2±3.0	12.1±9.4	31.4±4.9	30.3±3.3	3.6±1.3	5.7±1.0
1895	1.5±0.1	3.7±1.1	7.0±2.6	13.1±5.5	6.3±2.0	16.8±2.3	2.4±1.1	4.3±1.2
2115	1.2±0.01	3.3±0.8	5.8±3.1	13.8±2.6	8.2±1.6	15.8±1.2	4.7±1.4	4.1±1.4

CINEMA-SELECT slightly inferior to TOF-MRA; 3, CINEMA-SELECT comparable to TOF-MRA; 4, CINEMA-SELECT slightly superior to TOF-MRA; and 5, CINEMA-SELECT definitely superior to TOF-MRA). The levels of inter-observer agreement and inter-modality agreement (between consensus readings of CINEMA-SELECT and TOF-MRA) with respect to depiction of the detailed anatomy were determined by use of weighted kappa (κ) statistics. $\kappa < 0.20$ indicated poor agreement; 0.21–0.40 fair agreement; 0.41–0.60 moderate agreement; 0.61–0.80 good agreement; 0.81–0.90 very good agreement; and >0.90 excellent agreement.

3 Results

3.1 Signal intensity of the stationary tissues and blood stream

All volunteers had normal circle of Willis anatomy at TOF-MRA. The volunteer studies were performed successfully with clear depiction of the major intracranial vessels in all the studies. CINEMA-SELECT could extract the blood flow in the three vessels at an interval of about 200 ms and provide MIP images in three orthogonal directions with $0.98 \times 1.36 \times 1.00 \text{ mm}^3$ spatial resolution (Fig. 2b). The average CNR of stationary tissues and flowing blood among the 10 volunteers is shown in Fig. 3. The signal intensity of stationary tissue was almost completely suppressed, whereas the signal from flowing blood was satisfactory over the TI. Good blood-background tissue contrast was achieved consistently over the entire TI.

3.2 The signal intensity of flowing blood of CINEMA-SELECT compared to CINEMA-FAIR

The average signal pattern among the 10 volunteers is shown in Fig. 4. As shown by the signal intensity curve derived from four different locations, each of the flowing blood from CINEMA-SELECT data is very similar to those measured with the CINEMA-FAIR. With the CINEMA-FAIR approach, the arrival times to the peak signal (mean values \pm standard deviations) were $575 \text{ ms} \pm 20.5$, $795 \text{ ms} \pm 52.5$ and $1015 \text{ ms} \pm 52.5$ for M1, M2, and M3, and $575 \text{ ms} \pm 50.5$, $795 \text{ ms} \pm 34.5$, and $795 \text{ ms} \pm 20.2$ for the same locations obtained from CINEMA-SELECT labeled data. The CNR of the peak time among the 10 volunteers is shown in Fig. 5. A pair wise *t* test between CNR obtained with CINEMA-FAIR and CINEMA-SELECT showed no significant difference for all flowing blood territories ($P \geq 0.30$). The arrival time of the peak signal and the CNR from CINEMA-SELECT data was very similar to those measured with CINEMA-FAIR.

3.3 Image analysis volunteer study: image quality of CINEMA-SELECT compared to TOF-MRA in terms of detailed anatomy

For all subjects, we had examined both CINEMA-SELECT and TOF-MRA. Compared with 3D TOF-MRA, CINEMA-SELECT without contrast material was similarly successful at visualizing the branches of the cranial arteries. The mean scores for the normal cerebral arteries were 2.6 ± 0.5 , 2.7 ± 0.5 , 2.8 ± 0.7 , 2.7 ± 0.7 , 2.8 ± 0.7 , respectively, for the ICAs, middle cerebral arteries,

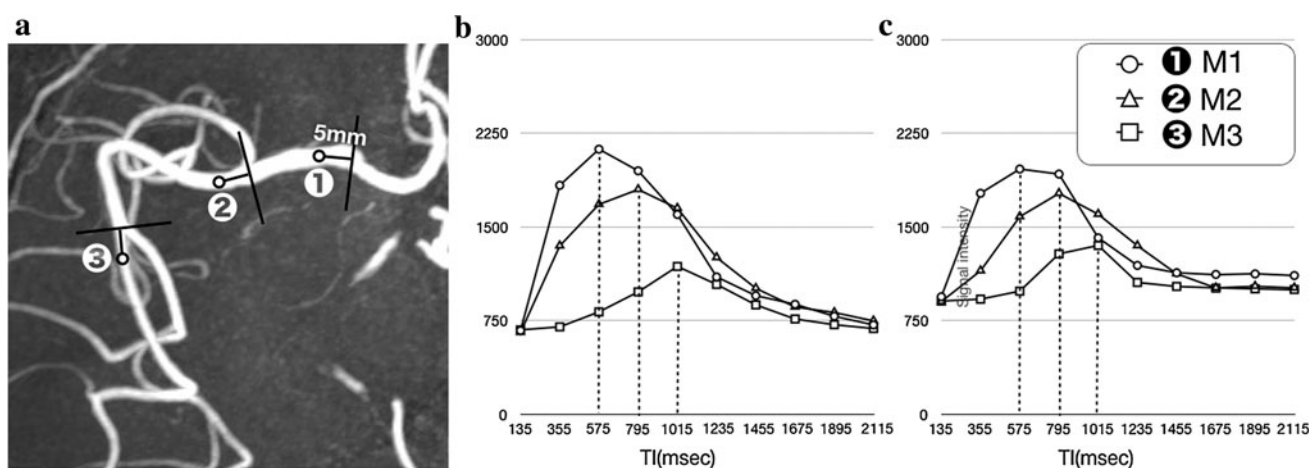
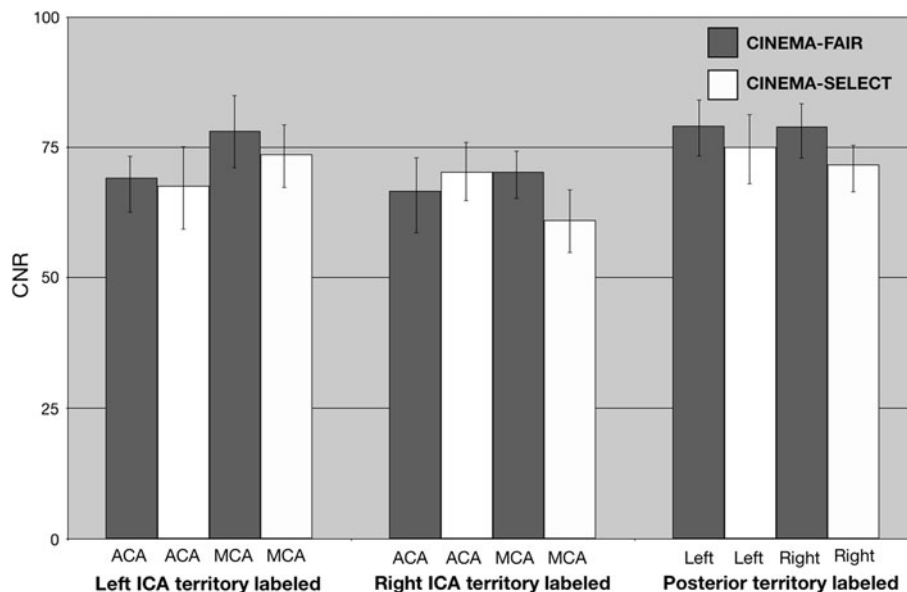


Fig. 4 Comparison of CINEMA-FAIR and CINEMA-SELECT in a volunteer. Signal intensity as a function of inversion time from three different positions residing from the proximal (M1) to distal segment (M3) of the same artery (b CINEMA-FAIR, c CINEMA-SELECT). Shown in the left figure are the locations of these sampling points (a).

The leading edge of labeled blood arriving at these positions (M1–M3) can be differentiated with incremental inversion times. The arrival time to peak signal of CINEMA-SELECT was very similar to that of CINEMA-FAIR

Fig. 5 Bar graph shows comparison of peak time of CNR of CINEMA-FAIR and CINEMA-SELECT. The peak time of CNR values measured in different arterial segments showed no significant differences between CINEMA-FAIR and CINEMA-SELECT



anterior cerebral arteries, posterior cerebral arteries, and basilar arteries (values represent mean score \pm standard deviations). The inter-modality agreement was excellent ($\kappa = 0.95$, 95 % confidence interval [CI] 0.61–1.0).

4 Discussion

In this study, a new vessel-selective time-resolved angiographic technique is demonstrated that can produce individual angiograms non-invasively by labeling the principal arterial vessels proximal to the circle of Willis. Clear vessel delineation was achieved, and the separation of the three vessels was evident in these healthy volunteers. Static tissue generally subtracted out well, and high temporal resolution and with spatial resolution was achieved simultaneously, without administration of any contrast agents.

In recent years, a number of ASL-based approaches have been developed that enable regional perfusion imaging by selective labeling of the blood in individual vessels [14, 15]. These methods have already found widespread application and made it possible to address several clinical questions regarding diagnosis, treatment, and therapy monitoring in acute cerebrovascular diseases such as stroke, as well as in chronic cerebrovascular disease, and on the same theoretical basis. The use of the PULSAR version as labeling scheme allowed us to achieve effective labeling of each individual major artery separately in this study.

Non-contrast MRA by use of ASL methods also has high clinical potential, and its utility has been widely reported [7–9]. With ASL, hemodynamic information can be acquired in different temporal phases by changing the delay time preceding data acquisition [16]. However,

repeated imaging with differing delay times prolongs imaging time substantially and thereby impedes its clinical use. CINEMA-SELECT uses Look-Locker sampling to allow continuous acquisition of multiple image data sets with differing delay times after one single inversion recovery pulse. The labeled blood arriving at four different positions could be differentiated with a temporal resolution of 220 ms in this study. Therefore, Look-Locker sampling allowed the acquisition of hemodynamic information without any substantial extension of imaging time.

A number of non-contrast, time-resolved MRA approaches have been developed that obtain hemodynamic information by FAIR-type labeling [17, 18]. However, it only allows visualizing all of the whole brain vessels together, and it cannot select the specific vessels. Further, in the result of comparing the labeling efficiency, both the FAIR-type (CINEMA-FAIR) and the PULSAR approaches yielded very similar arrival times and CNR. The similarity of the measured arrival time and CNR obtained with the FAIR-type and PULSAR approaches also indicate that the adiabatic inversion condition is not greatly affected by the different orientation and thickness of the inversion slabs. It is important to note that PULSAR data are the same as in the data acquired with the FAIR-type approach.

Visualization of anatomic structures with CINEMA-SELECT was not completely comparable to that with TOF-MRA, according to the results of this study. However, CINEMA-SELECT allows obtaining important hemodynamic information, which is not achievable with TOF-MRA. Such a capability may be clinically important for assessment and characterization of collateral flow patterns in steno-occlusive diseases.

The proposed CINEMA-SELECT technique has several limitations. First, CINEMA-SELECT suffers inherently

from poor visualization of the vessels at long TI values (similar to the late phase of conventional contrast-enhanced angiography). This occurs because of the limitation of T1 recovery of the magnetically labeled blood, which causes a gradual decrease of the subtracted signal. Therefore, long TI times such as those around 1200 ms or longer may impede complete peripheral observation of slow blood flow. Second, this technique requires a relatively longer acquisition time (up to 15 min) than that of typical TOF-MRA, which may cause motion artifacts. Therefore, this technique should directly benefit from further acceleration of data acquisition, as in current contrast-enhanced studies in which higher parallel imaging factors and/or advanced data sharing in the spatial and temporal domain are used. Thus, further sequence optimization is highly desirable. Finally, this approach relies on an angulated or translational positioning of the large inversion volumes. Selective labeling can be achieved by positioning of a labeling slab in such a way that the complete path of only a single artery is included in this technique. However, because this technique relies on labeling of the targeted artery over a long range, the selectivity is restricted to the major brain-feeding arteries, and it bears the risk of inclusion of other vessels in the labeling slab. Recently, continuous artery-selective spin labeling has been introduced on the basis of a rotating labeling plane for obtaining a localized effect that is limited to a single artery [19]. This method provides high selectivity and allows labeling of the ICA and vertebral arteries. Improved sequence design or other optimizations may lead to different solutions of the problem.

5 Conclusion

This study demonstrated the feasibility of the CINEMA-SELECT technique in the non-invasive evaluation of the selective angiograms of intracranial vessels. Relatively high quality temporal and spatial resolutions were achieved simultaneously. Although further sequence optimization and clinical studies are required, this technique could play an important role in assessment of the structure and hemodynamics of intracranial arteries without the use of contrast agents.

Conflict of interest The authors declare that they have no conflict of interest.

References

- Duran M, Schoenberg SO, Yuh WT, Knopp MV, van Kaick G, Essig M. Cerebral arteriovenous malformations: morphologic evaluation by ultrashort 3D gadolinium-enhanced MR angiography. *Eur Radiol.* 2002;12:2957–64.
- Hadizadeh DR, von Falkenhausen M, Gieseke J, Meyer B, Urbach H, Hoogeveen R, Schild HH, Willinek WA. Cerebral arteriovenous malformation: Spetzler–Martin classification at subsecond-temporal-resolution four-dimensional MR angiography compared with that at DSA. *Radiology.* 2008;246:205–13.
- Bendszus M, Koltzenburg M, Burger R, Warmuth-Metz M, Hofmann E, Solymosi L. Silent embolism in diagnostic cerebral angiography and neurointerventional procedures: a prospective study. *Lancet.* 1999;354:1594–7.
- Masaryk TJ, Modic MT, Ross JS, Ruggieri PM, Laub GA, Lenz GW, Haacke EM, Selman WR, Witznitzer M, Harik SI. Intracranial circulation: preliminary clinical results with three-dimensional (volume) MR angiography. *Radiology.* 1989;171:793–9.
- Moran PR. A flow velocity zeugmatographic interlace for NMR imaging in humans. *Magn Reson Imaging.* 1982;1:197–203.
- Dixon WT, Du LN, Faul DD, Gado M, Rossnick S. Projection angiograms of blood labeled by adiabatic fast passage. *Magn Reson Med.* 1986;3:454–62.
- Nishimura DG, Macovski A, Pauly JM, Conolly SM. MR angiography by selective inversion recovery. *Magn Reson Med.* 1987;4:193–202.
- Wang SJ, Nishimura DG, Macovski A. Multiple-readout selective inversion recovery angiography. *Magn Reson Med.* 1991;17:244–51.
- Edelman RR, Siewert B, Adamis M, Gaa J, Laub G, Wielopolski P. Signal targeting with alternating radiofrequency (STAR) sequences: application to MR angiography. *Magn Reson Med.* 1994;31:233–8.
- Kim SG, Tsekos NV. Perfusion imaging by a flow-sensitive alternating inversion recovery (FAIR) technique: application to functional brain imaging. *Magn Reson Med.* 1997;37:425–35.
- Look DC. Time saving in measurements of NMR and EPR relaxation times. *Rev Sci Instrum.* 1970;41:250–1.
- Nakamura M, Yoneyama M, Tabuchi T et al. Non contrast 3D volumetric time-resolved MRA combining multiple phase FAIR (CINEMA-FAIR). *ISMRM.* 2011;Proc:4036.
- Liebeskind DS. Collateral circulation. *Stroke.* 2003;34:2279–84.
- Xavier G, Esben T, Petersen FH. Pulsed star labeling of arterial regions (PULSAR): a robust regional perfusion technique for high field imaging. *Magn Reson Med.* 2005;53:15–21.
- Hendrikse J, van der Grond J, Lu H, van Zijl PC, Golay X. Flow territory mapping of the cerebral arteries with regional perfusion MRI. *Stroke.* 2004;35:882–7.
- Hori M, Shiraga N, Watanabe Y, Aoki et al. Time-resolved three-dimensional magnetic resonance digital subtraction angiography without contrast material in the brain: initial investigation. *J Magn Reson Imaging.* 2009;30:214–8.
- Bi X, Weale P, Schmitt P, et al. Non-contrast-enhanced four-dimensional (4D) intracranial MR angiography: a feasibility study. *Magn Reson Med.* 2010;63:835–41.
- Yan L, Wang S, Zhuo Y, et al. Unenhanced dynamic MR angiography: high spatial and temporal resolution by using true FISP-based spin tagging with alternating radiofrequency. *Radiology.* 2010;256(1):270–9.
- Wong EC. Vessel-encoded arterial spin-labeling using pseudo-continuous tagging. *Magn Reson Med.* 2007;58:1086–91.