TECHNICAL NOTE   **Open Access**

Altered saturation pulse with a high flip angle for venous saturation on 7 T time-of-flight magnetic resonance angiography

Sangwoo Kim[1]* and Chulhyun Lee[2]

Abstract

This study aimed to apply minimum-time variable-rate selective excitation (MinVER) to a presaturation pulse (PSP) with a high flip angle on 7 T time-of-flight magnetic resonance angiography (7T TOF-MRA), to attain a superior vessel-to-tissue contrast (VTCR), short acquisition time, and minor off-resonance effect. An altered PSP modified by using the 90° flip angle (FA)-MinVER was implemented in the 7 T TOF-MRA, and its performance was evaluated with a signal profile and vessel-tissue contrast ratios and compared to the conventional PSP and 45 FA-TOF. The 90 FA-MinVER showed a similar signal profile to that of the conventional PSP and improved the vessel-tissue contrast ratios (0.313 ± 0.80) compared to all conventional types (45 FA-TOF: 0.088 ± 0.84, 90 FA-TOF: 0.203 ± 0.72). Moreover, this noteworthy approach achieved substantially reduced total acquisition time (5 min and 55 s) with a short repeat-to-time (28 ms), indicating that at the 7 T TOF-MRA, the 90 FA-MinVER could be applied by default to suppress the venous signals regardless of individual human status and the specific absorption ratio constraint and with rapid imaging. Ultimately, its application could also help to observe subtle microvascular changes in the early stages and serve as key biomarkers in various vascular diseases.

Keywords: Presaturation pulse, Time-of-flight, Ultra-high field, Venous saturation, Magnetic resonance angiography

Introduction

Magnetic resonance angiography (MRA) based on time-of-flight (TOF) is an important non-invasive method for diagnosing intracranial vascular pathologies, such as aneurysm and moyamoya disease (Fushimi et al. 2006; Morelli et al. 2013; Oh et al. 2017). At present, in an ultra-high magnetic field (7 T), TOF-MRA MRI allows the precise detection of lenticulostriate arteries related to ischemic and hemorrhagic cerebral strokes (Cho et al. 2008; Hendrikse et al. 2008; Kang et al. 2009). This is attributed to better signal-to-noise ratio and spatial resolution in subtle arteries, higher saturation of background tissues, and lower signal loss of in-plane flow due

to prolonged T1 relaxation of bloodstreams compared to low-field MRA (Brinjikji and Young 2015). However, the application of 7 T TOF-MRA to humans has a critical disadvantage due to an elevated radiofrequency (RF) pulse: a high specific absorption rate (SAR) (Speck and Tempelmann 2010; van der Kolk et al. 2013). This causes repetition time (TR) increases to ameliorate SAR constraints (Kim and Rhim 2020). Although TOF-MRA should select the shortest possible TR intervals for high vessel-to-tissue contrast (VTCR) (Johst et al. 2012), the prolonged TR results in a reduction in the VTCR due to high background signals and a long acquisition time that can generate motion-related artifacts (Morelli et al. 2013). Importantly, the SAR accumulations in 7 T TOF-MRA are mostly induced by the presaturation pulse (PSP) for venous suppression (Schmitter et al. 2012). Hence, appropriate strategies to decrease the SAR level

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increased by PSP are needed to emphasize the superior advantages of 7 T TOF-MRA.

There are ways of resolving SAR restriction at 7 T TOF-MRA. A simple method is to reduce the RF power of the PSP, which requires several RF excitations to reach the low steady-state level of the venous signal. The excitation amount of the saturated pulses increases as the RF power decreases, and the specific numbers of RF deposits depend on subject-individual physiology, such as blood flow velocity, head size, and vascular disease status (Johst et al. 2012). Although a previous study, which combined low RF power and variable-rate selective excitation (VERSE) technique, has demonstrated an excellent imaging quality of 7T TOF-MRA, venous saturation is decreased in arteriovenous malformations and dural arteriovenous fistula (Wrede et al. 2014). This was probably caused by the effect on the low FA in relation to the patient-individual pathology mentioned above. In addition, segmented TOF-MRA using a sparse excitation of the PSP has demonstrated a low SAR and short acquisition time. This method is also dependent on an individual's conditions because the VTCR has an approximately 4–19% reduction in the human scan in comparison with the conventional PSP with a low FA (Zhang et al. 2015). Johst et al. have stated that an RF amplitude of 90° can be theoretically accomplished by only two excitations (Johst et al. 2012). Therefore, a saturation pulse with a 90° flipangle (FA) is required to achieve a reasonable state of the low venous signal, regardless of the individual status.

Applying the VERSE technique to the saturation pulse with the 90° FA has been demonstrated with approximately 50% or more improved VTCR with a sufficient SAR range at 7 T TOF-MRA (Schmitter et al. 2012). However, the VERSE that is implemented by RF shape change on resonance only, without spatial excitation (Conolly et al. 1969, 1991; Hardy and Cline 1989), is more sensitive to resonant shifts and RF/gradient timing (Hargreaves et al. 2004). Thus, it is especially important to resolve this issue in 7 T TOF-MRA. The off-resonance effects of the RF pulse cause FA variations (Ulmer et al. 1996), which could lead to an insufficient saturation effect of the venous phase. A prior study using a modified VERSE technique (called minimum-time VERSE, MinVER) implemented short-duration pulses with high FA and minor off-resonance sensitivity (Hargreaves et al. 2004). Thus, we hypothesized that, especially in 7 T TOF-MRA, the use of the MinVER can satisfy constant RF high energy for minimal intravenous signals within SAR constraints, without off-resonance effects, regardless of individual physiology.
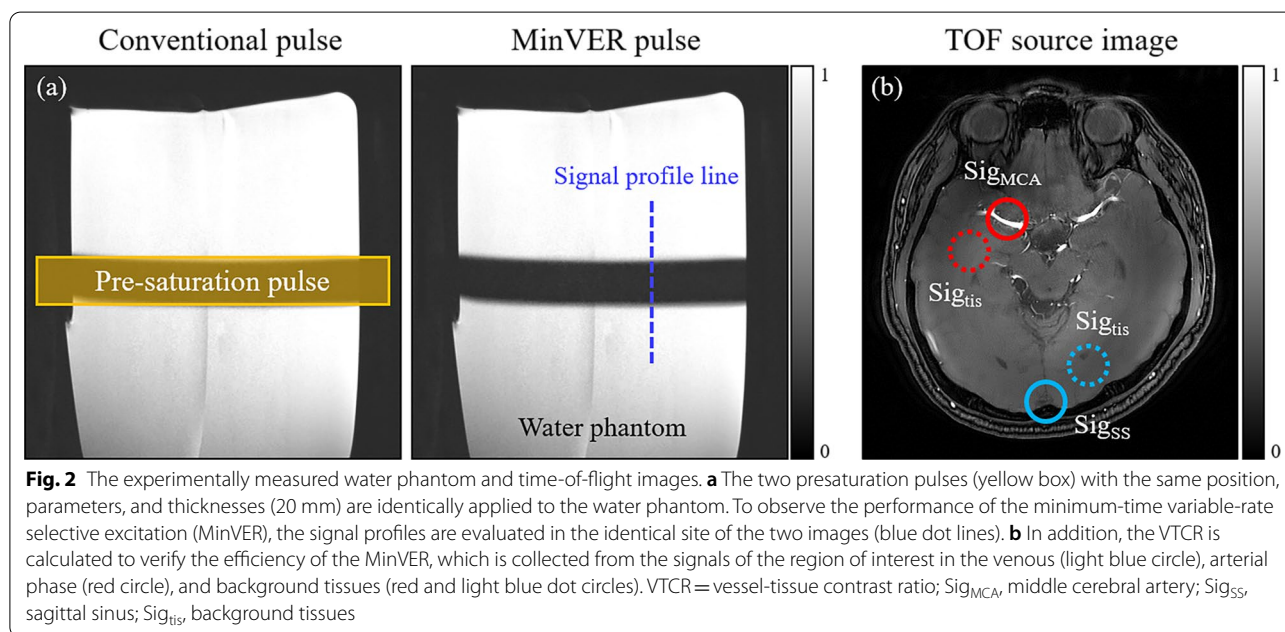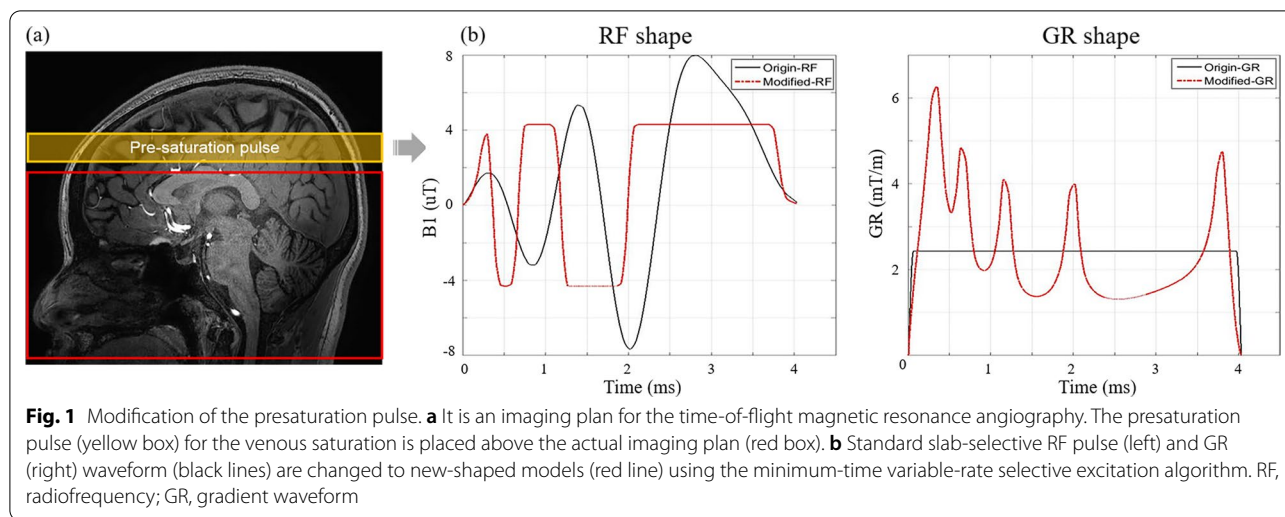
TOF-MRA requires the shortest possible TR to maintain a reasonable acquisition time and minor steady-state signals from background tissues (Morelli et al.

2013). However, the short TR allows rough RF excitations, leading to unstable contrasts in a slice (Hargreaves et al. 2004). In contrast, the TR increase mainly results in high background signals (low VTCR) and long acquisition times (Allison and Yanasak 2015; Morelli et al. 2013). The TR expansion in 7 T TOF-MRA arises from the SAR constraint, which is mainly occupied by the application of the PSP of venous signals (Schmitter et al. 2012). In addition, 7 T exhibits off-resonance effects more sensitively, causing high FA variations. The MinVER enables improved RF profiles with short duration and minor off-resonance effects, accompanied by RF power reduction (Hargreaves et al. 2004). Hence, this study employed the MinVER to the PSP and presented the excitation signal profile by comparing it with conventional PSP. Subsequently, the use of the PSP modified by the MinVER with high FA showed superior performance including higher VTCR and decreased acquisition time caused by the significantly short TR.

Methods
Application and evaluation of the minimum-time variable-rate selective excitation
First, the MinVER algorithm was downloaded from a site (http://mrsrl.stanford.edu/~brian/mintverse/). Subsequently, the file was compiled for use in MATLAB by utilizing the MEX function (MathWorks, MA, USA). The conventional RF shape was then extracted from the 7 T MRI scanner to apply the MinVER to the PSP (Philips, Achieva, Best, Netherlands). Using MinVER, the original RF and gradient waveform (GR) were modified to new-shaped shapes by selecting a parameter with approximately 70% attenuation of the RF power. In addition, the RF/GR durations were identical to those of the conventional one (Fig. 1) to only observe the performance of the changed RF/GR. All changed RF/GR models were entered into the whole-body 7 T MRI and updated to be used simultaneously with the conventional PSP. Furthermore, with the water phantom, each MR image was obtained to validate the performance of the conventional PSP and that of the MinVER, which was implemented in the 7 T MRI with a 32-channel phased-array head coil (Nova Medical, MA, USA). The scan parameters were as follows: TR = 42 ms in the conventional PSP and 28 ms in the MinVER, echo time = 1.6 ms, FA = 20, field of view = 320 × 240, matrix size = 800 × 400, bandwidth = 251 Hz/pixel, slice thickness = 1 mm/, slice numbers = 120, slab numbers = 3, number of averages = 1, and sense factor = 3. The excitation position of the PSP was placed at the center of the water phantom, and the imaging direction was planned as a sagittal view to clarify the saturation signs (Fig. 2a). Finally, an analysis of the

Fig. 1 Modification of the presaturation pulse. **a** It is an imaging plan for the time-of-flight magnetic resonance angiography. The presaturation pulse (yellow box) for the venous saturation is placed above the actual imaging plan (red box). **b** Standard slab-selective RF pulse (left) and GR (right) waveform (black lines) are changed to new-shaped models (red line) using the minimum-time variable-rate selective excitation algorithm. RF, radiofrequency; GR, gradient waveform

Fig. 2 The experimentally measured water phantom and time-of-flight images. **a** The two presaturation pulses (yellow box) with the same position, parameters, and thicknesses (20 mm) are identically applied to the water phantom. To observe the performance of the minimum-time variable-rate selective excitation (MinVER), the signal profiles are evaluated in the identical site of the two images (blue dot lines). **b** In addition, the VTCR is calculated to verify the efficiency of the MinVER, which is collected from the signals of the region of interest in the venous (light blue circle), arterial phase (red circle), and background tissues (red and light blue dot circles). VTCR = vessel-tissue contrast ratio; Sig_{MCA}, middle cerebral artery; Sig_{SS}, sagittal sinus; Sig_{tis}, background tissues

signal profile was performed to compare the difference between the MinVER and the conventional PSP.

Preliminary validation of in vivo study

Each in vivo image of the 7 T TOF-MRA was acquired from a subject, a responsible member, a total of three times over 2 weeks. The TOF-MRA images were all identical to the water phantom study, except for the position of the PSP and the imaging direction. The PSP was located above the excitation slab to saturate the venous signal, and the MR images were collected using an axial plane. Subsequently, the VTCR method presented in a study by Wrede et al. (2014) was utilized to verify the

efficiency of the PSP with the MinVER in comparison with the conventional method. Signal intensities were measured in the vein and both middle cerebral arteries and the background signals around the vessels, which were averaged with the standard deviation. Subsequently, the VTCRs were calculated for each value as follows:

$$VTCR\_SS = \frac{Sig_{tis} - Sig_{ss}}{Sig_{tis} + Sig_{tis}}, \quad VTCR\_MCA = \frac{Sig_{tis} - Sig_{MCA}}{Sig_{tis} + Sig_{MCA}}$$

where Sig_{tis} is the background tissue signal, Sig_{SS} is the signal intensity of the inferior sagittal sinus, and Sig_{MCA} is the signal intensity of both middle cerebral arteries (Fig. 2b). Moreover, the TRs in each method were

extracted from the Digital Imaging and Communications in Medicine files to indirectly observe the SAR decrease by the 90 FA-MinVER. A study has shown that the saturation FAs for low venous signals are 30°–50° within the TR ranges of 20–35 ms and the reasonable FA is the saturation FA + 15° in 7 T TOF-MRA; therefore, an additional examination of the conventional PSP at 45° was performed (Johst et al. 2012). The imaging analysis of the 45 FA TOF-MRA was identically performed as described above with the VTCRs and TR.

Results

With the ultra-high field TOF sequence, the signal profiles on the water phantom were first measured to compare the performance between the 90 FA-MinVER sequence and their original sequences. The signal profile obtained using the MinVER sequence was almost identical to that of the original state (Fig. 3). Subsequently,

background and vessel signals in all TOF images were quantified to demonstrate the efficiency of the 90 FA-MinVER sequence. The venous signal was lower in the 90 FA-MinVER (176.42 ± 27.71) compared to the original sequence (45 FA-TOF: 415.57 ± 33.54, 90 FA-TOF: 281.92 ± 29.37). In addition, the VTCR_SS in the MinVER (0.313 ± 0.80) showed a more excellent signal change (Fig. 4) compared to the conventional TOFs (45 FA-TOF: 0.088 ± 0.84, 90 FA-TOF: 0.203 ± 0.72). Moreover, the middle cerebral artery exhibited an identical signal (approximately 1622.94 ± 147.42) in all TOF sequences, which also observed similar contrast ratios (VTCR_MCA: 0.521 ± 0.86 vs. 0.527 ± 0.86 in the 90 FA-TOF and 0.539 ± 0.78 in the 45 FA-TOF). The individual values for all the TOF sequences are summarized in Table 1.
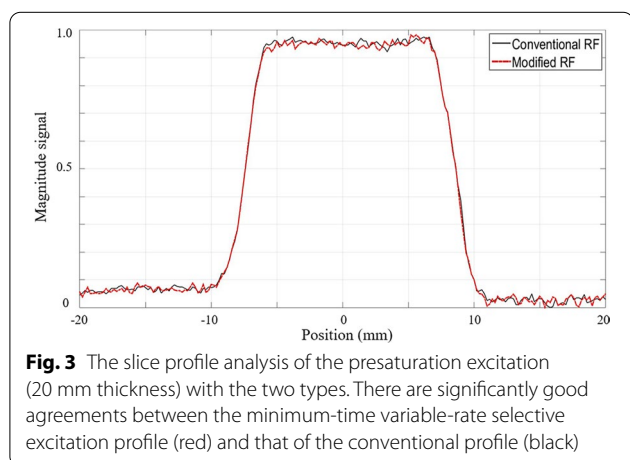

Fig. 3 The slice profile analysis of the presaturation excitation (20 mm thickness) with the two types. There are significantly good agreements between the minimum-time variable-rate selective excitation profile (red) and that of the conventional profile (black)

Table 1 Quantitative signal intensity measurements performed by region-of-interest analysis (values provided with averages and standard deviations)

	45 FA-cTOF	**90 FA-cTOF**	**90 FA-MinVER**
Sagittal sinus			
Tissues	348.53 ± 2.93	425.09 ± 4.77	336.99 ± 3.02
SS	415.57 ± 33.54	281.92 ± 29.37	176.42 ± 27.71
VTCR	0.088 ± 0.84	0.203 ± 0.72	0.313 ± 0.80
Middle cerebral arteries			
Tissues	462.20 ± 16.98	516.20 ± 10.00	522.61 ± 13.01
MCA	1541.44 ± 135.28	1666.45 ± 132.96	1660.95 ± 174.02
VTCR	0.539 ± 0.78	0.527 ± 0.86	0.521 ± 0.86

FA, flip angle; cTOF, conventional TOF; SS, sagittal sinus; MCA, middle cerebral artery; VTCR, vessel-to-tissue contrast ratio
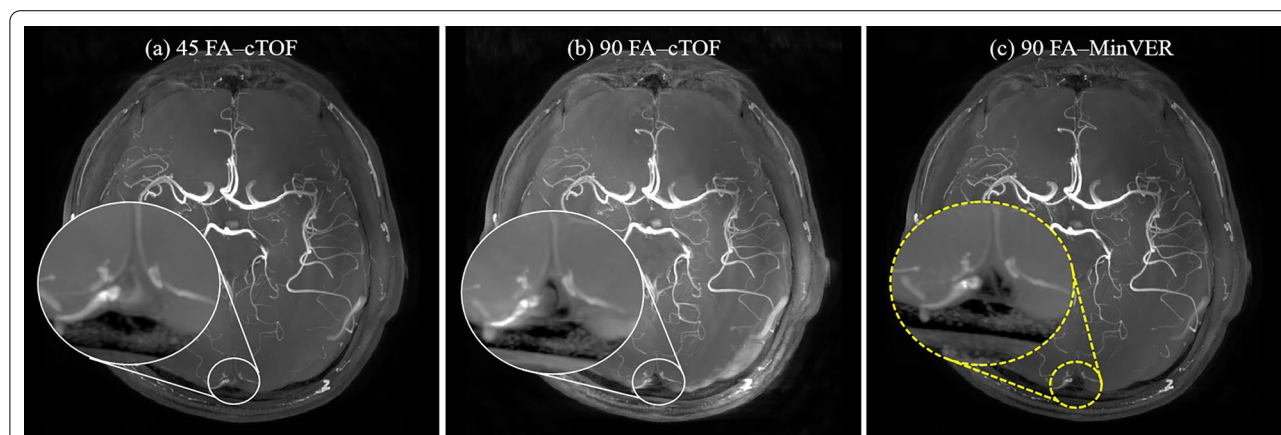
Fig. 4 Comparison of venous saturations among each presaturation pulse. All sagittal sinuses in each time-of-flight (TOF) image (white circles: cTOF, yellow dot circle: minimum-time variable-rate selective excitation [MinVER]) are enlarged to verify the saturation effects on the venous phase. It is fairly excellent in the MinVER (**c**) more than the conventional pulse with 45 (**a**) and 90 FA (**b**). FA, flip angle; cTOF, conventional TOF

The TR and total scan time were also observed to verify the usefulness of the 90 FA-MinVER sequences. The TR in the 90 FA-MinVER was substantially lower at approximately 66% (28 ms) compared to that of the 90 FA-TOF conventional one (42 ms) and was similar to the 45 FA-TOF-based sequence (26 ms). Furthermore, the 90 FA-MinVER (5 min and 55 s) had a shorter acquisition time than the original sequences (90 FA-TOF: 8 min and 50 s) and was comparable to the 45 FA-TOF (5 min and 23 s), which was attributed to the reduction in the TR.

Discussion

This study focused on observing the performance of the modified RF pulse and gradient shape on 7 T TOF-MRA. The 90 FA-MinVER not only showed a better vessel-tissue contrast ratio (0.313 ± 0.80) compared to the conventional types (45 FA-TOF: 0.088 ± 0.84 and 90 FA-TOF: 0.203 ± 0.72, Fig. 4 and Table 1), but also resulted in a substantially lower total acquisition time (5 min and 55 s) with a short TR (28 ms). The results obtained using 7 T TOF-MRA could be utilized to establish the early diagnosis of subtle vessel diseases, such as microinfarction and lacunar infarction, using superior vessel contrast ratios based on a reasonable scan time.

It is noteworthy that the 90 FA-MinVER achieved the lowest signal of the sagittal sinus, suggesting that 7 T TOF-MRA could be utilized to establish a superior venous saturation with the large FA and the short TR. Prior studies have stated that the application of the PSP with low FAs (approximately 30°–50°) is sufficient to suppress the venous signal owing to the longer T1 relaxation time at 7 T MRA (Johst et al. 2012; Wrede et al. 2014; Zhang et al. 2015), which was exhibited in the 45 FA-TOF of our findings (Fig. 4). In view of venous saturation, the reduced FA requires multiple RF excitations to reach the low steady-state signals, and its numbers depend on an individual's status, such as blood flow rate, shape, and head size. In contrast, an FA of 90° forms suppression effects within just two excitations (Johst et al. 2012). This supports our result that the venous signal of the 90 FA-MinVER is substantially lower compared to that of the 45 FA-TOF (Fig. 4 and Table 1). In addition, the TR range in the 90 FA-MinVER (28 ms) was similar to that of the 45 FA-TOF (26 ms). This result implies that both sequences could virtually produce equivalent SAR values, since the TR expansion is needed to release SAR restrictions when using a high FA to humans (Johst et al. 2012; Morelli et al. 2013; Schmitter et al. 2012). That is, the 7 T TOF-MRA combined with the 90 FA-MinVER could be applied to suppress the venous signals regardless of individual human status and the SAR constraint. Additional studies are, however, needed to further investigate the efficiency of the 90 FA-MinVER by measuring the RF-related

temperature changes because the SAR increase induces a temperature increase in vivo (Kim and Rhim 2020; Oh et al. 2014).

TOF-MRA requires the shortest possible TR selection for arterial visualization by reducing the background signals (Morelli et al. 2013). The 7 T MRA has the advantage of increasing static tissue suppression due to longer T1 relaxation times than low magnetic fields (van der Kolk et al. 2013), but the extended TR caused by the elevated RF deposits hardly brings the benefit of the ultra-high field MRA. The increased TR decreases background suppression in TOF-MRA, which is a cause of lower vessel-tissue contrasts (Johst et al. 2012; Wrede et al. 2014). In this study, the background signal of the 90 FA-MinVER (336.99 ± 3.02) was lower compared to that of the 90 FA-TOF (425.09 ± 4.77), leading to superior vessel-tissue contrast ratios (0.313 ± 0.80 versus 90 FA-TOF: 0.203 ± 0.72). This can be explained by the improved saturation effect of background tissues caused by the short TR at 7 T TOF-MRA, which suggests that the 90 FA-MinVER with the short TR could more sensitively detect microvascular changes with superior arterial visualization. It is based on which both TOF and phase-contrast angiography at the 7 T MRI have an excellent detection of small vessels due to the increased signal-to-noise ratio and spatial resolution (Morze et al. 2007; Stamm et al. 2013).

The increased TR also causes the total acquisition time to increase in TOF-MRA (Allison and Yanasak 2015; Johst et al. 2012; Morelli et al. 2013; van der Kolk et al. 2013). This study achieved a reasonable acquisition time with a short TR (5 min and 55 s with TR 26 ms vs. 90 FA-TOF: 8 min and 50 s with TR 42 ms) using the 90 FA-MinVER sequence. In clinical and/or research magnetic resonance imaging (MRI) settings, a long scan time induces motion artifacts related to the subject's discomfort and an involuntary condition (Kim and Lee 2020). Although 7 T TOF-MRA using prospective motion correction has been completed with better arterial visualization, the main limitation is the long scan time (Mattern et al. 2018). In addition, the saturation pulse together with the magnetic transfer pulse using the VERSE technique has demonstrated a considerable effect on SAR reduction; however, the study's authors have stated that simply applying the VERSE to the presaturation pulse can significantly decrease SAR levels (Schmitter et al. 2012). In this regard, a modified saturation pulse using the VERSE technique with a low FA has been attempted in an in vivo study with various vascular diseases, such as aneurysm, moyamoya disease, arteriovenous malformation, and arteriovenous fistula, which showed that venous saturation effects are decreased in arteriovenous malformations and fistulas (Wrede et al. 2014). This emphasizes

the necessity of 90° FAs that are independent of the individual's status (Johst et al. 2012). Consequently, it could be hypothesized that the use of the 90 FA-MinVER would certainly be desirable for 7 T TOF-MRA with not only an identical effect on venous saturation in any case but also for rapid imaging.

This study has some limitations. Several studies with temperature mapping using proton resonance frequency shift or optic-fiber thermography should be conducted to compare temperature differences induced by an original TOF sequence and the 90 FA-MinVER, thereby ensuring a thorough RF safety for the human body. This would also allow us to determine whether to apply the 90 FA-MinVER for 7 T TOF-MRA. Additionally, a large number of human subjects must be employed to validate that the 90 FA-MinVER achieves the same venous saturation in varying individual vessel conditions and vascular diseases, which could lead to the fundamental application of the 90 FA-MinVER to 7 T TOF-MRA. In addition, this study only investigated the modification of the PSP, not the magnetic transfer pulse on the excitation pulse (Schmitter et al. 2012), which requires additional studies that employ the MinVER for the two types of RF pulses. Moreover, since parallel RF transmission at the 7 T MRI enables the correction of B1 inhomogeneity and the decreases in RF deposition (Deniz 2019), TOF-MRA using the MinVER should be compared with that of the parallel transmission in the future.

Conclusion

This study implemented a novel method of applying a PSP with a high FA at 7 T TOF-MRA and achieved superior venous suppression, improved vessel-tissue contrast, and a reasonable acquisition time based on a short TR. This method enables the use of the same saturation effect of the venous system regardless of human-dependent physiological effects, and the fast TOF-MRA imaging can be used at 7 T MRI. Its application could also help to observe subtle microvascular changes in the early stages and to prevent motion-related artifacts.

Abbreviations
MRA: Magnetic resonance angiography; TOF: Time of flight; SAR: Specific absorption rate; RF: Radiofrequency; TR: Repetition time; VTCR: Vessel-to-tissue contrast; PSP: Presaturation pulse; VERSE: Variable rate selective excitation; FA: Flip angle; MinVER: Minimum-time variable-rate selective excitation; GR: Gradient waveform; SS: Sagittal sinus; MCA: Middle cerebral arteries.

Acknowledgements
Not applicable.

Authors' contributions
SW contributed to the writing of the original manuscript, the formal analysis, methodology, software, and visualization. CHL provided conceptualization, resources, and investigative contributions. All authors read and approved the final manuscript.

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