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Inflow Effect Correction in Perfusion Measurement of Normal Subjects with T1-Weighted Images Using Inversion Recovery Sequences

Background/Objective: A dynamic contrast-enhanced T1 technique has been applied for calculating cerebral blood flow (CBF) with MRI. Previous studies have shown that the CBF calculated from T1 techniques was lower than the expected CBF. One cause could be the change in MRI signal intensity due to blood flowing into the measurement slice. The aims of this paper were:
1. To quantify the effects of inflow on perfusion measurements using a phantom.
2. To apply a simple inflow correction to perfusion measurements taken from 11 healthy subjects.
Patients and Methods: A flow phantom was designed to produce different velocities covering the velocity range of small vessels and big arteries. The inflow effects were measured in the phantom. After the contrast administration for healthy subjects, CBF was calculated based on T1 technique.
Results: The inflow correction factor for the common carotid artery velocity and capillary level was calculated by the phantom as 1.23 and 1, respectively. The average value of CBF on the middle cerebral artery (MCA) grey matter territory of 11 healthy volunteers without any correction was 43.0 mL/100 g/min.
Conclusion: For measuring the absolute CBF, the inflow correction factor for the arterial input function and tissue should be known. After applying the inflow correction factors, the absolute CBF may be calculated as 52.9 mL/100 g/min. This value is in good agreement with those in the PET literature.

Keywords: Absolute Cerebral Blood Flow, Inflow Effect, Inversion Recovery, T1 Technique, T1-Weighted

Introduction

There are some instruments such as transcranial Doppler ultrasonography (TCD), dynamic or xenon-enhanced computed tomography (Xe-CT), single-photon emission computed tomography (SPECT), positron emission computed tomography (PET), and magnetic resonance imaging (MRI) that can be used for determining the hemodynamic parameters of the brain.[1-5]

Perfusion or the blood flow to an organ based on a T1 technique after injection of contrast agent may be calculated by measuring the gradients of the tissue signal intensity curve divided by the maximum signal intensity (SI) of the arterial input curve (AIF).[6]

The value of cerebral blood flow (CBF) using the T1 technique has been reported by Moody et al.[6] They stated that the measurement of the asymptomatic MCA grey matter (GM) territory was slightly low compared with the other quantitative techniques. Vallee et al.[7] and Montet et al.[8] measured the absolute renal blood flow based on the T1 technique. They also stated that the values of the perfusion were lower than the expected values. Since all absolute organ blood flow measurements were lower than the expected values, it seems that some corrections should be

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applied on the T1 technique equations.

It is necessary to mention that this method has been used for measuring the blood flow in a range of organs such as the liver, kidneys, spleen, pancreas and the brain in nuclear medicine and CT.[9-14]

Since the enhancement of the SI is dependent on velocity at a constant concentration,[15] the difference in velocity of the arterial input and tissue (organ) lead to difference in the inflow effect. If SI is used for calculation of the CBF, the effect of inflow should be considered. The image parameters may affect the SI and SI is sensitive to the inflow effect. The effect of blood flow into the neck during image acquisition was not corrected when measuring CBF in the previous studies using T1 technique.[6,16] This effect increases the measured SI in the arterial input, subsequently leading to a decrease in the calculated value of CBF.

Evaluation of T1 technique by a phantom after inflow correction was reported in our previous study.[17] The aim of this paper was to use the inflow correction factor from a flow phantom and to apply the inflow correction factor to the mean value of the CBF using the T1 technique from eleven normal volunteers.

Patients and Methods

Phantom

To estimate the inflow effect in normal human subjects, a flow phantom and a trolley were designed similar to our previous study.[17]

The phantom contains two parts; one is used for calibrating the flow, and the other contains one branch of Tygon tube (internal diameter=0.95 cm). This is approximately the same diameter as the human internal carotid artery.

A trolley, made by wood and aluminium, was used to carry the flow phantom to the MRI scanner room. It had three moveable shelves and two tanks on the shelves, one of which is the water reservoir above the other. In each experiment, the two tanks were full of the desired concentration (0.8 mmol/L). Different flow rates may be obtained without using a pump, by changing the height of the shelves or tap adjustments (Fig. 1).

The stationary state may be obtained from the steady-state flow when water flow is stopped. The inflow effect was calculated at different flow rates (0, 3.08, 4.81, 8.46, 9.82, 15.45, 17.55, 40.71, 57.08 and 57.97 mL/s).

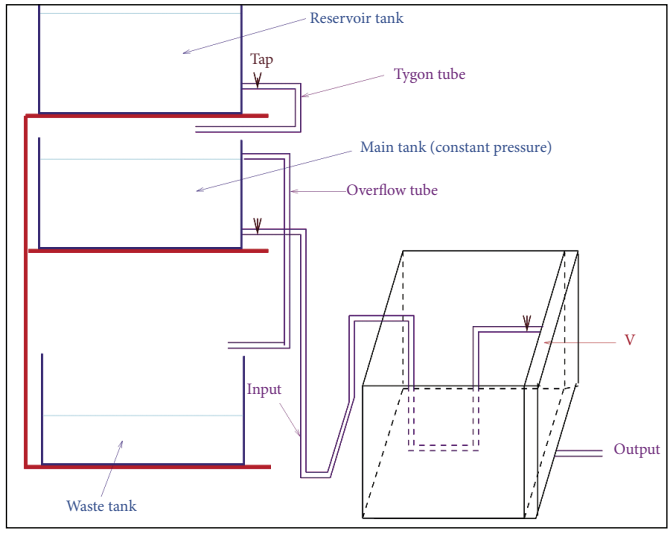

Fig. 1. Schematic diagram of MR flow phantom with reservoir and main tanks. Water pressure in the main tank is constant during the experiment as long as water is constantly flowing in the overflow tube. Volume (V) is used to calibrate the absolute flow. Flow can be calculated by measuring V and dividing it by the time taken to fill this volume. The velocity is calculated as a ratio of the flow of the object (tube) to its area (0.71 cm^3). The bulk of the phantom is filled with tap water or a saline solution.

The velocity was calculated as a ratio of the flow of the object (tube) to its area (0.71 cm3). The velocities (0, 4.34, 6.77, 11.91, 13.84, 21.76, 24.71, 57.34, 80.39 and 81.65 cm/s) cover the velocity range of small vessels and big arteries. Since the image parameters of the inflow measurement of the phantom were similar to the clinical data, the correction factor of the inflow effect may be applied to clinical data.

MRI T1-Weighted Technique

Moody et al.[6] have applied Peters'[18] radiolabeled microsphere technique for calculating the tissue blood flow to MR cerebral perfusion imaging.

The CBF can be calculated by the following expression on T1-weighted imaging:

$$CBF = \frac{Max\ gradient\ tissue\ (brain)}{Max\ intensity\ arterial\ input\ (neck)}$$

The correction factor for inflow can be calculated from the SI of the steady state flow divided by the SI of the stationary state at the same position.

Since the velocity, which depends on the flow rate,may affect SI, this effect should be considered when measuring the flow. To correct the CBF, the arterial input SI and gradient of the tissue should be divided by these factors. If the arterial input and tissue contain the same flow rate, the inflow does not have any effect on the flow, because the correction factors

will cancel out. But if the flow rates of the arterial input and tissue are not the same, the correction factors for both of them should be calculated and applied to the flow measurement. After applying the inflow effect, the corrected CBF may be calculated by

$$Corrected\ CBF = \frac{\frac{Max\ gradient\ tissue\ (brain)}{Inflow\ effect\ of\ the\ capilary}}{\frac{Max\ intensity\ arterial\ input\ (neck)}{Inflow\ effect\ of\ the\ artery}}$$

After perfusion image construction, the validity of the T1 technical acquisition should be checked by the quality control (QC), which was one of the requirements of the model of Bell et al.[10] The QC ensures that the integrated arterial input curve multiplied by the tissue blood flow paralleled that of the brain tissue SI time curve.

The T1 technique for measuring CBF has been applied to the MRI images acquired from eleven normal volunteers. The normal volunteers had a mean age of 32 with a range of 27 to 44 years (Standard deviation=4). The local ethics committee approval had been granted, and the inform consent of the healthy volunteers was obtained in all cases.

Blood Velocity

Soustiel et al.[19] measured the mean common carotid artery blood volume and its diameter using Doppler ultrasound. They mentioned that the mean values for common carotid artery blood flow and its diameter taken from 28 healthy volunteers (mean age=33.8 years) were 456±39 mL/min (range, 417-583 mL/min) and 6.7±0.7 mm (range, 5.8-8.7 mm), respectively. The velocity is the mean velocity range throughout the cardiac cycle. Since velocity of one organ is the ratio of the mean blood flow to its cross sectional area, the mean velocity of the common carotid is calculated as 21.57 cm/s. The mean velocity value of 23 cm/s was also reported by Savin et al.[20] Therefore, the average velocity of common carotid is assumed to be equal to 22.28 cm/s. In addition, the mean velocity value of 0.02 to 0.03 cm/s was reported by Smith and Kampine[21] for the capillaries.

Image Acquisition

1.5 T clinical MR scanner (Vision, Siemens Medical, Erhlangen, Germany) was used for this study. The phantom was placed centrally within a standard head and neck coil. T1-weighted TurboFLASH images were used to measure the SI of the steady flow and stationary state using the inversion recovery sequence (Linear Phase-Encoding). The acquisition parameters were as follows: echo time [TE]=4 ms, time for one FLASH line=8.5 ms, slice thickness=15 mm, matrix size=128×128, flip angle [α]=15°, inversion time set on scanner [TI]=300 ms, effective TI=844(300+8.5×128/2) ms. Images were acquired every 3 seconds. Magnetization preparation with a nonselective inversion pulse was performed.

One of the major sources of image non-uniformity in the MR scanners is the radio frequency (RF) coil inhomogeneity.[22] The RF coil should be uniform when the T1 technique is used for measuring the flow. That is because the technique is based on the maximum SI of the arterial input and the gradient of the tissue (organ) curves which are positioned at different places in the coil. Body coil (55 cm) was used for the CBF study. The body coil is assumed to be uniform and therefore no correction factor is required.[23]

After the contrast administration, T1-weighted TurboFLASH images were used to measure the SI change during the first passage of the bolus of contrast medium through the neck at the level of C4/C5 to include the common carotid arteries and through the brain at the level of the lateral ventricles. This means that slices were grouped in pairs (one measurement); one through the head and one through the neck.

A low dose (0.02 mL/kg) of Gd-DTPA contrast agent (Magnevist, Schering, Health Care Ltd, West Sussex, UK) was drawn up into a 10 mL syringe under a column of normal saline. It was injected via an antecubital vein after acquisition of the fifth image pair followed by a bolus flush. The contrast agent and flush were injected manually at the rate of 2 to 3 mL per second. Approximately, 1.5 mL of Gd-DTPA was injected for a 70-kg normal subject to give a concentration less than 0.8 mmol/L with the Linear Phase-Encoding acquisition.[6] The volume of injected contrast agent was about 1/10 of the normal suggested dose in T2-weighted perfusion imaging.

Temporal resolution was provided by the use of a gradient echo sequence, Linear Phase-Encoding (64×64 matrix interpolated to 128×128) sequence, (echo time [TE]=4 ms, time for one FLASH line=8.5 ms, slice thickness=15 mm, flip angle [α]=15°). Forty pairs of images were acquired after the fifth measurement with

neck-head image pairs being acquired every 3 seconds. Magnetization preparation with an inversion pulse was performed to null the signal from blood (inversion time set on scanner [TI]=300 ms, effective TI=844 ms).

Image Analysis

After transfering the image data from the MR scanner to a UNIX workstation, post processing was carried out with an in-house software developed using Interactive Data Language (IDL, Research Systems Inc. http://www.rsinc.com) and "C". This program could be run from either a UNIX workstation or a personal computer.

The programs were written to automatically find:

1- A region of interest (ROI) after discarding the first three pairs of images to reach a steady state around the brain, excluding the skull and scalp. The operator was given the opportunity to manually redefine the ROI when the automatic technique failed.

2- Arterial input curve, generated by using the images acquired through the common carotid artery of the neck. The maximum gradient of the brain tissue for each pixel during transit of the contrast bolus produces a gradient image.

3- To produce a perfusion image from the gradient image of the brain tissue divided by the peak value of the arterial input, which was calculated from the gamma fit curve. The scale of this image was then automatically adjusted, taking into consideration the known time interval between measures (3 seconds), to produce an image reflecting CBF in milliliters per 100 g per minute.

Results

Phantom

Figure 2 shows the effect of velocity on MR signal intensity at concentrations of 0.8 mmol/L, which is similar to the concentration of ROI in the human study. The figure also shows that an increase in the velocity is associated with increase in the SI. The error bars show the standard deviation of SI in the region of interest.

Figure 3 displays the relationship between the inflow correction factor and velocity at the concentration. The velocity varied between 0 and 81.65 cm/s. As it can be seen from figure 3, an increase in the velocity is associated with an increase in the inflow correction factor.

For the average common carotid artery velocity (22.28 cm/s), the inflow correction factor may be obtained as 1.23 at a concentration of 0.8 mmol/L (Fig. 3). In addition, the figure shows that the inflow correction factor for the capillary level (0.02 - 0.03 cm/s) is about 1 and therefore may be ignored for measuring the cerebral blood flow. Therefore, for measuring CBF, the maximum gradient of the tissue curve and the maximum SI of arterial curve should be divided by 1 and 1.23, respectively. In other words, CBF should be multiplied by 1.23.

Normal subjects

Figure 4 shows the right and left, upper and lower territories of the middle cerebral artery (MCA). CBF using the T1 technique was calculated for these areas.

After perfusion image construction, the validity of the technical acquisition was checked by the QC. The values of CBF were calculated using the T1 technique for the right and left, upper and lower portions of the MCA territory from eleven normal subjects, shown in Table 1. In addition, the total mean, which shows the mean value of the right and left MCA territories, can also be seen in Table 1. The average of CBF in the MCA grey matter territory measured by the T1 technique was 43.0 mL/100 g/min (SD=8.8). After applying the

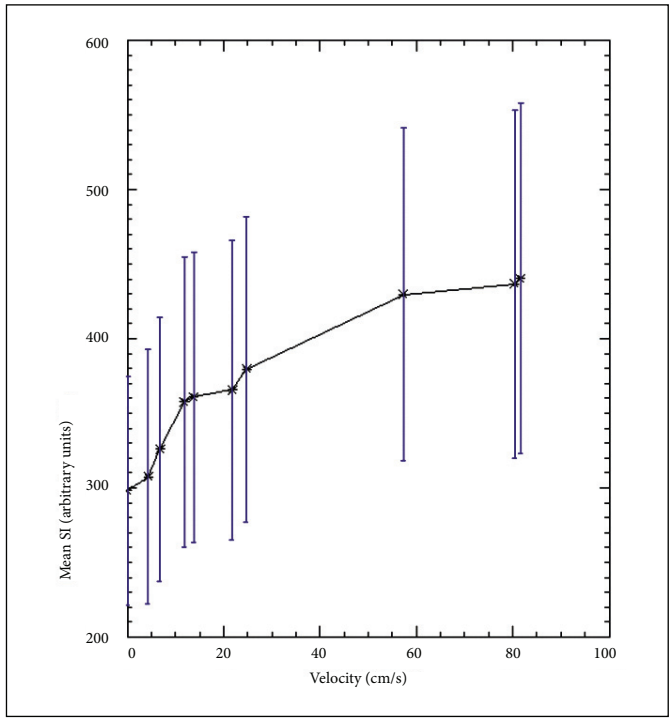

Fig. 2. The effect of velocity on MR signal strength. An increase in the velocity is associated with an increase in signal intensity (SI). The error bars show the standard deviation of SI in the region of interest.

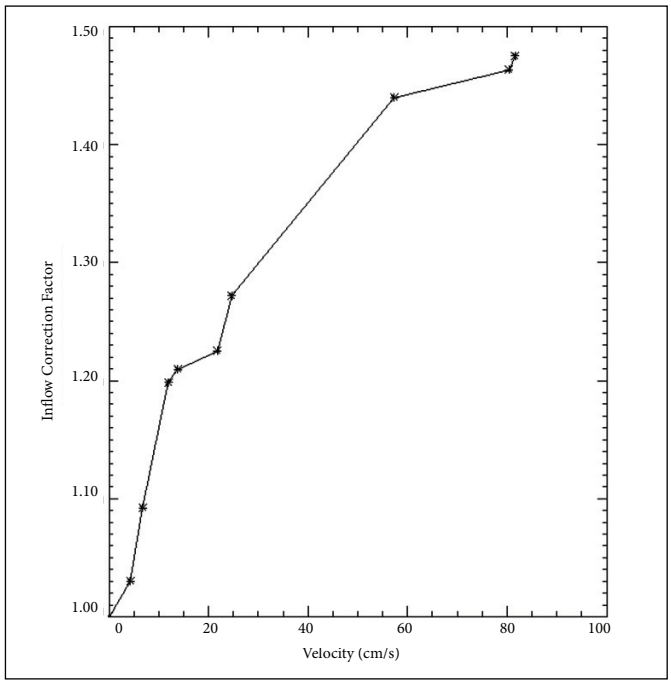

Fig. 3. Inflow correction factor, calculated by the steady state flow over stationary state against velocity at concentration of 0.8 mmol/L, using the Linear Phase-Encoding acquisition. An increase in the velocity is associated with an increase in the inflow correction factor.

inflow correction factor (1.23, Fig. 3), the corrected CBF was calculated as 52.9 mL/100 g/min.

Discussion

A large number of papers have discussed relative hemodynamic parameters, sufficient for many clinical applications. However, for precise evaluation of disease or drug treatment, absolute hemodynamic parameters need to be determined.

A T1 MRI technique was presented to measure the absolute CBF by Moody et al.[6] They reported that the asymptomatic MCA grey matter territory gave an average CBF of 42.6 mL/100 g/min. They compared this value with the SPECT value and showed that the average difference between the two techniques was -0.79% (SD=4.3%). They stated that the technique had not been compared with a quantitative technique such as PET or Xe-CT, and it appeared that the CBF values were slightly low.

Since the T1 technique is based on the maximum gradient of tissue and maximum amplitude of arterial curve, one reason for the low value for CBF could be due to the inflow effect of the arterial input. The effect of inflow on SI was investigated in this paper. The finding indicates that the blood velocity may affect the SI, leading to a change of the SI. Therefore, the effect

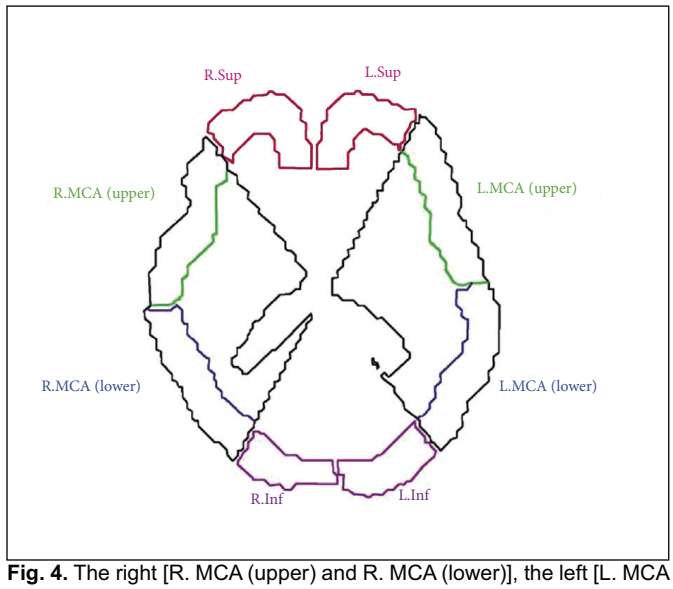

Fig. 4. The right [R. MCA (upper) and R. MCA (lower)], the left [L. MCA (upper) and L. MCA (lower)], and the middle cerebral artery (MCA) territories. In addition, the superior [left (L. Sup) and right (R. Sup)] and the inferior [left (L. Inf) and right (R. Inf)] territories can also be seen.

of inflow should be considered in CBF calculations.

The aim of this paper was to assess the accuracy of T1 technique for measuring the CBF after inflow correction.

Since the image parameters of this study were similar to Moody et al.'s[6] study, the inflow correction factor may be applied to their result. After applying the inflow correction factor of 1.23 on the CBF value in MRI, which was reported by Moody et al.,[6] the corrected CBF was equal to 52.4 mL/100 g/min. The MRI value has a good agreement with the value obtained from SPECT (53.9 mL/100 g/min). The finding of this study indicates that the average CBF in the MCA grey matter territory measured by the T1 technique was 43.0 mL/100 g/min (SD=8.8) for eleven normal subjects. After applying the inflow correction factor, the corrected CBF was calculated as 52.9 mL/100 g/min. Since PET is the gold standard for quantitative assessment of CBF,[24-27] different values of grey matter CBF have been extracted from PET studies. CBF varied between 47.7 and 69.8 mL/100 g/min for healthy subjects, which is in good agreement with those in the PET literature.

Although the CBF value from the T1 technique is comparable to the value obtained from the literature, it seems that it is slightly lower than the real CBF. Low CBF values could be the result of the gradient of the tissue curve being lower than ideal. This could be due to the dispersion of the bolus that takes place within the capillary bed, leading to an increase in the mean transit time. This leads to a decrease in the maximum gradient

Table 1. CBF Values (mL/100 g/min) for Different Parts of the Brain

Subject NO	Right Upper MCA	Right Lower MCA	Right Mean MCA	Left Upper MCA	Left Lower MCA	Left Mean MCA	Total Mean
1	23.9	26.7	25.3	28.5	27.3	27.9	26.6
2	38.6	34.7	36.7	37.5	43.2	40.4	38.5
3	37.7	38.1	37.9	49.3	42.5	45.9	41.9
4	36.2	48.1	42.2	40.9	55.0	48.0	45.1
5	40.8	39.3	40.1	39.6	44.3	42.0	41.0
6	60.7	45.1	52.9	62.4	48.8	55.6	54.3
7	35.8	34.3	35.1	34.1	32.7	33.4	34.2
8	45.4	47.8	46.6	47.3	44.2	45.8	46.2
9	33.2	39.2	36.2	47.3	38.9	43.1	39.7
10	49.5	50.1	49.8	40.7	50.6	45.7	47.7
11	57.6	56.2	56.9	52.8	66.3	59.6	58.2

Uncorrected CBF values (mL/100 g/min) for the upper and lower portions and the mean value of CBF for the right and left middle cerebral artery (MCA) territories from eleven normal subjects. In addition, the total mean, which shows the mean value of the right and left MCA, may be seen in the table.

of tissue and hence a reduction in the subsequent CBF.

Peters et al.[9] reported the influence of bolus spreading on blood flow measurement of the kidney with different arterial inputs from first pass time activity curves. They stated that the measured blood flow was different when using different arterial inputs, because some bolus spreading occurs between arterial inputs and the organ (tissue).

It should be noted that although the T1 technique suffers from dispersion of bolus in the tissue as does the deconvolution method, complex numerical analysis for measuring CBF is not required. In addition, the deconvolution process is also extremely sensitive to noise in the measured arterial and tissue enhancement curves.[28-29] Using T1-weighted images for a perfusion study needs about 1/10 of the contrast agent that is normally used for a T2-weighted acquisition. The use of small dose in T1-weighted imaging has some advantages. First, it does not need a pump injector and the contrast is delivered by simple hand injection. Second, small doses have a low cost. Third, it is possible to carry out repeated measurements. In addition, if other investigations require the use of additional doses of contrast agent such as MR angiography, they can be carried out during the same session without exceeding the maximum permissible contrast dose. Finally, the images may be acquired on a conventional MRI scanner.

It seems that in spite of dispersion, the T1 technique does suffer from a number of drawbacks as follows:

1- In contrast to T2-weighted techniques currently in use, the T1 technique acquires the image from only one brain slice, which means that whole-brain studies are not possible. This may be overcome by the use of echo planar imaging to provide a rapid multislice T1 technique that would also include a neck slice for the AIF.

2- The use of small volumes of contrast results in reduced signal-to-noise ratio (SNR). This ratio should be improved by using more contrast agent.

As mentioned in a previous study,[30] inversion time (TI) is one of the important parameters for measuring SI. These parameters may have an effect on the maximum linear relationship between SI and concentration. An increase in TI leads to a decrease in the maximum linearity. Therefore, the SNR may be improved by using a high volume of contrast agent with a low TI for inversion recovery sequences.

In conclusion, using the T1 technique for perfusion studies needs about 1/10 of the contrast agent that is normally used for a T2-weighted acquisition allowing additional contrast enhanced examinations to be performed. Since the values of CBF after applying the correction factor due to inflow have a better agreement with those obtained with PET in normal volunteers, the new T1 technique may be used to measure the absolute flow rate in MRI.

Conflict of Interest

The authors have no financial or personal relationship with other people or organizations that

could inappropriately influence (bias) this work.

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