Comparison of cerebral blood flow acquired by two-dimensional and three-dimensional Arterial Spin Labeling on one system at 3 Tesla

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Aims and objectives

Arterial spin-labeling (ASL) perfusion MRI enables absolute quantification of cerebral blood flow (CBF) without the use of contrast agents (1-5). Especially, pseudo-continuous arterial spin labeling (pCASL) was widely used because it provides continuous labeling of arterial blood with a low specific absorption ratio (SAR) via a train of rapidly repeating low-tip radiofrequency (RF) pulses. For pCASL, two-dimensional (2D) gradient-echo (GRE) planar imaging (EPI) and three-dimensional (3D) fast-spin echo interleaved stack-of-spirals (FSE spiral) are used as common readout schemes (2,4).

High signal-to-noise ratio (SNR) is usually required in ASL acquisition because ASL is encumbered by its intrinsically low SNR. Low SNR is caused by the short lifetime of the labeled blood by T1 decay and small volume fraction of blood vessels in the human brain, estimated as 3-5%, which is much smaller than other tissues (3). In addition, low SNR also has an influence lead to inaccurate quantification in calculation of CBF-values.

As one of the important approaches to improve SNR, the use of 3D readout module is widely recognized. One of weaknesses in 2D GRE EPI is high sensitivity of susceptibility effect, especially in the region of cerebellum, resulting in susceptibility artifacts and image distortion which leads to low SNR images (2-4,6). Additionally, another weakness is the different slice acquisition times and that each slice exhibits a longer effective post-labeling delay (PLD) compared to its previous slice. Such results in the different SNR between imaging slices. The 3D readout module can overcome these problems because it simultaneously obtains all imaging slices with identical PLD times, with numerous numbers of encode steps which lead to high SNR. Together, these allow for an improvement in ASL imaging in terms of sequence efficiency, slice coverage, SNR, physiologic timing, substantially reduced measurement times, reduced distortion, and susceptibility artifacts (2,4,6). As a 3D readout in pCASL, FSE spiral readout was frequently used. This readout module provides high SNR images because the largest signal through the signal sampling was placed in the center of k-space. However, this readout is sometimes problematic because peripheral signal level in k-space is very low. This can lead to images with blurred outline.

Recently, pCASL using turbo spin-echo (TSE) with pseudo-steady state (PSS) readout module has become available. The advantage of TSE with PSS readout module is that PSS obtains the high signal echo in the periphery of k-space as well as its center by using an optimized variables flip angle (FA) scheme in this readout. A low refocusing FA is continuously served to adjust the effective rate of \( T_2 \) relaxation.

It is expected that 3D-pCASL using PSS readout module provides high SNR and spatial resolution with sharpened outlines. In our knowledge, there is no report which has described 3D-pCASL using TSE with PSS readout module.
The aim of the current study is to assess and compare the CBF-value obtained from 2D pCASL using GRE-EPI and 3D pCASL using TSE with PSS readout module with some FA patterns by one system as well as to compare CBF-value by these techniques with 3D pCASL using FSE spiral readout module by another vendor.
Methods and materials

Subjects

Ten healthy volunteers (7 men, 3 women, mean age, 29 years; range 24-36 years) participated in this study after signing a written informed consent and ten patients (3 men, 7 women, mean age, 48 years; range 10-70 years, 4 aneurysm, 2 moyamoya disease, 1 stroke, 1 subarachnoid hemorrhage, 1 systemic lupus erythematosis, 1, aortic valve stenosis, 1) who underwent 3-tesla MRI scanning including pCASL sequence were investigated.

MRI data acquisition

All subjects were scanned on a 3-tesla MR scanner (Achieva TX; Philips Medical Systems, Best, The Netherlands) using an 8-channel head coil. In addition, all volunteers also received an additional MR scan by different 3-tesla unit (Discovery MR750w, GE Healthcare, Milwaukee, WI, US) using 12-channel head coil on the same day.

pCASL by Philips scanner was performed using the following readout modules and scanning parameters:

- 2D GRE-EPI: repetition time (TR), 4500 ms; echo time (TE), 15 ms; FA, 90°; number of signal average (NSA), 10; slice thickness, 5 mm; slice gap, 0.5 mm; sensitivity encoding (SENSE) factor, 2.5; field of view (FOV), 240 mm; image matrix, 80×80; number of slice, 25; label duration, 1650 ms; post labeling delay (PLD), 1525 ms; PLD increase per slice, 28.3 ms; background suppression, which consisted of a saturation pulse before labeling and inversion pulses at 1710 ms and 2860 ms after the saturation pulse; scan time, 1:38.

- 3D TSE with PSS readout modules at refocusing FA 120°-180°, Constant FA of 120°, and 130°: TR, 5393 ms/4639 ms/4869 ms; TE, 19 ms; FA, 90°; refocusing FA, which trains with explicit control of that from minimum FA of 120° to maximum FA of 180° (PSS120°-180°), constant FA of 120° and 130°; NSA, 1; slice thickness, 3 mm; TSE factor, 100; SENSE factor, 2.5; FOV, 240 mm; image matrix, 80×80; number of slice, 40; label duration, 1650 ms; PLD, 1525 ms; background suppression, which consisted of a saturation pulse before labeling and inversion pulses at 1680 ms and 2730 ms after the saturation pulse; scan time, 1:47/1:32/1:37.

pCASL by GE scanner was performed using the following readout modules and scanning parameters:
- 3D FSE spiral: TR, 5393 ms; TE, 19 ms; FA, 90°; refocusing FA 111°; NSA, 1; slice thickness, 4 mm; FOV, 240 mm; image matrix, 8 spirals×512 sampling points; number of slice, 36; label duration, 1450 ms; PLD, 1525 ms; scan time, 1:47.

The scanning range of these four pCASL acquisitions were planned to cover the whole brain including the cerebellum at the lower end. Labeling slab was set 20 mm below the lowest image slices.

**Refocusing FA modulation techniques**

(1) PSS readout module using a variable refocusing FA

Fig. 1 shows that transition of refocusing FA with PSS readout module using the variable refocusing FA. In the PSS readout module with the variable refocusing FA, at first, the refocusing FA rapidly decreases from around 180° to the minimum (\(\#_{\text{min}}\)). Then remains constant for the specified number of echoes to place in the center of k-space (\(\#_{\text{cen}}\)), at the same time PSS conditions can be established. (8). As shown in Fig. 2, the signal intensity approaches a temporary steady state condition due to T\(_2\) and T\(_1\) relaxation, this condition is called a PSS condition because of the steady state condition is actually only temporary (7).

Thereafter, the refocusing FA gradually increases linearly until the end of the echo train, when the refocusing FA arrvies at\(\#_{\text{max}}\). In this study, we set the details of input in refocusing FA as follows; \(\#_{\text{min}}=120°, \#_{\text{cen}}=120°, \#_{\text{max}}=180°\).

By using this style of refocusing FA, output signal intensity accomplished is illustrated in the solid line of Fig. 2.

In this style of refocusing FA, higher signal at the first echo can be accomplished by using a refocusing FA of near 180° than using a refocusing FA of low angles (10).

(2) PSS readout module using a constant refocusing FA

Fig. 3 shows that transition of refocusing FA with PSS readout module using the constant refocusing FA. In the PSS readout module with constant refocusing FA, refocusing FA at the first echo is the same as that of the PSS readout module described above. The refocusing FA trains from around 180° to the constant refocusing FA set. The constant refocusing FA trains were used until the end of the echo train. The disadvantage of this method is that the signal intensities around the end of echo train decrease more than the PSS readout module described above (7-10). In this study, we set the input of refocusing FA as follows; \(\#_{\text{min}}=120°\) and 130°.

By using this style of refocusing FA, output signal intensity accomplished is illustrated in the dotted line of Fig. 2.
Fig. 1: Refocusing FA modulation model: The PSS readout module with variable refocusing FA.

*References:* - Sapporo/JP
Fig. 2: This figure shows signal intensities produced by the PSS readout modules. Transition of signal intensities with PSS readout modules by variable refocusing FA (solid line), and constant refocusing FA (dotted line).

References: - Sapporo/JP
**Fig. 3:** Refocusing FA modulation model: The PSS readout module with constant FA.

*References:* Sapporo/JP

**Post-processing**

For the data obtained by Philips scanner, labeled and control images were pairwise subtracted and averaged to obtain perfusion-weighted images.

The CBF was calculated using this equation (2)(Fig. 4):

\[
CBF = \frac{6000 \times \lambda_{GM} \times (SI_{control} - SI_{label}) \times e^{\frac{PLD}{T_{1,blood}}} \times e^{\frac{T_{1,blood}}{\tau}}}{2 \times \alpha \times T_{1,blood} \times SI_{PD} \times \left(1 - e^{-\frac{T_{1,blood}}{T_{1,blood}}}\right)} \quad [mL/100 \ g/\min]
\]
The CBF was calculated using this equation (2): where $\#_{GM}$ is the gray matter (GM) brain/blood partition coefficient in mL/g (0.9), $S_{I_{control}}$ and $S_{I_{label}}$ are the time-averaged signal intensities in the control label images, respectively, $T_{1,blood}$ is the longitudinal relaxation time of blood (1650 ms), $\#$ is the labeling efficiency (0.85), $S_{I_{PD}}$ is the signal intensity of a proton density-weighted image, and $\tau$ is the label duration (1650 ms). PLD is the posy labeling delay (1525 ms).

References: - Sapporo/JP

For the data obtained by GE scanner, the perfusion-weighted images obtained by subtracting labeled images from control images, these were provided directly from the console with the scanner.

The CBF was calculated using this following equation (1)(Fig. 5):

$$CBF = \frac{6000 \times \Delta M \times e^{\frac{-PLD}{T_{1,blood}}}}{2 \times \alpha \times \alpha_{inv} \times M_{0,blood} \times T_{1,blood} \times \left(1 - e^{\frac{-\tau}{T_{1,blood}}}ight)} [mL/100 g/min]$$

Fig. 5: The CBF was calculated using this equation (1): where $\#M$ represents the difference of signal intensity between control and labeled images. $M_{0,blood}$ is the equilibrium magnetization of arterial blood. $T_{1,blood}$ is the longitudinal relaxation time of blood (1650 ms) in seconds,$\#$ is the labeling efficiency (0.8), $\#_{inv}$ corrects for the decrease in labeling efficiency due to background suppression pulses (0.75), and $\tau$ is the label duration (1650 ms). PLD is the posy labeling delay (1525 ms).

References: - Sapporo/JP

where $\#M$ represents the difference of signal intensity between control and labeled images. $M_{0,blood}$ is the equilibrium magnetization of arterial blood. $T_{1,blood}$ is the longitudinal relaxation time of blood (1650 ms) in seconds,$\#$ is the labeling efficiency (0.8),$\#_{inv}$ corrects for the decrease in labeling efficiency due to background suppression pulses (0.75), and $\#$ is the label duration (1650 ms). PLD is the posy labeling delay (1525 ms).
M_{0,\text{blood}} was calculated using this following equation (1)(Fig. 6):

\[
M_{0,\text{blood}} = \frac{PD}{\lambda_{GM} \times \left(1 - e^{-\frac{t_{\text{sat}}}{T_{1GM}}} \right)}
\]

**Fig. 6:** M_{0,\text{blood}} was calculated using this equation (1): PD was the image signal intensity of control images that was provided by the console with the scanner. tsat is the saturation recovery time (2000 ms), T1GM is the relaxation time of GM tissue (1200 ms) and #GM is the gray matter (GM) brain/blood partition coefficient in mL/g (0.9).

**References:** Sapporo/JP

PD was the image signal intensity of control images that was provided by the console with the scanner. tsat is the saturation recovery time (2000 ms), T1GM is the relaxation time of GM tissue (1200 ms) and #GM is the gray matter (GM) brain/blood partition coefficient in mL/g (0.9).

**Data analysis**

The labeled and control images by Philips scanner and the control and subtraction images by GE scanner obtained with all readout modules of pCASL sequences were outputted in the digital imaging and communication in medicine (DICOM) format. The CBF calculation was performed using Microsoft Excel on a personal computer. Data analysis was conducted using Image J software (NIH Image, Bethesda, MD, USA). The volunteer’s and patient’s data were analyzed individually (Fig. 7-9).

In each imaging, manual regions of interest (ROI) was placed bilaterally on gray matter (GM) in the flow territory of the anterior (ACA), middle (MCA), and posterior cerebral artery (PCA); white matter (WM) on parietal and basal areas; and GM in the cerebellum (Fig. 10).
**Fig. 7:** Images acquired by pCASL using 2D-GRE EPI and 3D-TSE by Philips scanner at the Parietal level.

**References:** - Sapporo/JP
**Fig. 8**: Images acquired by pCASL using 2D-GRE EPI and 3D-TSE by Philips scanner at the Basal level.

*References:* - Sapporo/JP
Fig. 9: Images acquired by pCASL using 2D-GRE EPI and 3D-TSE by Philips scanner at the Cerebellum level.

References: - Sapporo/JP
**Fig. 10**: Images of the manual region of interest (ROI); the ROIs were placed bilaterally on gray matter (GM) in the flow territory of the anterior (ACA), middle (MCA), and posterior cerebral artery (PCA); white matter (WM) on parietal and basal areas; and GM in the cerebellum.

**References**: - Sapporo/JP

The coefficient of variation (CV) was calculated using this following equation (1). The CV-values were also calculated as the ratio of SD_{CBF} to the mean CBF. The mean CBF and standard deviation (SD_{CBF}) were calculated with those 16 segments in each pCASL images (Fig. 11).
The coefficient of variation (CV) was calculated using this equation (1). The CV-values were also calculated as the ratio of SDCBF to the mean CBF. The mean CBF and standard deviation (SDCBF) were calculated with those 16 segments in each pCASL images.

References: - Sapporo/JP

**Statistical analysis:**

Both of the CBF-values and CV-values were respectively compared between the readout modules using Steel-Dwass' test.

Correlation of CBF-values between different readout modules and correlation of CBF-values between different vendors were respectively analyzed using Pearson's correlation coefficient.

All statistical analyses were performed using the JMP® 11 (SAS Institute Inc., Cary, NC, USA). Statistical significance was set to P<0.05 for all tests.

**For Data analysis (1): Comparison of CBF-values in all segments and slice levels obtained by Philips scanner**

To assess the readout module differences, the CBF-values obtained by 2D-pCASL and the three readout modules of 3D-pCASL on a Philips scanner were compared in all segments and each slice levels by Steel-Dwass' test.

**For Data analysis (2): Comparison of the CV-value of GM in parietal and basal levels**

To assess the readout module differences, the CV-value of GM were calculated from the mean CBF and SD_{CBF} of GM obtained from 2D-pCASL and the three readout modules of 3D-pCASL on a Philips scanner in parietal and basal level. The CV-value of GM were compared in each these slice levels by Steel-Dwass' test.

\[
CV = 100\% \times \frac{SD_{CBF}}{mean\ CBF}
\]
For Data analysis (3): Correlation of the CBF-values between the different vendors (volunteer group only)

To assess the differences of CBF-values between different vendors, the linear correlation coefficient was calculated to estimate the correlation of CBF-values by Pearson's correlation coefficient between these combinations; 2D-pCASL (Philips) and FSE spiral of 3D-pCASL (GE), 3D-pCASL with PSS readout (120° constant) (Philips) and FSE spiral of 3D-pCASL (GE), 3D-pCASL with PSS readout (130° constant) (Philips) and FSE spiral of 3D-pCASL (GE), 3D-pCASL with PSS readout (120°-180°) (Philips) and FSE spiral of 3D-pCASL (GE).
Fig. 1: Refocusing FA modulation model: The PSS readout module with variable refocusing FA.

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**Fig. 2:** This figure shows signal intensities produced by the PSS readout modules. Transition of signal intensities with PSS readout modules by variable refocusing FA (solid line), and constant refocusing FA (dotted line).

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**Fig. 3:** Refocusing FA modulation model: The PSS readout module with constant FA.

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\[ CBF = \frac{6000 \times \lambda_{GM} \times (SI_{control} - SI_{label}) \times e^{\frac{PLD}{T_{1,\text{blood}}}}}{2 \times \alpha \times T_{1,\text{blood}} \times SI_{PD} \times \left(1 - e^{-\frac{\tau}{T_{1,\text{blood}}}}\right)} \text{ [mL/100 g/min]} \]

**Fig. 4:** The CBF was calculated using this equation (2): where \#GM is the gray matter (GM) brain/blood partition coefficient in mL/g (0.9), SIcontrol and SIlabeled are the time-averaged signal intensities in the control label images, respectively, T1,blood is the longitudinal relaxation time of blood (1650 ms), \#is the labeling efficiency (0.85), SIPD is the signal intensity of a proton density-weighted image, and \# is the label duration (1650 ms). PLD is the posy labeling delay (1525 ms).

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Fig. 5: The CBF was calculated using this equation (1): where $\Delta M$ represents the difference of signal intensity between control and labeled images. $M_{0,\text{blood}}$ is the equilibrium magnetization of arterial blood. $T_{1,\text{blood}}$ is the longitudinal relaxation time of blood (1650 ms) in seconds, $\#$ is the labeling efficiency (0.8), $\#_{\text{inv}}$ corrects for the decrease in labeling efficiency due to background suppression pulses (0.75), and $\#$ is the label duration (1650 ms). PLD is the posy labeling delay (1525 ms).

$CBF = \frac{6000 \times \Delta M \times e^{\frac{-PLD}{T_{1,\text{blood}}}}}{2 \times \alpha \times \alpha_{\text{inv}} \times M_{0,\text{blood}} \times T_{1,\text{blood}} \times \left(1 - e^{\frac{-\tau}{T_{1,\text{blood}}}}\right)}$ [mL/100 g/min]

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Fig. 6: $M_{0,\text{blood}}$ was calculated using this equation (1): PD was the image signal intensity of control images that was provided by the console with the scanner. $t_{\text{sat}}$ is the saturation recovery time (2000 ms), $T_{1GM}$ is the relaxation time of GM tissue (1200 ms) and $\#_{\text{GM}}$ is the gray matter (GM) brain/blood partition coefficient in mL/g (0.9).

$M_{0,\text{blood}} = \frac{PD}{\lambda_{\text{GM}} \times \left(1 - e^{\frac{-t_{\text{sat}}}{T_{1GM}}}\right)}$

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Fig. 7: Images acquired by pCASL using 2D-GRE EPI and 3D-TSE by Philips scanner at the Parietal level.

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**Fig. 8:** Images acquired by pCASL using 2D-GRE EPI and 3D-TSE by Philips scanner at the Basal level.

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Fig. 9: Images acquired by pCASL using 2D-GRE EPI and 3D-TSE by Philips scanner at the Cerebellum level.

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**Fig. 10:** Images of the manual region of interest (ROI); the ROIs were placed bilaterally on gray matter (GM) in the flow territory of the anterior (ACA), middle (MCA), and posterior cerebral artery (PCA); white matter (WM) on parietal and basal areas; and GM in the cerebellum.

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**Fig. 11:** The coefficient of variation (CV) was calculated using this equation (1). The CV-values were also calculated as the ratio of SDCBF to the mean CBF. The mean CBF
and standard deviation (SDCBF) were calculated with those 16 segments in each pCASL images.

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Results

Results of data analysis (1): Comparison of CBF-values in all segments and slice levels obtained by Philips scanner:

In both volunteer's and patient's data, in all regions except the cerebellum, significant differences in GM CBF-values were found between 2D-pCASL and the three modules of 3D-pCASL obtained by Philips scanner (P<0.05) (Table 1). There were no significant differences of the WM CBF-values between 2D-pCASL and the three modules of 3D-pCASL obtained by the Philips scanner (Table 2).

Results of data analysis (2): Comparison of the CV-value of GM in parietal and basal levels

In patient's data, the smallest GM CV-value was obtained in the 3D-pCASL using PSS120°-180° method in each slice levels.

In contrast, in the volunteer's data, the smallest GM CV-value was obtained in the 3D-pCASL using PSS120°-180° method, only in parietal level.

In both volunteer's and patient's data, significant differences of CV-value in GM were found between 2D-pCASL and the three readout modules of 3D-pCASL in each slice levels (P<0.05) (Table 3).

Results of Data analysis (3): Correlation of the CBF-values between the different vendors (volunteer group only):

Significant correlation was found in all regional GM CBF-values except the parietal level between all of the three readout modules of 3D-pCASL obtained with Philips scanner and FSE spiral 3D-pCASL obtained with GE scanner. In these correlations, the correlation coefficient between 3D-pCASL using PSS120°-180° and FSE spiral 3D-pCASL on the cerebellum level was the largest (cerebellum; r=0.83, P<0.0001)(Fig. 12).

There was no significant correlation of the GM CBF-values between 2D-pCASL obtained with Philips scanner and 3D-pCASL obtained with GE scanner.

There was only one significant correlation in the WM CBF-values; it was between 3D-pCASL using PSS 120°-180° readout module obtained with Philips scanner and FSE spiral 3D-pCASL obtained with GE scanner on the basal level (r=-0.46, P<0.05) (Fig. 13).
Table 1: The GM CBF-values in each slice level; Volunteer's data and Patient's data. GM: gray matter; WM: white matter; CBF: cerebral blood flow; SD: standard deviation 2D: 2D-GRE EPI; PSS120-180: 3D-pCASL using PSS120°-180° method; rfc120, 130: 3D-pCASL using constant FA of 120° and 130° method GE: 3D-pCASL by GE scanner

References: - Sapporo/JP
Table 2: The WM CBF-values in each slice level; Volunteer’s data and Patient’s data

References: - Sapporo/JP

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Table 3: The GM CV-values in each slice level; Volunteer's data and Patient's data

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Fig. 12: Comparison between Philips and GE CBF measurements: 3D-pCASL using PSS120°-180° by Philips scanner (P CBF) and 3D-pCASL by GE scanner (GE CBF). The correlation of GM CBF-value on the cerebellum level. Good correlation was observed between P CBF and GE CBF in GM with statistical significance at cerebellum level (r=0.83, P<0.0001).

References: - Sapporo/JP
Fig. 13: The correlation of WM CBF-value on the basal level. Good correlation was observed between P CBF and GE CBF in WM with statistical significance at basal level ($r=-0.46$, $P<0.05$).

References: - Sapporo/JP
### GM CBF-value in each slice level

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**Table 1**: The GM CBF-values in each slice level; Volunteer's data and Patient's data. GM: gray matter; WM: white matter; CBF: cerebral blood flow; SD: standard deviation 2D: 2D-GRE EPI; PSS120-180: 3D-pCASL using PSS120°-180° method; rfc120, 130: 3D-pCASL using constant FA of 120° and 130° method GE: 3D-pCASL by GE scanner
### Table 2: The WM CBF-values in each slice level; Volunteer's data and Patient's data

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### GM CV-value

#### Volunteer's Data

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<td>CV</td>
<td>SD</td>
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<tr>
<td>PSS120–180</td>
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<tr>
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<td>rfc130</td>
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#### Patient's Data

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<th>Basal Level</th>
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<td>SD</td>
</tr>
<tr>
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</tbody>
</table>

**Table 3:** The GM CV-values in each slice level; Volunteer's data and Patient's data

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Fig. 12: Comparison between Philips and GE CBF measurements: 3D-pCASL using PSS120°-180° by Philips scanner (P CBF) and 3D-pCASL by GE scanner (GE CBF). The correlation of GM CBF-value on the cerebellum level. Good correlation was observed between P CBF and GE CBF in GM with statistical significance at cerebellum level ($r=0.83$, $P<0.0001$).

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Fig. 13: The correlation of WM CBF-value on the basal level. Good correlation was observed between P CBF and GE CBF in WM with statistical significance at basal level ($r=-0.46$, $P<0.05$).

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Conclusion

Several significant differences of the CBF-values, except with the cerebellum level and GM CV-values in all slice levels, were observed between 2D-pCASL and three readout modules of 3D-pCASL obtained by the Philips scanner. Especially, the CBF-values and CV-values of the largest difference were observed when using 3D-pCASL with PSS 120°-180° method. The smallest value of CV in GM was observed by 3D-pCASL using PSS 120°-180° method.

In addition, a good correlation was observed in the CBF-values between all readout modules of 3D-pCASL obtained by Philips scanner and 3D-pCASL by GE scanner.

2D-pCASL using GRE EPI did not obtain a good correlation with the cerebellum level, probably because the GRE EPI sequence has high sensitivity for susceptibility variations (e.g. Tissue-air interfaces). In addition, geometric distortions were expected in such regions when using EPI readout.

In contrast, 3D-TSE by Philips scanner and 3D-FSE spiral by GE scanner, use FSE-based readout. The advantage of this readout, the spin dephasing caused by inhomogeneities in the B\textsubscript{0} field at every spin-echo time are rephased to use the refocusing FA (4). For these reasons, 3D-pCASL with PSS readout module or with FSE spiral is considered superior in regions such as the cerebellum compared 2D-GRE EPI sequence.

This study had several limitations. First, only the CBF and CV value were used for image evaluation. In 3D-pCASL, the advantage of PSS readout is that high signal echo is placed in the periphery of k-space as well as center, and thus will be expected to provide sharpened outlined images as well as high SNR. This sequence presents a streamlined technique to generate a sequence of refocusing FA on a per-prescription basis, that produces relatively high SNR and limits blurring in a wide range of materials encountered in vivo. Additional image evaluation relating to image blurring is expected in further studies.

Second, we did not compare the CBF-values obtained from pCASL to those obtained from the referent gold standard, H\textsubscript{2}\textsuperscript{15}O positron emission tomography (PET), for validation (11).

In conclusion, the results of this study showed it was more useful to evaluate CBF by 3D-pCASL, especially using PSS 120°-180°, than by 2D-pCASL.
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