## DIAGNOSTIC NEURORADIOLOGY

# Intracranial artery velocity measurement using 4D PC MRI at 3 T: comparison with transcranial ultrasound techniques and 2D PC MRI

Stephan Meckel • Lorenz Leitner • Leo H. Bonati • Francesco Santini • Tilman Schubert • Aurelien F. Stalder • Philippe Lyrer • Michael Markl • Stephan G. Wetzel

Received: 1 June 2012 / Accepted: 3 October 2012 / Published online: 10 November 2012 © Springer-Verlag Berlin Heidelberg 2012

#### **Abstract**

Introduction 4D phase contrast MR imaging (4D PC MRI) has been introduced for spatiotemporal evaluation of intracranial hemodynamics in various cerebrovascular diseases. However, it still lacks validation with standards of reference. Our goal was to compare blood flow quantification derived from 4D PC MRI with transcranial ultrasound and 2D PC MRI.

Methods Velocity measurements within large intracranial arteries [internal carotid artery (ICA), basilar artery (BA), and middle cerebral artery (MCA)] were obtained in 20 young healthy volunteers with 4D and 2D PC MRI, transcranial Doppler sonography (TCD), and transcranial colorcoded duplex sonography (TCCD). Maximum velocities at peak systole (PSV) and end diastole (EDV) were compared using regression analysis and Bland–Altman plots.

Stephan Meckel and Lorenz Leitner contributed equally to content of manuscript.

S. Meckel (\subseteq)

Department of Neuroradiology, University Hospital Freiburg, Breisacher Strasse 64, 79106, Freiburg, Germany e-mail: stephanmeckel@gmail.com

L. Leitner · T. Schubert Institute of Radiology, University Hospital Basel, Basel, Switzerland

L. H. Bonati · P. Lyrer Department of Neurology, University Hospital Basel, Basel, Switzerland

F. Santini

Department of Radiological Physics, Institute of Radiology, University Hospital Basel, Basel, Switzerland Results Correlation of 4D PC MRI measured velocities was higher in comparison with TCD (r=0.49–0.66) than with TCD (0.35–0.44) and 2D PC MRI (0.52–0.60). In mid-BA and ICA C7 segment, a significant correlation was found with TCD (0.68–0.81 and 0.65–0.71, respectively). No significant correlation was found in carotid siphon. On average over all volunteers, PSVs and EDVs in MCA were minimally underestimated compared with TCD/TCCD. Minimal overestimation of velocities was found compared to TCD in mid-BA and ICA C7 segment.

Conclusion 4D PC MRI appears as valid alternative for intracranial velocity measurement consistent with previous reference standards, foremost with TCD. Spatiotemporal averaging effects might contribute to vessel size-dependent mild underestimation of velocities in smaller (MCA), and overestimation in larger-sized (BA and ICA) arteries,

A. F. Stalder

Department of Radiology, Xuanwu Hospital—Capital Medical University, Beijing, China

M. Markl

Departments of Radiology and Biomedical Engineering, Northwestern University Feinberg School of Medicine, Chicago, USA

S. G. Wetzel

Neuroradiology, Swiss Neuro Institute, Klinik Hirslanden, Zurich, Switzerland



respectively. Complete spatiotemporal flow analysis may be advantageous in anatomically complex regions (e.g. carotid siphon) relative to restrictions of ultrasound techniques.

**Keywords** Phase contrast (PC) MR imaging · 4D PC MRI · Intracranial artery velocity measurement · Cerebral circulation · Transcranial ultrasound

## Introduction

Flow-sensitized 4D phase contrast magnetic resonance imaging (4D PC MRI) has been recently introduced to assess the hemodynamics in the normal carotid and intracranial arteries as well as in cerebrovascular pathologies such as intracranial aneurysms [1–8].

This method was developed to measure 3D blood flow and to determine its temporal evolution within larger arteries such as the aorta and to study cardiovascular pathologies [9, 10]. Besides studying spatiotemporal flow properties including complex flow, it can provide secondarily derived flow parameters such as wall shear stress, flow waveform, pulsatility, or resistance index. Such information can be of great relevance for cerebrovascular diseases, e.g. give important clues about conditions of atherosclerotic plaques or cerebral aneurysm development [5, 7, 11–13].

Transcranial ultrasound is an established reference for intracranial blood flow measurement. However, it has various drawbacks: correct localization of vessels and lacking angle correction of measured velocities with transcranial Doppler sonography (TCD), as well as operator dependency and anatomical boundaries of insonation windows with both TCD and transcranial colorcoded duplex sonography (TCCD) [14-16]. 2D PC MRI has been validated to measure velocities in intracranial arteries [11, 17-19]. However, most 2D PC MRI applications employ unidirectional velocity encoding and provide only limited spatial coverage, whereas 4D PC MRI allows velocity encoding multi-directionally inside a 3D volume. Combined with the temporal information during the cardiac cycle, comprehensive qualitative and quantitative hemodynamic information can be analysed at any site within the measured arterial tree using advanced postprocessing methods (e.g. velocity fields, streamlines, or virtual particle traces).

Hitherto, 4D PC MRI has been tested demonstrating its feasibility and advantageous 3D capabilities within geometrically complex vessels or cerebral aneurysms [1, 2, 4–7, 12]. Our aim was to compare measured velocities in intracranial arteries between 4D PC MRI and TCD/TCCD as well as 2D PC MRI in young healthy volunteers as an in vivo validation of the technique. We hypothesized that flow velocities obtained

with 4D PC MRI correlate well with those of reference modalities at specific intracranial artery locations.

## Patients and methods

Study population

Twenty healthy volunteers (11 male and 9 female; mean age, 23.0 years; range, 20-27 years) were investigated with 4D PC MRI, 2D PC MRI, and TCD/TCCD. Intracranial velocity measurements were obtained from 4D PC MRI and TCD at seven predefined locations in the circle of Willis: internal carotid artery (ICA) C5 (carotid siphon), and C7 (supraclinoid) segments (according to Bouthillier classification of ICA segments [20]), middle cerebral artery (MCA) proximal M1 segment bilaterally, and basilar artery (BA) midbasilar segment. For 2D PC MRI and TCCD, measurements were only obtained in MCA M1 bilaterally and BA. All locations were selected because of their anatomically stable position and reliable access via ultrasound insonation windows. Both MRI and transcranial ultrasound studies were performed at different time points (mean interval between MRI and ultrasound studies, 62.6 days; range, 0–450 days; >1 month in eight subjects). The study was approved by the ethics review committee of the University of Basel/Switzerland, and written informed consent was obtained from all subjects.

## MR imaging

All examinations were performed on a 3-T head system (Magnetom Allegra, Siemens, Erlangen, Germany) by using a single-channel standard head coil. Both 2D and 4D PC MRI sequences were acquired during the same scan session in direct succession. For positioning of the axial 3D slab of the 4D PC MRI sequence as well as for placement of slices on the respective vessels of interest in 2D PC MR, a standard MPRAGE sequence was acquired as a vessel localizer. 4D PC MRI consisted of a k-space segmented 3D radiofrequency-spoiled gradient echo sequence with prospective ECG gating and interleaved 3D velocity encoding. Data acquisition resulted in a series of 3D volumes representing 3D blood flow in consecutive timeframes within the cardiac cycle with a temporal resolution of 54.4–56.0 ms [5, 6]. Thereby, the number of frames varied with the patients' individual heart rate (13–16 frames) resulting in acquisition times of 25-30 min, and was determined as following: temporal resolution=RR interval/number of frames (no view sharing factor applied). Further imaging parameters were: TR/TE 6.8-7.0/4.0-4.4 ms, flip angle 15°, band width 450 Hz/pixel, velocity encoding sensitivity (VENC) 100 cm/s along all three encoding directions. The axial 3D



slab was positioned to cover the centre of carotid siphon equidistant to the upper and lower boundary of acquired data volume [ $220 \times 176 \text{ mm}^2$  rectangular field of view (FOV), 28 sections,  $1.0 \times 0.7 \times 1.2 \text{ mm}^3$ ].

2D PC MRI flow measurements were acquired from sections placed perpendicular to vessel of interest at target points (MCA and BA) with the following imaging parameters: TR/TE 5.3/2.83–2.86 ms, flip angle 15°, band width 450 Hz/pixel, FOV 220×176 mm², in-plane resolution 0.9×0.7 mm², slice thickness 5 mm, temporal resolution 21.2 ms, and VENC 100 cm/s (unidirectional velocity encoding). In one volunteer, the BA measurement with 2D PC MRI could not be obtained due to technical problems.

## MR flow velocity data postprocessing

Automated postprocessing of 2D and 4D PC MRI datasets using an in-house software tool based on Matlab (Math-Works, Natick, MA, USA) included noise masking, antialiasing, and eddy current correction as previously described [21–23].

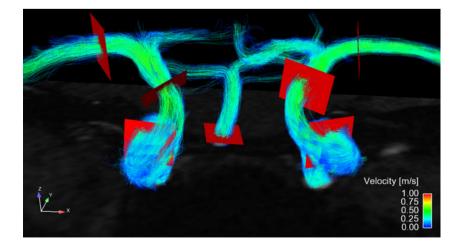
The 4D PC MRI data were further processed using a commercially available 3D visualization software package (EnSight, CEI, Apex, NC, USA). Thereby, the points of maximum velocity within all predefined arterial segments were first determined by manual inspection of the 3D streamlines of the whole measured arterial tree. This approach was chosen in order to obtain velocity measurements from locations along the lines of transcranial ultrasound. Then, velocity measurements were obtained by retrospectively placing 2D analysis planes transecting the arterial lumen perpendicular to vessel axis (Fig. 1). From these planes, time-resolved velocity data for all three spatial velocity components were imported into an in-house software tool (MathWorks, Natick, MA, USA) enabling frame-wise interactive segmentation of the vessel lumen as previously

described [5, 13]. Based on the segmented vessel lumen contour, peak systolic velocity (PSV), and end-diastolic velocity (EDV) values were extracted. These values represent the spatial maximum of the velocity vectors in the z-direction, i.e. transversal to the defined vessel plane, at the respective time frames during the cardiac cycle. The 2D PC MRI flow data were directly processed with the in-house software tool, and PSV and EDV values were extracted likewise.

#### Transcranial ultrasound studies

TCD/TCCD examinations were performed by two experienced neurologists with expertise in transcranial ultrasound (L.H.B. and P.L.). The TCD studies were acquired on a Pioneer TC8080 Doppler (VIASYS Healthcare Inc., Madison, WI, USA) using a 2-MHz PW transducer (sample volume, 10 mm). For TCCDs, an ACUSON Sequoia 512 (Siemens, Erlangen, Germany) with a 3-MHz transducer (sample volume, 1.5 mm) was utilized. The ICA C5 segments were insonated through a transorbital window. For ICA C7/MCA M1 segments and for BA, a standard transtemporal and transforaminal window, respectively, was chosen. On TCD, the M1 measurements were obtained at proximal location (centred 2-4 mm distal to ICA terminus). To locate the C5 segment on TCD, the highest ICA flow signal directed towards the probe proximal to the ophthalmic artery origin was chosen. The C7 segment was measured at the site of the highest flow signal directed towards the probe, within 2–10 mm proximal to ICA terminus. For BA measurements, the most distal signal directed away from the probe was chosen. In TCCD studies, the most proximal detectable signal in the M1 segment was chosen on the plain visualizing the longest part of the M1 in 2D Duplex mode. The BA measurements with TCCD were obtained in the most distal BA section visualized on the plain showing both vertebral artery V4 segments as well as

Fig. 1 3D streamline visualization of circle of Willis from 4D PC MRI velocity data. *Red planes* indicate areas of velocity measurement obtained in ICA C5 and C7, MCA M1, and mid-BA segments





the proximal BA. In one volunteer, TCCD measurements in both MCAs were not possible due to poor transtemporal ultrasound penetration. In another volunteer, the transforaminal window quality was insufficient for BA TCD measurement. With both ultrasound techniques, the maximum velocity values from the measured spatial profile within the respective vessel were obtained during peak systole (PSV) and at end diastole (EDV).

## Statistical analysis

Mean values and standard deviation (SD) over all volunteers PSV and EDV samples were compared between the different imaging modalities for the corresponding arterial segments. For the agreement of measured blood flow velocities between modalities, mean differences were calculated with accompanying two-sided 95 % confidence interval (CI). The difference was considered statistically significant at 5 % level, if the 95 % CI did not contain 0. Linear regression for each arterial segment using PSV and EDV, and combined PSV and EDV values was performed between 4D PC MRI and the other three imaging modalities. A Pearson r was calculated for PSV and EDV values. A P value <0.01 for the correlation coefficient was considered statistically significant (two-tailed test). Bland-Altman plots were also generated to visualize the agreement between 4D PC MRI and the other techniques. In these plots, the differences between the individual velocity measurements that were performed by the two compared modalities (TCD, TCCD, or 2D PC MRI versus 4D PC MRI) within the respective vessel are plotted against the mean values of the two compared velocity measurements. Thereby, the three continuous lines represent the bias estimated by the mean and the two standard deviations of calculated velocity differences from all volunteer velocity measurements (EDV

**Table 2** Mean differences in velocities between 4D PC MRI and three other imaging techniques

	2D PC MRI	4D PC MRI vs. TCCD mean Δ velocity (lower; upper limits of 95 % CI) (m/s)	TCD
MCA (M1)			
PSV	-0.067 (-0.136; 0.003)	0.269 (0.186; 0.351) <sup>a</sup>	$0.062 (0.000; 0.125)^a$
EDV	-0.019 (-0.055; 0.017)	0.091 (0.057; 0.126) <sup>a</sup>	$0.053 (0.025; 0.081)^a$
BA (mid)			
PSV	-0.042 (-0.176; 0.093)	-0.107 (-0.222; 0.007)	$-0.177 (-0.254; -0.100)^{a}$
EDV	$-0.065 (-0.109; -0.021)^{a}$	-0.028 (-0.080; 0.025)	$-0.044 (-0.085; -0.004)^{a}$
ICA (C5)			
PSV	N/A	N/A	-0.120 (-0.188; -0.053) <sup>a</sup>
EDV	N/A	N/A	-0.041 (-0.087; 0.004)
ICA (C7)			
PSV	N/A	N/A	-0.133 (-0.185; -0.080) <sup>a</sup>
EDV	N/A	N/A	$-0.047 (-0.077; -0.017)^{a}$

<sup>a</sup>Significant difference at 5 % level



Table 1 Mean velocities measured with four different imaging techniques

	4D PC MRI mean velocity (±SD) (m/s)	2D PC MRI mean velocity (±SD) (m/s)	TCCD mean velocity (±SD) (m/s)	TCD mean velocity (±SD) (m/s)		
MCA (M1)						
PSV	0.88 (0.13)	0.82 (0.20)	1.15 (0.20)	0.94 (0.15)		
EDV	0.38 (0.08)	0.36 (0.10)	0.47 (0.08)	0.43 (0.09)		
BA (mid)						
PSV	0.78 (0.19)	0.74 (0.26)	0.68 (0.21)	0.61 (0.11)		
EDV	0.36 (0.11)	0.30 (0.10)	0.33 (0.08)	0.32 (0.08)		
ICA (C5)						
PSV	0.83 (0.12)	N/A	N/A	0.70 (0.10)		
EDV	0.35 (0.06)	N/A	N/A	0.30 (0.06)		
ICA (C7)						
PSV	0.98 (0.14)	N/A	N/A	0.84 (0.14)		
EDV	0.44 (0.09)	N/A	N/A	0.39 (0.09)		

Mean values and SDs for PSV and EDV measurements in 20 healthy volunteers

and PSV values) [24]. All statistical analysis was performed using SPSS (PASW Statistics version 18.0.2).

#### Results

The mean velocity values from all 20 volunteer measurements using all four imaging modalities are summarized in Table 1. The mean differences of measured blood flow velocities between 4D PC MRI and each of the three other modalities including their statistical significance are summarized in Table 2: In the MCA M1 segment, 4D PC MRI mildly underestimated flow velocities compared to both

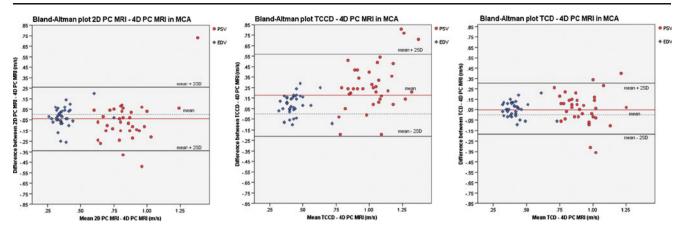


Fig. 2 Bland-Altman plots of 4D PC MRI compared with 2D PC MRI, TCCD, and TCD in M1 segment

ultrasound methods. The differences between 2D and 4D PC MRI were not statistically significant. In both ICA segments, a mild overestimation of flow velocities was observed compared with TCD. These results were significant for both PSV, and EDV values in the ICA C7 segment, but only for PSV values in the ICA C5 segment. In the mid-BA, measured flow velocities were mildly higher with 4D PC MRI compared to all three methods. However, these differences were only significant for the comparison with TCD (for both EDV and PSV values). Bland–Altman plots comparing velocity measurements of 4D PC MRI with the other techniques in MCA M1 segment, the mid-BA, and the ICA C5 and C7 segments are shown in Figs. 2, 3, and 4, respectively. The respective values of agreement (mean difference of velocities and 95 % CIs of the bias) are provided in Table 2.

The correlation analysis of measured flow velocities per arterial segment showed a significant correlation between 4D PC MRI and all three other modalities in the MCA M1 segment, and for the comparison with TCD only in the mid-BA and ICA C7 segments (Table 3, Figs. 5, 6, and 7). Thereby, moderate to strong correlation was found between 4D PC MRI and TCD in the BA (0.68–0.81). In the MCA

M1, a mild to moderate correlation (0.49–0.66) was observed for the comparisons of 4D PC MRI with TCD as well as with 2D PC MRI. Correlation was found weaker for the comparison with TCCD measurements in the M1 segments (0.35–0.44). In the ICA C7 segment, correlation was moderate with TCD measurements (0.65–0.71). In the ICA C5 segment, 4D PC MRI did not correlate with TCD measurements.

#### Discussion

Our results represent a quantitative validation of the recently introduced 4D PC MRI technique for intracranial blood flow measurements. Thus, 4D PC MRI velocity measurements in the MCA M1 segment correlated with all three reference standards but was found to be best with TCD and 2D PC MRI. Further, in the ICA C7 and mid-BA, moderate to strong correlation with TCD was observed. Thereby, 4D PC MRI may be advantageous not being restricted by insonation angles and anatomic windows compared to transcranial ultrasound

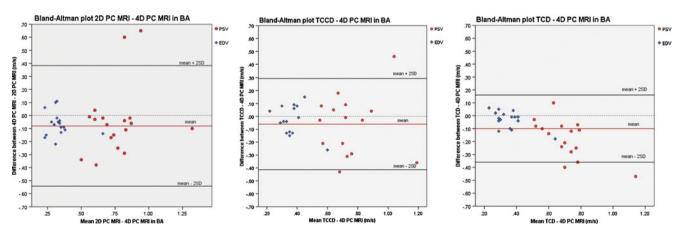


Fig. 3 Bland-Altman plots of 4D PC MRI compared with 2D PC MRI, TCCD, and TCD in the mid-BA

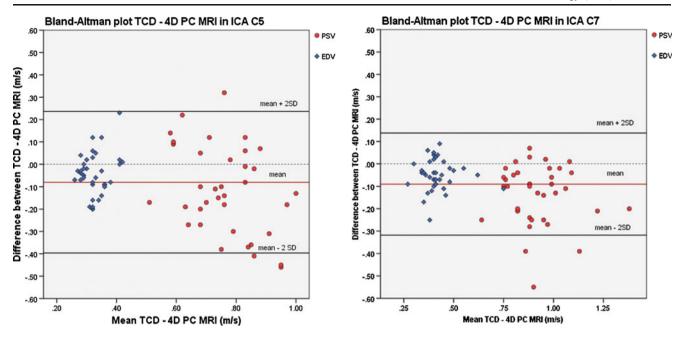


Fig. 4 Bland-Altman plots of 4D PC MRI compared with TCD for ICA C5 (left panel) and C7 (right panel) segments

techniques [14, 15, 25]. These limitations may attribute to the somewhat lower and lacking correlation between 4D PC MRI and ultrasound techniques in the BA/MCA M1 (TCCD) and ICA C5 segment (TCD), respectively. In the vertebrobasilar system, these drawbacks remain critical which may possibly lead to an underestimation of true flow velocities, in particular with TCD [14, 25, 26]. In the ICA C5 segment which is located in the centre of the carotid siphon, non-axial, helical flow patterns may also impair the accuracy of velocity analysis with transcranial ultrasound [6, 14]. Overall, our TCD and TCCD velocity data agree with previously published reference data for healthy subjects [1, 14, 25–28].

Moreover, 4D PC MRI enables complete 3D analysis of blood flow covering the entire circle of Willis, as well as a dynamic visualization of the spatiotemporal flow evolution within the entire sampled region. This is a clear benefit as compared to 2D PC MRI that only allows measurements within 2D planes placed at predefined points within the arterial tree, as well as compared to transcranial ultrasound which is anatomically restricted by the area of insonation. Our results disclosed moderate correlation between both MRI methods for most velocity measurements, and our 2D PC MRI measurements seem to be in agreement with previously reported 2D PC MRI data [29, 30]. Spatiotemporal averaging effects related to differences in resolutions of both sequences may contribute to possible discordant velocity measurements. Thereby, the temporal resolution in 2D PC MRI was markedly higher compared to 4D PC MRI (21.2) vs. 54.4-56 ms) which may result in a lower estimation of peak velocities by 4D PC MRI. On the other hand, spatial averaging effects related to higher slice thickness of 2D PC MRI compared to 4D PC MRI (0.9×0.7 mm in-plane resolution, 5 mm slice thickness vs. 1.0×0.8×1.2 mm) may lead to averaging and subsequent reduction of velocities by 2D PC MRI. The latter effect can possibly exceed the former resulting in the mostly non-significantly lower velocity measurements by 2D PC MRI. Likewise, Enzmann et al. found only an overall poor correlation for PSVs in major

**Table 3** Correlation analysis of measured velocities between 4D PC MRI and three other imaging modalities

	4D PC MRI vs.				
	2D PC MRI r (n)	$TCCD \ r \ (n)$	TCD r(n)		
MCA (M1)					
PSV	$0.524 (38)^a$	0.353 (37) <sup>a</sup>	0.487 (37) <sup>a</sup>		
EDV	$0.595 (38)^a$	$0.444(37)^{a}$	$0.664 (37)^{a}$		
BA (mid)					
PSV	0.315 (18)	0.340 (19)	$0.683 (18)^a$		
EDV	$0.642 (18)^a$	0.462 (19)	$0.805 (18)^{a}$		
ICA (C5)					
PSV	N/A	N/A	0.118 (36)		
EDV	N/A	N/A	-0.226 (36)		
ICA (C7)					
PSV	N/A	N/A	0.645 (37) <sup>a</sup>		
EDV	N/A	N/A	$0.713 (37)^{a}$		

r Pearson correlation coefficient, (n) number of velocity samples



<sup>&</sup>lt;sup>a</sup> Significant at the 0.01 level (two-tailed test)

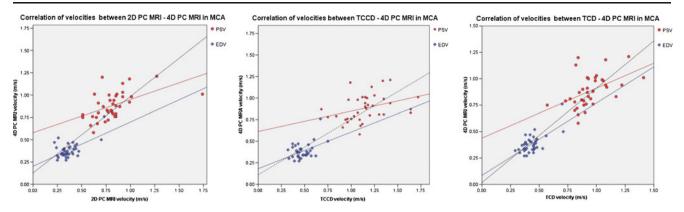


Fig. 5 Linear regression analysis for 4D PC MRI measured blood flow velocities compared with three other imaging modalities in MCA M1 segment. *Dotted lines* indicate combined correlation for PSV and EDV values

arteries of the circle of Willis measured with 2D PC MRI compared to TCD [17]. Our 2D PC MRI measurements were only obtained from the MCA M1 and midbasilar artery segments. In general, 2D PC MRI may also be used in more complex regions such as the carotid siphon by careful placement of individual measurement planes transversal to the respective vessel curvature. However, this might imply multiple measurements and is still restricted by not being capable to display complex 3D flow phenomena such as helical flow (see below) as well as by spatial averaging effects due to the relatively thicker slices [1].

The major limitation of the 4D PC MRI method as implemented in our study is its long acquisition time. In order to reduce scan time, several scan parameters may be altered which in turn could impact the accuracy of velocity measurements. Bammer et al. have underlined the importance of maintaining a high temporal resolution in intracranial 4D PC MRI flow measurements as reduced temporal resolution causes a low-pass filtering of the velocity time course with subsequent underestimation of peak velocities and broadening of the systolic phase [1]. Note that no parallel imaging was used in our study. Future studies are thus necessary to investigate the possibility to achieve a

clinically reasonable scan time (10 min or less) at 3 T or 7 T by employing parallel imaging with an acceleration factor of up to 3 [1, 4, 31]. Subsampling of k-space with the exclusion of corners may be another potential approach for scan time reduction as velocity-induced phase shifts are encoded mainly in central k-space [4, 32]. Temporal averaging of flow data represents another limitation of 4D PC MRI as the ECG-gated data acquisition over many heartbeats does not enable real-time flow measurement but reconstruction of images representing phases of the cardiac cycle. This effect may mask small dynamic flow features such as beat-to-beat variations of flow and cause a low-pass filtering of peak flow velocities [1, 5, 6]. Spatial averaging effects also need to be considered as a limitation of the accuracy of measured velocities with the given voxel size of 1.0×0.7×1.2 mm. The latter effect may preferentially play a role for measurements within smaller-sized arteries. This is underlined by our results that showed a significant underestimation of flow velocities (on average by 0.05-0.27 m/s) in the smaller calibered MCA M1 segment (mean luminal diameter of M1 segment, 2.1±0.41 mm) compared to TCD and TCCD measurements, whereas velocity measurements in the larger-sized arteries (BA, ICA segments;

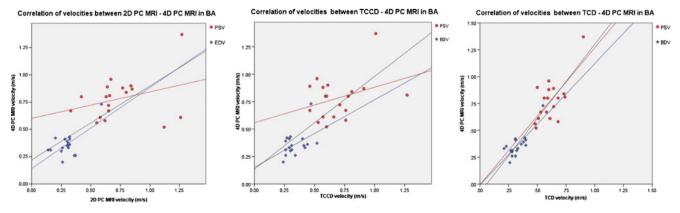


Fig. 6 Linear regression analysis for 4D PC MRI measured blood flow velocities compared with three other imaging modalities in mid-BA segment. *Dotted lines* indicate combined correlation for PSV and EDV values



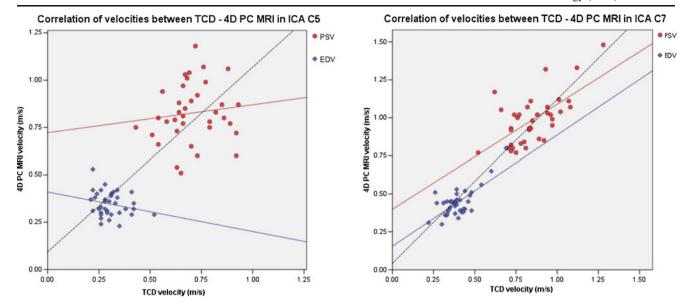


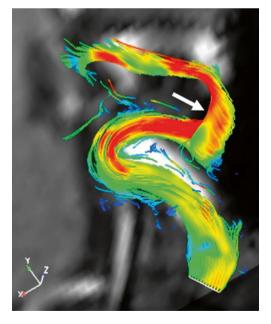
Fig. 7 Linear regression analysis for 4D PC MRI measured blood flow velocities compared with TCD in ICA C5 (*left panel*) and C7 (*right panel*) segments. *Dotted lines* indicate combined correlation for PSV and EDV values

mean luminal diameter of ICA C7, 2.8±0.49 mm) were mildly overestimated (on average by 0.03-0.18 m/s) when compared to the ultrasound-based measurements [33]. These observations are consistent with previous reports comparing 2D PC MRI with TCD-derived intracranial velocity measurements [17, 34]. However, the mentioned lack of angle correction may also contribute to lower velocities on TCD in the BA and ICA C7 segment. 4D PC MRI measurements with flow visualization in small intracranial arteries may also be improved by increasing field strength up to 7 T due to the increased SNR [31]. Compared to our results, a recent study by Bammer et al. with 4D PC MRI measurements showed a more pronounced underestimation of maximum velocities in the MCA M1 segment and BA as compared to transcranial ultrasound reference data (no direct comparison was performed in their study) [1]. These differences may be attributed to slight differences in spatiotemporal resolutions compared to our 4D PC MRI implementation, lower magnetic field strength (velocity measurements in MCA were only performed at 1.5 T in their study), as well as to parallel imaging utilised with acceleration factors up to 3, for which they have shown a marked decrease in SNR up to 68 % at 1.5 T.

In addition, the time interval between the MRI and ultrasound studies was rather long in a few subjects in our study. However, major intra-individual hemodynamic variations may not be expected in young healthy volunteers under similar examination conditions (lying position, no physical exertion, normal respiration) as cerebral autoregulatory mechanisms keep intracranial blood flow velocities constant as long as the arterial  $P_a\mathrm{CO}_2$  is kept constant. This is underlined by several studies that found only small, non-significant variations

in measured intracranial artery velocities by TCD and TCCD for short-time or day-to-day repeated measurements [14, 35, 36]. Moreover, other investigators found that PSVs and EDVs measured in major intracranial arteries are relatively constant in younger adults (between 20 and 40 years old), whereas over the age of 40 years a slow age-related decline of peak velocities may occur related to increased arterial stiffness [28, 37].

Alternatively to 4D PC MRI, intracranial artery velocity measurements as well as comprehensive 4D hemodynamic



**Fig. 8** 3D streamline visualization of blood flow within carotid siphon obtained from 4D PC MRI of a healthy volunteer depicting helical flow pattern at supraclinoid ICA segment (*arrow*)



analysis of vascular pathologies such as AVMs may be possible using a different recently introduced PC MRA method with radial readout called phase-contrast vastly undersampled projection reconstruction. This technique has been validated only for velocity measurements in MCA M1 segments enabling high-resolution measurements at relatively shorter scan times (5–6 min) [38–40].

Overall, our results serve as important prerequisite for the use of 4D PC MRI as a robust alternative method for intracranial flow velocity measurements within large arteries of the circle of Willis. Further, this study also emphasizes its advantages compared to the other studied modalities in geometrically complex regions such as the carotid siphon (Fig. 8) [12]. Given its excellent dynamic 3D capabilities for comprehensive flow analysis including secondary flow-derived parameters, 4D PC MRI appears as valuable and attractive tool for hemodynamic studies of cerebrovascular diseases. Moreover, it may serve as a reliable instrument for validation of blood flow modelling in intracranial aneurysms using computational fluid dynamics [2, 5].

## Conclusion

In summary, correlation of intracranial velocity measurements was highest between 4D PC MRI and TCD in MCA M1, mid-BA, and ICA C7 segments. The lacking correlation in the carotid C5 segment (TCD) and considerable lower agreement with TCCD in the MCA M1 and BA are most likely due to anatomical and technical restrictions of the ultrasound technique. Spatiotemporal averaging effects of 4D PC MRI may likely contribute to a vessel diameter-dependent mild velocity underestimation and overestimation in smaller-sized arteries (M1 segment) and larger-sized arteries (ICA/BA), respectively. The results emphasize the value of 4D PC MRI as a robust method for complete 3D flow analysis within major cerebral arteries for further studies of cerebrovascular diseases.

**Acknowledgments** We thank Gabriele Ihorst, Ph.D., Biostatistician, for valuable statistical support. This work was supported in part by a grant from the Swiss National Science Foundation (SNF 320000-113492/1).

Conflict of interest We declare that we have no conflict of interest.

# References

 Bammer R, Hope TA, Aksoy M, Alley MT (2007) Timeresolved 3D quantitative flow MRI of the major intracranial vessels: initial experience and comparative evaluation at 1.5 T and 3.0 T in combination with parallel imaging. Magn Reson Med 57(1):127–140

- Boussel L, Rayz V, Martin A, Acevedo-Bolton G, Lawton MT, Higashida R, Smith WS, Young WL, Saloner D (2009) Phasecontrast magnetic resonance imaging measurements in intracranial aneurysms in vivo of flow patterns, velocity fields, and wall shear stress: comparison with computational fluid dynamics. Magn Reson Med 61(2):409–417. doi:10.1002/mrm.21861
- Harloff A, Albrecht F, Spreer J, Stalder AF, Bock J, Frydrychowicz A, Schollhorn J, Hetzel A, Schumacher M, Hennig J, Markl M (2009) 3D blood flow characteristics in the carotid artery bifurcation assessed by flow-sensitive 4D MRI at 3 T. Magn Reson Med 61(1):65–74. doi:10.1002/mrm.21774
- Hope MD, Purcell DD, Hope TA, von Morze C, Vigneron DB, Alley MT, Dillon WP (2009) Complete intracranial arterial and venous blood flow evaluation with 4D flow MR imaging. AJNR 30(2):362–366. doi:10.3174/ajnr.A1138
- Meckel S, Stalder AF, Santini F, Radu EW, Rufenacht DA, Markl M, Wetzel SG (2008) In vivo visualization and analysis of 3-D hemodynamics in cerebral aneurysms with flow-sensitized 4-D MR imaging at 3 T. Neuroradiology 50(6):473–484. doi:10.1007/ s00234-008-0367-9
- Wetzel S, Meckel S, Frydrychowicz A, Bonati L, Radue EW, Scheffler K, Hennig J, Markl M (2007) In vivo assessment and visualization of intracranial arterial hemodynamics with flowsensitized 4D MR imaging at 3 T. AJNR 28(3):433–438
- Yamashita S, Isoda H, Hirano M, Takeda H, Inagawa S, Takehara Y, Alley MT, Markl M, Pelc NJ, Sakahara H (2007) Visualization of hemodynamics in intracranial arteries using time-resolved threedimensional phase-contrast MRI. J Magn Reson Imaging 25 (3):473–478
- Markl M, Wegent F, Zech T, Bauer S, Strecker C, Schumacher M, Weiller C, Hennig J, Harloff A (2010) In vivo wall shear stress distribution in the carotid artery: effect of bifurcation geometry, internal carotid artery stenosis, and recanalization therapy. Circ Cardiovasc Imaging 3(6):647–655. doi:10.1161/ CIRCIMAGING.110.958504
- Markl M, Chan FP, Alley MT, Wedding KL, Draney MT, Elkins CJ, Parker DW, Wicker R, Taylor CA, Herfkens RJ, Pelc NJ (2003) Time-resolved three-dimensional phase-contrast MRI. J Magn Reson Imaging 17(4):499–506
- Markl M, Draney MT, Hope MD, Levin JM, Chan FP, Alley MT, Pelc NJ, Herfkens RJ (2004) Time-resolved 3-dimensional velocity mapping in the thoracic aorta: visualization of 3-directional blood flow patterns in healthy volunteers and patients. J Comput Assist Tomogr 28(4):459–468
- Hoppe M, Heverhagen JT, Froelich JJ, Kunisch-Hoppe M, Klose KJ, Wagner HJ (1998) Correlation of flow velocity measurements by magnetic resonance phase contrast imaging and intravascular Doppler ultrasound. Invest Radiol 33(8):427–432
- Schubert T, Santini F, Stalder AF, Bock J, Meckel S, Bonati L, Markl M, Wetzel S (2011) Dampening of blood-flow pulsatility along the carotid siphon: does form follow function? Ajnr 32 (6):1107–1112. doi:10.3174/ajnr.A2426
- Stalder AF, Russe MF, Frydrychowicz A, Bock J, Hennig J, Markl M (2008) Quantitative 2D and 3D phase contrast MRI: optimized analysis of blood flow and vessel wall parameters. Magn Reson Med 60(5):1218–1231. doi:10.1002/mrm.21778
- Baumgartner RW, Mathis J, Sturzenegger M, Mattle HP (1994) A validation study on the intraobserver reproducibility of transcranial color-coded duplex sonography velocity measurements. Ultrasound Med Biol 20(3):233–237
- Hoksbergen AW, Legemate DA, Ubbink DT, Jacobs MJ (1999) Success rate of transcranial color-coded duplex ultrasonography in visualizing the basal cerebral arteries in vascular patients over 60 years of age. Stroke 30(7):1450–1455
- Tsuchiya T, Yasaka M, Yamaguchi T, Kimura K, Omae T (1991)
  Imaging of the basal cerebral arteries and measurement of blood



- velocity in adults by using transcranial real-time color flow Doppler sonography. Ajnr 12(3):497–502
- Enzmann DR, Ross MR, Marks MP, Pelc NJ (1994) Blood flow in major cerebral arteries measured by phase-contrast cine MR. Ajnr 15(1):123–129
- McCauley TR, Pena CS, Holland CK, Price TB, Gore JC (1995) Validation of volume flow measurements with cine phase-contrast MR imaging for peripheral arterial waveforms. J Magn Reson Imaging 5(6):663–668
- Zananiri FV, Jackson PC, Halliwell M, Harris RA, Hayward JK, Davies ER, Wells PN (1993) A comparative study of velocity measurements in major blood vessels using magnetic resonance imaging and Doppler ultrasound. Br J Radiol 66(792):1128–1133
- Bouthillier A, van Loveren HR, Keller JT (1996) Segments of the internal carotid artery: a new classification. Neurosurgery 38 (3):425–432, discussion 432–423
- Bock J, Kreher BW, Hennig J, Markl M (2007) Optimized preprocessing of time-resolved 2D and 3D Phase Contrast MRI data. In Proc: ISMRM 2007, May; Berlin, Germany p # 3138
- Buonocore MH (1998) Visualizing blood flow patterns using streamlines, arrows, and particle paths. Magn Reson Med 40 (2):210-226
- Walker PG, Cranney GB, Scheidegger MB, Waseleski G, Pohost GM, Yoganathan AP (1993) Semiautomated method for noise reduction and background phase error correction in MR phase velocity data. J Magn Reson Imaging 3(3):521–530
- Bland JM, Altman DG (1986) Statistical methods for assessing agreement between two methods of clinical measurement. Lancet 1 (8476):307–310
- Schoning M, Walter J (1992) Evaluation of the vertebrobasilarposterior system by transcranial color duplex sonography in adults. Stroke 23(9):1280–1286
- Martin PJ, Evans DH, Naylor AR (1994) Transcranial color-coded sonography of the basal cerebral circulation. Reference data from 115 volunteers. Stroke 25(2):390–396
- Bartels E, Fuchs HH, Flugel KA (1995) Color Doppler imaging of basal cerebral arteries: normal reference values and clinical applications. Angiology 46(10):877–884
- Shambal S, Grehl H, Zierz S, Lindner A (2003) Age dependence of Doppler parameters in the basal cerebral arteries evaluated by transcranial color-coded duplex sonography. Reference data from 290 volunteers. Fortschr Neurol Psychiatr 71(5):271–277. doi:10.1055/s-2003-39064
- Mattle H, Edelman RR, Wentz KU, Reis MA, Atkinson DJ, Ellert T (1991) Middle cerebral artery: determination of flow velocities with MR angiography. Radiology 181(2):527–530

- Stock KW, Wetzel SG, Lyrer PA, Radu EW (2000) Quantification of blood flow in the middle cerebral artery with phase-contrast MR imaging. Eur Radiol 10(11):1795–1800
- van Ooij P, Zwanenburg JJ, Visser F, Majoie CB, Vanbavel E, Hendrikse J, Nederveen AJ Quantification and visualization of flow in the circle of Willis: time-resolved three-dimensional phase contrast MRI at 7 T compared with 3 T. Magn Reson Med. doi:10.1002/mrm.24317
- Markl M, Hennig J (2001) Phase contrast MRI with improved temporal resolution by view sharing: k-space related velocity mapping properties. Magn Reson Imaging 19(5):669–676
- Piepgras A, Bise K, Schmiedek P (1993) Morphometry of intraluminal side-to-side differences in human basal cerebral arteries. Ultrasound Med Biol 19(3):193–195
- Marks MP, Pelc NJ, Ross MR, Enzmann DR (1992) Determination of cerebral blood flow with a phase-contrast cine MR imaging technique: evaluation of normal subjects and patients with arteriovenous malformations. Radiology 182(2):467–476
- Maeda H, Etani H, Handa N, Tagaya M, Oku N, Kim BH, Naka M, Kinoshita N, Nukada T, Fukunaga R et al (1990) A validation study on the reproducibility of transcranial Doppler velocimetry. Ultrasound Med Biol 16(1):9–14
- Sorteberg W, Langmoen IA, Lindegaard KF, Nornes H (1990) Side-to-side differences and day-to-day variations of transcranial Doppler parameters in normal subjects. J Ultrasound Med 9 (7):403–409
- 37. Krejza J, Mariak Z, Walecki J, Szydlik P, Lewko J, Ustymowicz A (1999) Transcranial color Doppler sonography of basal cerebral arteries in 182 healthy subjects: age and sex variability and normal reference values for blood flow parameters. AJR Am J Roentgenol 172(1):213–218
- Chang W, Landgraf B, Johnson KM, Kecskemeti S, Wu Y, Velikina J, Rowley H, Wieben O, Mistretta C, Turski P (2011) Velocity measurements in the middle cerebral arteries of healthy volunteers using 3D radial phase-contrast HYPRFlow: comparison with transcranial Doppler sonography and 2D phase-contrast MR imaging. Ajnr 32(1):54–59. doi:10.3174/ajnr.A2240
- 39. Chang W, Loecher MW, Wu Y, Niemann DB, Ciske B, Aagaard-Kienitz B, Kecskemeti S, Johnson KM, Wieben O, Mistretta C, Turski P (2012) Hemodynamic changes in patients with arteriovenous malformations assessed using high-resolution 3D radial phase-contrast magnetic resonance angiography. Ajnr. doi:10.3174/ajnr.A3010
- Gu T, Korosec FR, Block WF, Fain SB, Turk Q, Lum D, Zhou Y, Grist TM, Haughton V, Mistretta CA (2005) PC VIPR: a highspeed 3D phase-contrast method for flow quantification and highresolution angiography. AJNR 26(4):743–749

