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BLOOD FLOW

Blood flow quantification in adults by phase-contrast MRI combined with SENSE—a validation study

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Purpose. To evaluate the feasibility of rapid free-breathing phase-contrast MRI (PC-MRI) at different in-plane resolutions combined with sensitivity encoding (SENSE) for flow quantification in the great arteries in healthy adult volunteers. *Methods.* In 13 volunteers (mean age 33.0 ± 7.4 years), blood flow rates in the pulmonary artery (Q_p), ascending aorta (Q_s), and flow ratio Q_p/Q_s were determined by PC-MRI with SENSE reduction-factor 2 and 3 (SF-2, SF-3). Additionally, we used PC-MRI with higher spatial in-plane resolution (1.6*2.1 mm vs. 2.3*3.1 mm) with/without SF-3. Standard (= reference) PC-MRI, which used two excitations (NEX = 2), was compared with PC-MRI sequences with NEX = 1. *Results.* Reduction of signal averages and application of SENSE accelerated flow measurements by a factor of 3.8 (5.5) using PC-MRI with SF-2 (SF-3): Scan time was 36 sec (SF-2) and 25 sec (SF-3) at average heart rate of 69/min. The mean Q_p/Q_s by reference PC-MRI was 1.03 ± 0.07 (range, 0.89–1.16), and 1.08 ± 0.11 (range, 0.86–1.24) by PC-MRI + SF-3, respectively. For blood flow rate through the pulmonary artery and aorta, and for Q_p/Q_s ratio, we found differences of −3% to + 4%. The lower limits of agreement (mean −2 SD) ranged between −14% and −21%, and upper limits (mean + 2 SD) between +9% and +30%, demonstrating clinically acceptable agreement with standard PC-MRI (Bland-Altman analysis). PC-MRI at higher in-plane resolution both with/without SENSE yielded slightly smaller aortic and pulmonary flows (mean differences 5% to 7%, $p < 0.05$). *Conclusions.* In adults, PC-MRI may be safely combined with SENSE to reduce scan time for a quantitative flow measurement in the great arteries to ∼30 seconds. High in-plane resolution was not advantageous.

Key Words: Heart defects; Congenital; Magnetic resonance imaging; Parallel imaging; Blood flow quantification; Phase-contrast MRI

1. Introduction

Blood flow quantification by cine phase-contrast magnetic resonance imaging (PC-MRI) has become a valuable diagnostic method to assess hemodynamics in congenital heart disease (1). Clinical examples include quantification of pulmonary regurgitation in Tetralogy of Fallot (2), venous and pulmonary flows after Fontan-type palliation in patients with a single-ventricle physiology (3), and the assessment or exclusion of cardiac left-to-right shunts in adult (4) and pediatric (5, 6) patients. Conventional flow measurements are usually ECG-gated and acquired over multiple heart beats. Scan time for each measurement is dependent on the number of phase-encoding steps, the heart rate and the number of signal averages, and usually lasts for 2.5–5 minutes in adults. However, repeated measurements at different sites are desirable in a variety of clinical conditions (1, 3, 5), thus rendering a thorough hemodynamical investigation time consuming.

With the advent of parallel imaging techniques, MR scanning may be accelerated considerably if no signal-to-noise limitations are present. Recently, we have demonstrated the reliability of rapid flow quantification protocols in sedated children with left-to-right shunt (7) using PC-MRI combined with the sensitivity encoding (SENSE) approach (8).

However, safe conclusions from pediatric data to an adult measurement environment are difficult for a number of reasons. With larger body size, the increased distance of the coil elements to the vessel of interest may introduce a signal-to-noise limitation (9). Moreover, the breathing pattern in adults is less regular and has a higher motion amplitude compared with sedated children. Respiration is known to contribute to stroke volume variation (10, 11), which in turn may introduce errors in volumetric phase-contrast measurements (12). Additionally, there is generally more heart rate

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variability (e.g., sinus arrhythmia with respiration) in conscious vs. sedated subjects due to a different level of autonomic nervous activity (13, 14). These factors are of potential relevance for measurement accuracy (12, 15).

This was the motivation to carry out an additional validation study in healthy adult volunteers to evaluate rapid free-breathing PC-MRI protocols in combination with SENSE at different in-plane resolutions for blood flow quantification in the great arteries. We used comparable protocols to our pediatric study (7), because in vitro validation data and calculations of signal-to-noise and velocity-to-noise ratios are available (7) for comparison. There were two hypotheses behind this investigation: 1) SENSE reconstruction would allow for faster imaging in adults with reliable flow measurement results; 2) a higher spatial resolution—as theoretically advantageous for flow measurements (16, 17)—would yield reliable measurement results, while the time penalty can be compensated using SENSE, without critical SNR limitations. The results were compared with conventional standard PC-MRI measurements used as a clinical reference (7).

2. Materials and methods

2.1. *Study population*

We enrolled into the study 13 healthy adult volunteers without any clinical signs of congenital or acquired heart disease, as taken from their medical history, physical examination, and transthoracical echocardiography. The mean age was 33.0 ± 7.4 years (median age 31.9 years). Ten subjects were female. All volunteers were in sinus rhythm. The study was approved by the institutional review committee and informed, written consent was obtained from the study subjects.

2.2. *Study design*

Each subject underwent MRI to measure through-plane flow in the ascending aorta and pulmonary artery (Fig. 1). A standard PC-MRI measurement (reference PC-MRI, Table 1) was repeated twice in each location to serve as a clinical reference method (5, 7), and to determine repeatability (i.e., precision, Fig. 2). The mean value of both measurements was compared with four research PC-MRI pulse sequences (see below, Table 1) that were not repeated for the sake of total imaging time. In all subjects, reference and research PC-MRI flow measurements were independently reanalyzed by two experienced observers to determine interobserver variability.

2.3. *MR imaging technique*

All examinations were performed on a 1.5 Tesla whole body MR scanner (Philips, ACS-NT, maximum gradient performance 30 mT/m amplitude, slew rate 150 T/m/s). After the survey scans, a SENSE reference scan was performed: Fast

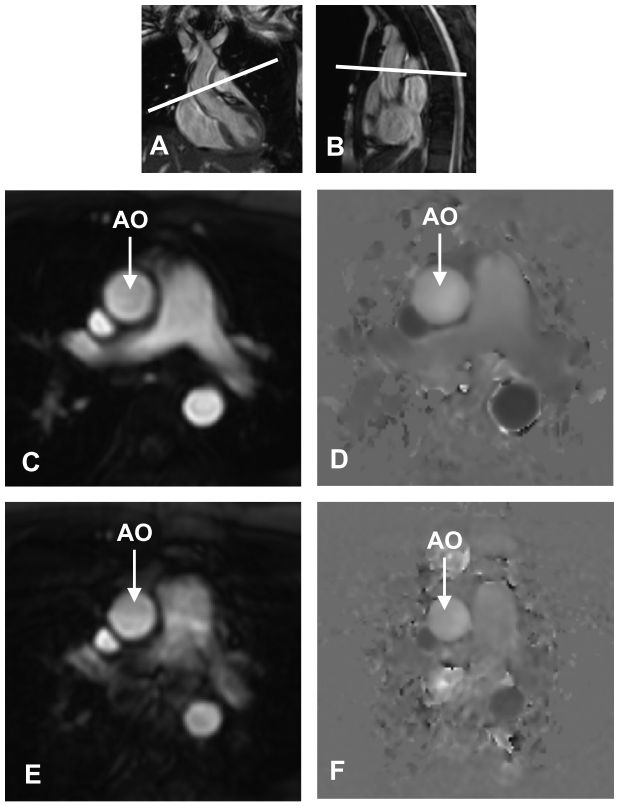

Figure 1. PC-MRI for determination of flow rate in the ascending aorta. Upper row: Plan scans (panel A, frontal/coronal view, and panel B, sagittal view) for flow quantification in the ascending aorta used steady-state free-precessing gradient echo (field of view 530 mm, matrix 125*256, 8-mm slice thickness, echotime 2.4 ms, repetition time 1.2 ms, flip angle 60°). Middle row: Standard phase-contrast MRI (without SENSE), used as reference method. In phase images (panel D), flow information is encoded through-plane for each pixel in the cross-sectional area. Panel C is the corresponding magnitude image displaying anatomical information (AO = ascending aorta, arrows, panels C and D). Bottom row: Magnitude (panel E) and phase images (panel F) by PC-MRI with SENSE reduction-factor 2 in the same patient (scan parameters, see Table 1). Please note the discrete reduction of signal-to-noise ratio in the magnitude images (panel E) compared with standard/reference PC-MRI (panel C).

field-echo, coronal orientation, repetition time (TR) 8.0 ms, echo time (TE) 0.6 ms, flip-angle 7°, voxel size (mm) 16.5*16.5*18, eight signal averages, water-fat-shift 0.06 pixels, free breathing, scan duration < 1 min. Multislice steady-state free-precessing sequences in three orthogonal planes covering the entire mediastinum were used for planning purposes and to exclude enlargement of cardiac chambers and thoracic vesssels.

The conventional standard PC-MRI pulse sequence for flow measurements (“reference PC-MRI”) was based on a protocol recently validated in children with left-to-right shunt (5) (Table 1), and served as reference method in our study. The four research PC-MRI protocols included a combination

Table 1. Scan protocols for reference PC-MRI and research PC-MRI with SENSE[a]

Parameters	PC-MRI (Reference)	PC-MRI + SF-2	PC-MRI + SF-3	$PC\text{-}MRI_{HR}$ (without SENSE)	$PC\text{-}MRI_{HR}$ + SF-3
Field of view (FOV) [mm]	300	380	380	300	380
In-plane resolution [mm^2]	2.3*3.1	2.3*3.1	2.3*3.1	1.6*2.1	1.6*2.1
Rectangular FOV [%]	80	80	80	80	80
Echo time TE [ms]	6.5	6.5	6.5	5.5	5.5
Signal averages	2	1	1	2	1
SENSE reduction factor (SF)	–	SF-2	SF-3	–	SF-3
Scan time [min:sec] @ mean heart rate 69/min	2:17	0:36	0:25	3:20	0:36
Relative scan time [% of ref. PC-MRI = Index-PC-MRI*100/ref.PC-MRI]		26%	18%		18%[b]
Acceleration factor		3.8	5.5		5.5[c]

[a]*All sequences:* Free-breathing, retrospective vector-ECG-(VCG) gating, repetition time (TR) 15 ms, 25 reconstructed heart phases, slice thickness 6 mm, flip angle 30°, velocity-encoded value 200 cm/sec. Please refer to text (MR Imaging Technique) for abbreviations of pulse sequence names.
[b]In % of scan time of $PC\text{-}MRI_{HR}$ without SENSE.
[c]Related to $PC\text{-}MRI_{HR}$ without SENSE.

of standard PC-MRI with SENSE reduction-factor (SF) of 2 (''PC-MRI + SF-2''), SF of 3 (''PC-MRI + SF-3''), and a PC-MRI protocol with higher spatial resolution with SF of 3 (''$PC\text{-}MRI_{HR}$+ SF-3'') and without SENSE (''$PC\text{-}MRI_{HR}$''). In-plane resolution was 2.3×3.1 mm^2 for PC-MRI with/without SENSE, and 1.6×2.1 mm^2 for $PC\text{-}MRI_{HR}$ with/without SENSE, respectively (Table 1). In PC-MRI techniques using SENSE, special care was taken to avoid backfolding due to the SENSE reconstruction algorithm (8). In all sequences, we used retrospective vector-ECG (18) gating to include end-diastole flow, repetition time (TR) $\sim$ 15 ms, 25–35 reconstructed heart phases depending on the heart rate, slice thickness 6 mm, flip-angle 30°, and velocity-encoded value (VENC) 200 cm/sec. The reference PC-MRI measurements had two numbers of excitation, whereas the PC-MRI sequences that were combined with SENSE had only one excitation (Table 1). The body coil was used for signal transmission, and a five-element phased-array surface (''cardiac'') coil was used for signal detection, with three elements placed in the back and two on the chest (patients positioned supine and head-first in the scanner). All flow measurements used a phase correction algorithm provided by the manufacturer.

Data analysis was performed off-line on a computer workstation using a computer algorithm for semiautomatical vessel border detection (5) to accelerate image analysis and optimize measurement reproducibility (19).

2.4. *Statistical analysis*

All data are expressed as mean ± SD. The analysis of Bland and Altman (20) was used to determine PC-MRI interobserver variability and to evaluate the agreement between the different PC-MRI techniques and the mean of both reference PC-MRI measurements for flow rate in the pulmonary artery (Q_p) and aorta (Q_s) and flow ratio Q_p/Q_s. The differences between research and reference flow measurements were tested using a paired two-tailed Student's t-test. A p-value of < 0.05 was considered significant.

3. Results

PC-MRI studies were completed within $\sim$ 30 minutes. The mean heart rate was 69 ± 15/min. Scan time was reduced to 26% with PC-MRI + SF-2 and to 18% with PC-MRI + SF-3 compared with the standard PC-MRI protocol, and to 18% with $PC\text{-}MRI_{HR}$+ SF-3 compared with $PC\text{-}MRI_{HR}$ without SENSE, respectively (Table 1). Thus, scanning was accelerated by a factor of 3.8, 5.5, and 5.5 for PC-MRI + SF2, PC-MRI + SF-3, and $PC\text{-}MRI_{HR}$+ SF-3, respectively. This was achieved by reduction of signal averages and by application of SENSE. Thus, at a heart rate of 69/min, scan time was 25 seconds with PC-MRI + SF-3 and 36 seconds with PC-MRI + SF-3, respectively (Table 1).

In healthy adult volunteers, the mean Q_p/Q_s was 1.03 ± 0.07 (range, 0.86–1.16) by reference PC-MRI, 1.05 ± 0.13 (range, 0.90–1.27) by PC-MRI + SF-2, and 1.08 ± 0.11 (range, 0.86–1.24) by PC-MRI + SF-3. With high-resolution PC-MRI the mean Q_p/Q_s was 1.05 ± 0.09 (range, 0.89–1.20), and it was 1.05 ± 0.10 (range, 0.84–1.20) with high-resolution PC-MRI + SF-3.

3.1. *Comparison of reference with research PC-MRI*

The Bland-Altman analysis was applied to the log-transformed data (20), since differences have been shown to increase linearly with mean stroke volumes (5). Estimation of precision of the limits of agreement (defined as mean ± 2

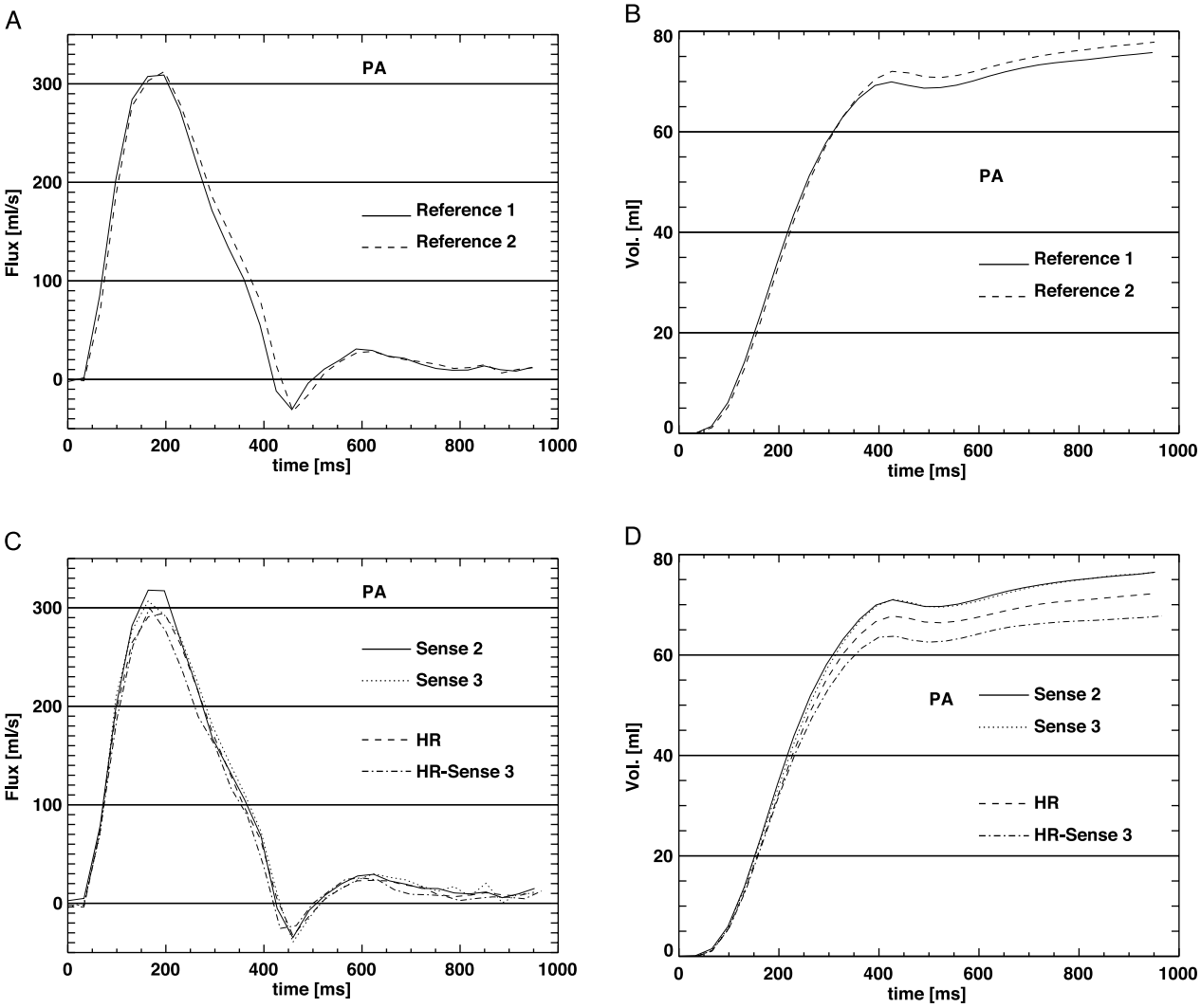

Figure 2. Flow-vs.-time curves and integrals: pulmonary artery. Mean flow volumes at multiple instants (25–35 phases) during an average cardiac cycle yield a flow-vs.-time curve (panels **A** and **C**). The corresponding integrals of the flow-vs.-time curves are given in panels B and D. The area under the curve (resp. the integral) represents the stroke volumes of the pulmonary artery (= PA). Two reference flow measurements (= reference 1 and 2, panel A and B; flow volumes in the pulmonary artery: 75.8 mL and 77.9 mL, respectively) were obtained with the standard PC-MRI technique, to serve as reference method and to assess repeatability (= precision). For each research flow scan using SENSE and/or high-resolution, only one measurement was obtained (panel C and D). Sense 2 = PC-MRI + SENSE reduction factor of 2, flow volume 76.5 mL; Sense 3 = PC-MRI + SENSE reduction factor of 3, flow volume 76.4 mL; HR = PC-MRI at high in-plane resolution, flow volume 72.2 mL; HR-Sense 3 = PC-MRI at high in-plane resolution with SENSE reduction factor of 3, flow volume 67.8 mL (Panels C and D). See also Table 1 for pulse sequence details.

SD) was based on calculation of 95% confidence intervals (c.i.). A mean value of 1.0 after antilog transformation (dimensionless ratio) is expected in the case of no difference between two tested methods. All calculated values are detailed in Table 2 for pulmonary artery (Q_p), ascending aorta (Q_s), and the flow ratio Q_p/Q_s.

For through-plane flow measurements (in-plane resolution 2.3*3.1 mm) in the pulmonary artery (Fig. 1), ascending aorta and for the flow ratio Q_p/Q_s, we found differences of −3% to + 4% (mean 0.97–1.04) between the reference protocol and PC-MRI combined with SENSE-reduction factor 2 and 3 (Table 2, Fig. 3). The upper limits of agreement were in the range of 1.08 to 1.29, and lower limits of agreement between 0.79 and 0.86, respectively. Thus, reference and research PC-MRI sequences assessing cardiac stroke volumes and Q_p/Q_s may differ by 9–30% above and 14–21% below in 95% of the cases. Scatter was smaller in the single vessel flow measurements than in the Q_p/Q_s ratio (Table 2). Overall, there was good agreement of reference and research PC-MRI in the single vessels, and clinically acceptable agreement between flow ratios Q_p/Q_s as assessed by reference and research PC-MRI. Some of the scatter may be explained by one subject

Table 2. Comparison of standard PC-MRI (= reference) with research PC-MRI (Bland-Altman analysis, data log-transformed[a])

	Bland-Altman category	PC-MRI + SF-2	PC-MRI + SF-3	$PC\text{-}MRI_{HR}$ (without SENSE)	$PC\text{-}MRI_{HR}$+ SF-3
Pulmonary artery					
	Mean	0.99	0.99	0.94	0.93
	Upper limit of agreement (mean + 2 SD)	1.18	1.20	1.07	1.15
	Lower limit of agreement (mean − 2 SD)	0.83	0.82	0.83	0.75
	Upper confidence interval (c.i.)	1.09–1.29	1.09–1.32	1.01–1.14	1.04–1.28
	Lower confidence interval (c.i.)	0.76–0.90	0.74–0.89	0.78–0.88	0.68–0.84
	p-value[b] (Reference vs. Research)	N.S.	N.S.	0.005	0.04
Aorta					
	Mean	0.99	0.97	0.95	0.94
	Upper limit of agreement (mean + 2 SD)	1.15	1.09	1.03	1.04
	Lower limit of agreement (mean − 2 SD)	0.84	0.86	0.86	0.84
	Upper c.i.	1.07–1.24	1.03–1.15	0.99–1.08	0.99–1.10
	Lower c.i.	0.78–0.91	0.82–0.91	0.83–0.90	0.80–0.89
	p-value (Reference vs. Research)	N.S.	0.05	0.002	0.004
Flow ratio Qp/Qs					
	Mean	1.01	1.04	1.02	1.03
	Upper limit of agreement (mean + 2 SD)	1.30	1.29	1.15	1.30
	Lower limit of agreement (mean − 2 SD)	0.79	0.84	0.91	0.81
	Upper c.i.	1.15–1.47	1.17–1.43	1.09–1.22	1.15–1.46
	Lower c.i.	0.70–0.89	0.76–0.94	0.86–0.96	0.72–0.91
	p-value (Reference vs. Research)	N.S.	N.S.	N.S.	N.S.

[a]After antilog transformation, a mean value of 1.0 would reflect a close agreement between reference-PC-MRI and any research PC-MRI pulse sequence, whereas a mean of 1.05 would reflect an overestimation of 5%. Please refer to text (MR Imaging Technique) for abbreviations of pulse sequence names.
[b]Paired two-tailed Student's t-test, to compare the differences between reference and research PC-MRI. A p-value < 0.05 was considered significant.

(included into the Bland/Altman comparison), where one of the two conventional reference PC-MRI measurements in the pulmonary artery yielded an apparently incorrect result (88 mL), whereas all PC-MRI + SENSE flow measurements in the aorta and pulmonary artery agreed closely (stroke volumes ranging between 63–72 mL). In another subject (also included in the Bland/Altman comparison), flow measurement in the aorta using PC-MRI + SF-3 deviated by 17%, but did not do so in the pulmonary artery. With this latter deviation, differences between reference and PC-MRI + SF-3 reached borderline significance in the aorta (Student's t-test, $p = 0.05$), but not in the pulmonary artery ($p = 0.66$).

When using a higher in-plane resolution (1.6*2.1 mm) both with and without SENSE, however, there was a small but statistically significant difference: Measurements in the pulmonary artery and ascending aorta generally yielded smaller flow values (mean difference, −5% to −7%, $p < 0.05$, Table 2, Fig. 4), although the scatter did not increase. The flow ratio Q_p/Q_s, however, showed no relevant difference between high-resolution PC-MRI and reference protocol, because flow underestimation was present in both arteries and thus cancelled out in the calculation of the flow ratio Q_p/Q_s.

3.2. *Repeatability and interobserver variability*

Repeatability (= precision or absence of random error) of the two reference PC-MRI flow measurements was excellent for the pulmonary artery (aorta) with a mean deviation of 2.0 ± 0.3% (1.7 ± 1.3%). Reevaluation of all standard and research PC-MRI flow measurements by two observers (Bland-Altman analysis, data log-transformed) revealed negligible mean differences of 0.0–1.3%, with lower and upper

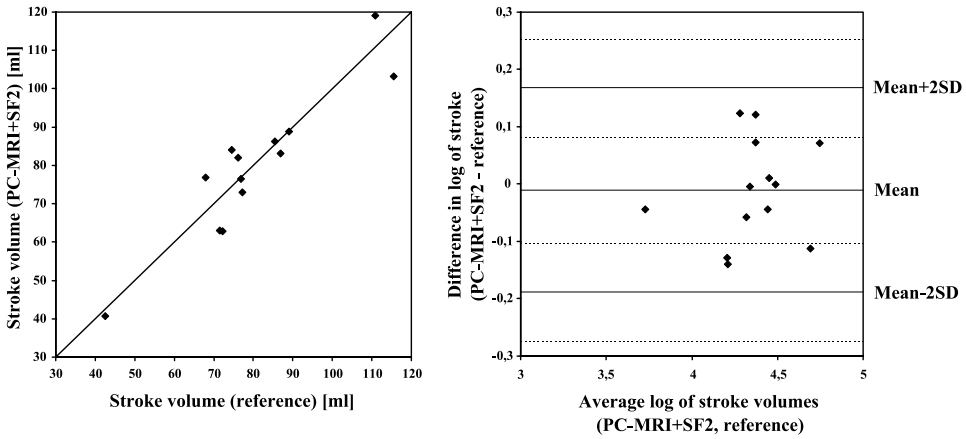

Figure 3. Standard-PC-MRI vs. PC-MRI + SF-2: pulmonary artery. The left panel is a plot of pulmonary stroke volumes by standard (= reference) PC-MRI vs. pulmonary stroke volumes by PC-MRI + SENSE reduction factor of 2. The right panel shows the results of Bland-Altman analysis of agreement for blood flow rate in the pulmonary artery: Plot of difference against mean for pulmonary stroke volumes by standard (= reference) PC-MRI vs. pulmonary stroke volumes by PC-MRI + SENSE reduction factor of 2, data log-transformed (20). Upper and lower limits of agreement: Mean ± 2SD (see also Table 2). SF-2 = SENSE reduction factor of 2.

limits of agreement (= mean ± 2 SD) ranging from −8.6% to +7.8%, demonstrating low interobserver variability.

4. Discussion

In the sensitivity encoding (SENSE) approach, an array of multiple, simultaneously operated receiver coils for signal acquisition (e.g., cardiac five-element phased-array surface coil) is used to spatially encode the MR signal as a function of the sensitivity of each coil element (8). This allows the reduction of the number of phase-encoding steps by increasing the distance of readout lines in k-space and thus accelerate acquisition, but at the expense of a lower signal-to-noise (SNR) ratio.

4.1. *PC-MRI with SENSE: signal-to-noise issues*

Recently, we have demonstrated in pediatric patients with left-to-right shunt that sensitivity encoding may be favorably used to substantially reduce imaging time for blood flow quantification by phase-contrast MRI (PC-MRI) (7), using an adult-size five-element cardiac coil. Although signal-to-noise ratio (SNR) was significantly reduced in the magnitude images, this was apparently no limiting factor for measurement precision in vivo and accuracy in vitro (7).

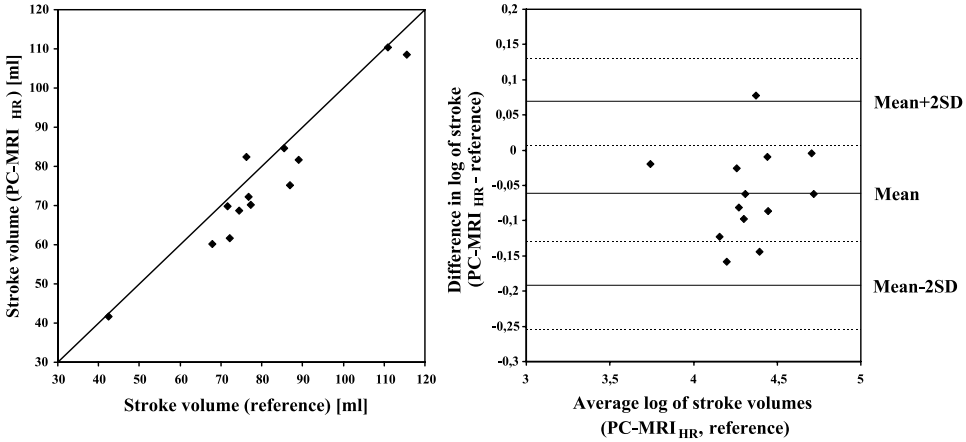

Figure 4. Standard-PC-MRI vs. PC-MRI$_{HR}$: pulmonary artery. The left panel is a plot of pulmonary stroke volumes by standard (= reference) PC-MRI vs. pulmonary stroke volumes by PC-MRI$_{HR}$. The right panel shows the results of Bland-Altman analysis of agreement for blood flow rate in the pulmonary artery: Plot of difference against mean for pulmonary stroke volumes by standard (= reference) PC-MRI vs. pulmonary stroke volumes by PC-MRI$_{HR}$, data log-transformed (20). Upper and lower limits of agreement: Mean ± 2SD (see also Table 2). PC-MRI$_{HR}$ = PC-MRI with high in-plane resolution (see also Table 1 for pulse sequence details). Note the moderate underestimation of flow rates when using PC-MRI$_{HR}$ as compared with standard PC-MRI as reference.

In adults, SNR may be even more an issue of concern. Theoretically, less signal should be available with the same coil design, because signal intensity fades with increasing distance between surface coil elements and vessel of interest, given a certain coil diameter (9).

The results of this study, however, suggest that the combination of standard PC-MRI with SENSE is also advantageous in adults. Quantitative flow measurements in thoracic vessels can be accelerated by a factor of 3.8 to 5.5 by reduction of signal averages and application of SENSE, with clinically well-acceptable results. Hence, at a heart rate of 69/min (= mean heart rate in this study), the scan time can be as short as 25 seconds with PC-MRI + SF-3, and 36 seconds with PC-MRI + SF-2, respectively. The agreement of flow measurements in the single vessels both with/without SENSE was very good. The scatter of Q_p/Q_s was only slightly higher when using SENSE, compared with standard PC-MRI, but not of clinical importance.

Some reduction of signal-to-noise ratio was apparent in the magnitude images (Fig. 1), but there was no degradation of flow measurement results or limitation to quality and speed of flow data postprocessing. It has been shown that useful phase-angle information can still be extracted when SNR in magnitude images is reduced, because phase-angle images principally have a better dynamic range compared with magnitude images (21).

4.2. *Respiratory motion*

In free-breathing adults, motion artifacts from respiration may play a greater role than in the sedated children of our previous study, where breathing pattern was highly regular (7). Theoretically, the amplitude of the diaphragm and chest wall movement should be greater in absolute terms, and the breathing pattern more irregular at times in nonsedated subjects (14).

In a rapid flow acquisition with SENSE, the averaging of any respiratory irregularity or heart rate variability is very limited, thus rendering a flow acquisition at a higher risk for bias. Hence, the shorter the flow scan, the higher is probably the susceptibility to motion artifacts. Although not obvious from the magnitude or phase images, it is likely that this contributed to the slightly higher scatter of flow measurement results in this adult study compared to the pediatric study, where we used the same flow protocols (7).

On the other hand, rapid scanning using SENSE is advantageous, because motion artifacts have simply less time to occur. If irregular breathing pattern or cardiac arrhythmia should be obvious from patient supervision, a SENSE flow study can be repeated at once in a very short time to yield a better result. In fact, it may be generally advisable to routinely perform a PC-MRI flow measurement twice at any location, to confirm results and assess measurement precision of any chosen flow protocol. Using SENSE allows this to be done very rapidly. In our opinion, 2 PC-MRI and SENSE flow measurements performed in a row with very similar results are probably clinically more reassuring and reliable than one single conventional PC-MRI measurement.

Although not yet possible with the protocols used in this study, breath-hold flow measurements seem to be a logical solution to the problem of potentially increased motion susceptibility with rapid flow scanning. Possible techniques to achieve this goal include, on the one hand, realtime flow acquisitions such as phase-contrast MRI using EPI and SENSE (22), and on the other hand, non-realtime gated sequences such as PC-MRI with segmented k-space/SENSE and new sequences based on spiral phase-contrast (23) or steady-state free-precessing (24). It remains to be determined, however, to what extent flow rates obtained by PC-MRI are attenuated during inspiratory or expiratory breathholding, compared to free-breathing conditions. A change in the heart rate during breath holds may also occur and be of potential relevance for flow measurement accuracy.

4.3. *PC-MRI with SENSE: clinical issues*

The proposed rapid flow protocols should be almost generally applicable in adults. The size of the field-of-view (FOV) was appropriate, and no FOV or matrix adjustments were necessary, for example with double-oblique angulation for flow assessment in the pulmonary artery. This is important to avoid severe image degradation from backfolding due to the SENSE reconstruction process. An anterior-posterior phase-encoding direction is most favorable when using SENSE. Some misalignment between flow-encoding gradient and blood flow direction may be tolerated to achieve this goal, because the resulting bias has been demonstrated to be of no clinical relevance (16).

The considerable time benefit is likely to be generally available for hemodynamical evaluations in the growing number of adults with congenital heart disease. For instance, the near equivalence of Q_p and Q_s and the overall limited scatter suggest that PC-MRI with SENSE may be used to exclude or quantify significant cardiac shunting in little more than a minute. Other possible applications of PC-MRI with SENSE include quantification of residual pulmonary valve regurgitation after surgery for Tetralogy of Fallot (2), and the quantification of flows in the venae cavae and branch pulmonary arteries after Fontan palliation in patients with "single-ventricle" physiology (25). Thus, either an examination can be shortened (reduced duration of sedation/anesthesia in children, increased patient throughput) or more comprehensive flow information may be collected in a given amount of time (see above).

4.4. *PC-MRI with higher resolution was not advantageous*

When using high-resolution PC-MRI, however, we observed a small but statistically significant underestimation of flow

rates in the aorta and pulmonary artery. This observation was in agreement with results from in vitro testing using a pulsatile flow phantom as recently reported by our group, where similar high in-plane resolution PC-MRI sequences both with/without SENSE significantly underestimated the "true" flow rate as assessed by stop-watch and graduated cylinder (7). Standard PC-MRI sequences both with/without SENSE, on the other hand, showed excellent correlation with the flow phantom (7). Therefore, the smaller flow rates by high-resolution PC-MRI do not seem to represent the "correct" values, as might be attributable to the reduced partial volume effects (16, 17, 19). Moreover, the effect of flow underestimation at high resolution was apparently not related to the SENSE reconstruction process, because it occured both with and without use of SENSE. We speculate that the increased gradient strength needed to obtain the higher spatial resolution introduces some artificial nonflow related effect on the phase shift, such as from residual eddy currents (26) and concomitant gradient fields, which may rather explain the small underestimation bias.

4.5. *Limitations*

No conclusions from our data are applicable to subjects with arrhythmia and valvular stenosis with turbulent blood flow. Theoretically, undetected shunts may have been present in our volunteers. However, no clinical signs were suggestive, and no evidence for left-to-right shunting was detected by echocardiography in any subject. Although there is no "gold standard" available for assessing accuracy of PC-MRI flow measurements in vivo, comparable PC-MRI protocols to the one used here as reference have been extensively validated both in vitro and in vivo (5, 6, 16, 19). Quantitative signal-to-noise measurements were not carried out, because filtering for noise reduction is automatically performed along with the application of SENSE. Hence, comparison with non filtered standard flow data may be misleading. In vitro flow-phantom testing of PC-MRI flow protocols similar to this study was performed in our previous study in children (7). Repeatability (i.e., precision) of the research flow sequences was not assessed for the sake of total imaging time. Therefore, the impact of any possible increase of intraindividual scatter of measurement results on the total scatter of measurement results was not determined.

5. Conclusions

Standard PC-MRI for flow quantitation may be safely combined with SENSE in free-breathing adults. Measurements can be accelerated by a factor of 3.8–5.5 using SENSE and one instead of multiple numbers of excitation. Thus, a scan time of ~30 seconds can already be achieved, and even breath-hold flow measurements may become possible in the future. A high in-plane resolution was not advantageous in our population.

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