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Repeatability and Internal Consistency of Abdominal 2D and 4D Phase Contrast MR Flow Measurements

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Abstract

RATIONAL AND OBJECTIVES: The aim of this study was to assess the repeatability and internal consistency of flow measurements in the renal arteries and pararenal aorta with the use of standard 2D and novel 4D phase contrast (PC) magnetic resonance imaging (MRI).

MATERIALS AND METHODS: Ten healthy volunteers were imaged with a radially-undersampled 4D PC technique centered over the renal arteries and with four 2D PC slices placed in the supra/infrarenal aorta and the left/right renal arteries; this MR exam was performed twice on each subject. Flow measurements in all four vessels were computed from 2D and 4D PC data sets. Student's t-tests ($p < 0.05$) were used to assess differences between in-flow (suprarenal aorta) and out-flow (infrarenal aorta + left renal artery + right renal artery) for the 2D and 4D techniques, to compare in- and out-flow, and to compare repeated measurements of 2D and 4D flow measurements.

RESULTS: No significant differences were found in repeated measurements of 2D ($p = 0.15$) or 4D ($p = 0.39$) data. No significant difference was found between 2D (3.4 ± 2.8 ml/cardiac cycle) and 4D (3.5 ± 2.7 ml/cardiac cycle) in- and out-flow differences ($p = 0.88$). Out-flow was greater than in-flow for 2D measurements ($p = 0.003$); no difference was found for 4D measurements.

CONCLUSION: The 2D and 4D techniques demonstrated strong repeatability and internal consistency of flow measurements in the renal arteries and pararenal aorta.

Keywords

4D PC MRI; reproducibility; phase contrast; repeatability; flow

INTRODUCTION

In recent years 4D phase contrast (PC) magnetic resonance imaging (MRI) has become more common as a research tool to investigate anatomy, angiography, and flow and velocity information. 4D PC acquisitions provide large volumetric coverage and three-directional velocity encoding for multiple time points in the cardiac cycle. Additionally, 4D PC data sets can be used to derive various flow-related parameters, including pulse wave velocity, pressure gradients, and wall shear stress (1). A number of studies have been performed to validate 4D PC flow measurements, such as the comparison of 4D PC flow measurements to flow phantoms (2, 3) and to 2D flow measurements as a reference standard (2, 4-7). 4D PC flow measurements have also been compared with laser Doppler velocimetry (8) and with ultrasound flow measurements in the cranial vessels (9) and the left ventricle (5). Furthermore, pressure gradients derived from 4D PC data sets have been validated with invasive pressure probes (10). Initial studies showed that pressure gradients measured with

4D PC and invasive pressure probes were found to be in strong agreement in the carotid and iliac arteries. Such studies are useful for demonstrating the feasibility of using 4D PC flow techniques clinically.

Navigator-based respiratory gating, as well as continuously adapting respiratory gating with bellows, has allowed for 4D PC data sets to be collected during free breathing (11-13). However, respiratory gating further prolongs the already lengthy acquisitions. Furthermore, the high demands for spatial resolution and large volume coverage needed to assess the complicated anatomy of the abdominal vasculature (Figure 1) have hampered the use of 4D PC MRI in the abdomen. Radial undersampling has been promising as a means to overcome these limitations; radial undersampling has allowed for the assessment of renal flow in addition to the acquisition of high quality PC angiograms without the need for an external contrast agent (11, 12). Given the potential for artifacts arising from respiratory and peristaltic motion in abdominal exams, further evaluation is needed to assess the performance of 4D PC techniques in the abdomen.

The purpose of this study was to assess and compare the repeatability and internal consistency of 2D and 4D PC flow measurements in the renal arteries and pararenal aorta. To evaluate the internal consistency of flow measurements, flow in the suprarenal aorta (SRA) was compared to the sum of flow measurements in the renal arteries and infrarenal aorta (IRA). Given that no gold standard exists for human in vivo flow measurements, 2D PC flow measurements were used as a reference standard for assessing the 4D PC flow measurements. There are a number of advantages to 4D PC imaging compared to 2D PC imaging; 4D PC provides volumetric three-dimensional anatomic and angiographic information, volumetric three-directional velocity information over time, the ability to acquire data during free breathing, and the ability to derive three-dimensional hemodynamic parameters, such as helices, vortices, wall shear stress, pulse wave velocity, pressure gradients, among other parameters. Furthermore, the comparison of 2D and 4D PC flow measurements is pertinent, given that the placement of 2D slices is subject to user error—as when slices are not placed double-obliquely and when a slice intersects a branching vessel. Since any plane can be extracted retrospectively from the 4D PC data sets, such user errors during scan prescription are mitigated. Furthermore, radially undersampled 4D PC acquisitions may require less total scan time than a series of 2D PC acquisitions, given that an angiogram is needed for accurate 2D slice prescriptions and rest is needed between multiple breath holds. We have also addressed in this study the technical challenges of comparing 2D and 4D PC measurements, given that the frame duration can differ between the acquisitions. Coverage of the cardiac cycle can also differ between the acquisitions, particularly when using the commonly used prospective gating for the 2D PC acquisition and retrospective gating for 4D flow imaging—as with our radial approach. To our knowledge this is the first comparison of 2D and 4D PC flow measurements in the renal/pararenal vasculature and the first assessment of the repeatability of 4D PC flow measurements in any vascular territory.

MATERIALS AND METHODS

Subjects

Ten healthy volunteers (6 men, 4 women, ages 24 – 31 years, mean age (±1 SD): 27.4 ± 2.3 years) with no history of cardiovascular disease, no history of smoking, and no current use of medications were included in this HIPAA-compliant study. The study protocol was approved by the local institutional human subjects review board (IRB). Written informed consent was obtained from all subjects prior to inclusion. Subjects refrained from food and drink for a minimum of four hours prior to the MR examination to mitigate the effects of

food and drink on blood volume status and hemodynamics. All subjects had a single renal artery supplying each of the kidneys.

MR Imaging

Subjects were imaged on a 3T clinical MR scanner (MR750, GE Healthcare, Waukesha, WI) using a 32-channel torso coil (NeoCoil, Pewaukee, WI). 4D PC data were acquired in the abdomen with the field of view centered on the take-off of the renal arteries. 2D PC slices were acquired in the supra- and infrarenal aorta as well as in each renal artery as shown in Figure 1. Slices were prescribed double-obliquely based on reformatted images from a non-contrast MR angiogram (inhance inflow inversion recovery [IFIR]). Planes in the supra- and infrarenal aorta were placed approximately 5-10 mm away from the takeoff of the renal arteries. Planes in the renal arteries were placed 10-15 mm distal to the ostia of the renal arteries. Slice prescription of the 2D PC scans was performed during the acquisition of 4D PC data. After the acquisition of 2D and 4D PC data, the subjects were asked to exit the scanner for five minutes and then re-enter the scanner; the entire procedure described above was then repeated.

2D PC data were acquired with a product 2D sequence with prospective cardiac gating and rectilinear k-space sampling. Typical scan parameters were: VENC (velocity encoding) = 100 cm/s for renal arteries, VENC = 150 cm/s for the aorta, through-plane velocity encoding, TR/TE/flip = 4.92 ms/2.91 ms/20°, FOV = 34 × 34 cm^2, slice thickness = 6 mm, bandwidth = 488.3 Hertz/pixel, 192 × 140 encoding matrix, breath-holding, temporal resolution = ~20 ms, in-plane spatial resolution = 1.33 × 1.33 mm^2, 25 heart beats required for scan time. 4D PC data were acquired with a dual-echo 5-point velocity encoded sequence with radial undersampling, termed PC VIPR (phase contrast with vastly undersampled isotropic projection reconstruction), in combination with retrospective ECG gating (2, 14, 15). Typical scan parameters were: VENC = 150 cm/s, three-directional velocity encoding, TR/TE/flip = 6.1 ms/2.4 ms/8°, reconstructed imaging volume = 34 × 34 × 34 cm^3, bandwidth = 488.3 Hertz/pixel, readout = 256 samples, resulting in 1.32 mm isotropic spatial resolution. The acquisition was conducted with an axial excitation and a slab thickness of 16 cm. Respiratory gating with a bellow signal was used with a 50% acceptance window that continuously adapted to the expiration position. The scan time was on the order of 11 minutes. During post-processing, data were reconstructed to 16 time frames with temporal filtering in the RR-cycle (16), similar to view sharing, to yield a temporal resolution of ~71.5 ms on average (depending on the subject's heart rate). This filter provides a temporal window equal to ~71.5 ms in the central spatial frequencies of k-space and a temporal window equal to 5*71.5 = 357.5 ms in the higher frequency regions of k-space.

Data Analysis

Header information from the 2D PC slices were used to extract identical planes from the 4D data sets with the use of a custom MATLAB-based software tool (The MathWorks, Natick, MA). Flow was measured from 2D and 4D slices with the use of a custom MATLAB-based software tool; regions of interest (ROIs) were drawn manually on magnitude images and subsequently copied to the corresponding phase difference images by the software. Regions of interest were propagated across all time frames and adjusted for any movement of the vessel that may have occurred during the cardiac cycle. Mean flow for each time frame was exported from the software.

The 4D PC acquisition was acquired with retrospective cardiac gating in which the ECG trigger pulses were recorded; trigger pulses did not affect the acquisition view ordering. Therefore, data were acquired over the entire cardiac cycle. In contrast, the 2D acquisition

was acquired with prospective cardiac gating, which requires a trigger delay and an arrhythmia rejection window. As a result, the cardiac cycle is not completely sampled with the 2D series of time frames and the resultant flow waveform is incomplete and shorter in duration compared to the 4D flow waveforms. Additionally, the trigger delay of the 2D acquisition, and the difference in temporal resolution between the 2D and 4D techniques, result in the flow waveform being shifted along the cardiac cycle relative to the 4D flow waveform. To compare flow measurements between the 2D and 4D techniques, the flow waveforms should be compared over the same portions of the cardiac cycle. Therefore, to compensate for the abbreviated cardiac cycle and temporal shift of the 2D flow waveform, a custom MATLAB-based software tool was created to align the 2D flow waveform with the 4D flow waveform; this waveform shift was performed by first upsampling both flow waveforms to 400 data points using a cubic spline interpolant. Points at the peak, 50% of maximum, and the foot (defined as the intersection between the x-axis and a line fitted to data along the upstroke between 20 and 80% of maximum) were identified on each flow waveform. A minimization problem was processed with the software tool to minimize the distance between these three waveform points on the 2D and 4D flow waveforms. Once the two waveforms were aligned, the 4D flow waveform was cropped such that the temporal window was the same for both the 2D and 4D flow waveforms. The adjusted waveforms were integrated such that total flow over the cardiac cycle (ml/cardiac cycle) was measured. Differences between in-flow (suprarenal aorta) and out-flow (infrarenal aorta + left renal artery [LRA] + right renal artery [RRA]) were tabulated for the 2D and 4D data.

Statistical Analysis

2D and 4D flow measurements from the two exams in each subject were compared and plotted with Bland-Altman analysis (17). 2D and 4D flow measurements were also compared with a paired Student's t-test ($p < 0.05$) for each individual vessel and for all vessels combined. Stacked box plots were created for the 2D and 4D data from the first exam in each subject to compare in- and out-flow differences. 2D and 4D in- and out-flow differences were compared with an unpaired equal-variance Student's t-test ($p < 0.05$). In- and out-flow were compared with a paired Student's t-test ($p < 0.05$) for both the 2D and 4D approaches. The percent differences between in- and out-flow measurements were computed via the absolute value of the difference between in-flow and out-flow, divided by the mean of the in-flow and out-flow. The overall percent differences for in- and out-flow were reported as the mean ± 1 SD and compared between the 2D and 4D techniques with an unpaired equal-variance Student's t-test. Bland-Altman plots were created for both the 2D and 4D data to assess the repeatability of flow measurements from the two exams in each subject. The percent differences of repeated 2D and 4D measurements were computed as the absolute value of the difference between the first and second flow measurements in each vessel, divided by the mean of the two flow measurements. The overall percent differences were reported for the 2D and 4D techniques as the mean ± 1 SD. The percent differences were compared between the 2D and 4D techniques with an unpaired equal-variance Student's t-test. A paired Student's t-test ($p < 0.05$) was performed to compare repeated measurements for both the 2D and 4D data. Linear regression of the repeated measurements of 2D and 4D data was performed using data from all four vessels (SRA, IRA, LRA, and RRA); R- and p-values ($p < 0.05$) were recorded.

RESULTS

For the first examination in each subject, mean (±1 SD) flow measurements from the 2D data were 28.6 ± 6.7, 16.0 ± 3.8, 7.6 ± 2.2, and 8.4 ± 2.0 ml/cardiac cycle for the SRA, IRA, LRA, and RRA vessels, respectively. For the second examination in each subject, mean 2D flow measurements were 30.7 ± 7.3, 17.4 ± 5.0, 7.3 ± 2.1, and 8.0 ± 2.2 ml/cardiac cycle for

the four vessels, respectively. Similarly for the first examination in each subject, 4D flow measurements were 26.8 ± 6.9, 15.5 ± 4.5, 5.1 ± 1.5, and 5.9 ± 1.3 ml/cardiac cycle for the SRA, IRA, LRA, and RRA vessels, respectively; for the second examination, measurements averaged 28.8 ± 7.7, 14.5 ± 3.8, 5.4 ± 2.1, and 6.2 ± 1.7 ml/cardiac cycle, respectively. Bland-Altman analysis comparing 2D and 4D flow measurements for all four vessels demonstrated an overall mean flow difference (±2 SD) of 2.0 ± 4.3 ml/cardiac cycle (Figure 2). Overall, 2D flow measurements were significantly greater than 4D flow measurements ($p = 2.0 \times 10^{-12}$). In each individual vessel, 2D flow measurements were significantly greater than 4D flow measurements for the SRA ($p = 4.89 \times 10^{-3}$), IRA ($p = 9.60 \times 10^{-3}$), LRA ($p = 3.81 \times 10^{-5}$), and RRA ($p = 1.70 \times 10^{-7}$).

No significant difference was found between 2D (absolute value of mean ± 1 SD: 3.4 ± 2.8 ml/cardiac cycle) and 4D (absolute value of mean ± 1 SD: 3.5 ± 2.7 ml/cardiac cycle) in- and out-flow differences (Figure 3; p = 0.88). The mean (±1 SD) percent difference for in- and out-flow measurements was 11.3 ± 9.4 % for the 2D data and 12.6 ± 8.8 % for the 4D data. No significant difference was found in the percent difference between the 2D and 4D results (p = 0.65). For 2D data, in-flow tended to be less than out-flow measurements, whereas for 4D data, in-flow tended to be greater than out-flow measurements. Out-flow measurements were significantly greater than in-flow measurements with the 2D technique (p = 0.003); no significant difference was found between in-flow and out-flow measurements for the 4D technique (p = 0.13)

For repeatability, Bland Altman analysis in all four vessels demonstrated a mean difference (±2 SD) of 0.8 ± 6.2 ml/cardiac cycle for 2D data (Figure 4a) and a mean difference (±2 SD) of 0.4 ± 6.2 ml/cardiac cycle for the 4D data (Figure 4b). The mean (±1 SD) percent difference for repeated flow measurements was 14.0 ± 12.5 % for the 2D data and 15.1 ± 15.6 % for the 4D data. No significant difference was found in the percent difference between the 2D and 4D results (p = 0.72). For all four vessels, no significant differences were found in repeated measurements of 2D (p = 0.15) or 4D (p = 0.39) data. For repeated measurements in each individual vessel, significant differences were found in neither the 2D (SRA: p = 0.06; IRA: p = 0.36; LRA: p = 0.60; RRA: p = 0.13) nor the 4D data (SRA: p = 0.12; IRA: p = 0.48; LRA: p = 0.47; RRA: p = 0.36). Linear regression demonstrated strong agreement between repeated measurements for both 2D ($R = 0.96$, $p = 2.6 \times 10^{-22}$) and 4D ($R = 0.96$, $p = 9.9 \times 10^{-22}$) data.

DISCUSSION

The results of this study demonstrate the repeatability of flow measurements in the abdominal vasculature, as well as the internal consistency of in- and out-flow measurements in the renal arteries and pararenal aorta, with both the 2D and 4D PC techniques. For repeatability, 2D data demonstrated a mean difference (±2 SD) of 0.8 ± 6.2 ml/cardiac cycle and 0.4 ± 6.2 ml/cardiac cycle for 4D data. No significant differences were found ($p > 0.05$) and correlation coefficients showed very strong agreement ($R = 0.96$) in repeated measurements of 2D and 4D data. However, repeated 2D and 4D flow measurements varied an average of 14-15%. For measurements of internal consistency, differences were found between in- and out-flow (2D: 3.4 ± 2.8 ml/cardiac cycle; 4D: 3.5 ± 2.7 ml/cardiac cycle); no significant differences were found in comparing 2D and 4D in- and out-flow measurements. In- and out-flow varied by 11.3 ± 9.4 % for the 2D data and 12.6 ± 8.8 % for the 4D data. Out-flow measurements were significantly greater than in-flow measurements with the 2D technique (p = 0.003); no significant difference was found between in-flow and out-flow measurements for the 4D technique (p = 0.13). These findings demonstrate stronger repeatability and internal consistency for the 2D and 4D techniques than reported in the study by Bax et al. (18). Bax et al. used a retrospectively cardiac gated 2D approach with

free breathing to measure repeatability and in-/out-flow differences in the renal arteries and pararenal aorta. Blurring secondary to respiratory motion led to a lesser degree of repeatability and internal consistency, as well as a limited technical success rate (78 - 85%) (18).

Flow measurements from the 4D approach were significantly lower than flow measurements from the 2D approach ($p = 2.0 \times 10^{-12}$), which is consistent with previous studies comparing 2D and 4D flow measurements (7, 19). The lower temporal resolution of the 4D approach (~71.5 ms) compared to the 2D approach (~20 ms) may explain these differences in flow measurements. The temporal filter used in the reconstruction of 4D data creates temporal blurring of higher spatial frequencies; the lower temporal resolution with the 4D approach will more often fail to sample the true peak systolic flow and therefore tend to underestimate the total flow over the cardiac cycle. Additionally, the 4D acquisition lasts more than 10 minutes; thereby, data are combined from many heartbeats and may include variations in the length of the cardiac cycle. Therefore, the scan duration may also contribute to the temporal blurring effect and lead to a decrease in peak flow. The in-plane spatial resolution of the 2D and 4D approaches was identical; however, the 4D approach provides isotropic spatial resolution, and therefore, the slice thickness of extracted 4D slices (1.32 mm) is less than the 2D slice thickness (6 mm). Out-of-plane partial voluming is more likely to have contributed to errors in flow for the 2D technique than for the 4D technique. Furthermore, flow measurements from the 4D data were acquired on planes extracted from the imaging volume. The extraction of a 2D plane from a 4D volume could lead to interpolation effects that affect flow measurements. Nevertheless, there was no non-invasive gold standard to demonstrate whether either the 2D or 4D flow values were more accurate compared to the true flow rates within the vessels. The extraction of planes from the 4D data set is potentially advantageous, as it doesn't rely on proper slice prescription during the acquisition. Slice prescription can be problematic with 2D acquisitions, since it takes time to acquire proper localizers and prescribe slices double-obliquely; 2D slices may also intersect branching vessels. For example, prescription of a suprarenal aortic slice without intersecting the superior mesenteric artery is difficult. Hence, the selection of slices retrospectively is a significant advantage of 4D PC data sets. Even with the retrospective selection of a plane with the 4D PC technique, an individual's anatomy can make it difficult to obtain a slice in the suprarenal aorta that doesn't intersect the superior mesenteric artery. Because of the difficulty in selecting a plane in the suprarenal aorta, and because of hemodynamic disturbances resulting from the complex geometry around the suprarenal aorta and superior mesenteric artery, flow measurements in the suprarenal aorta were more variable than flow measurements in the three other vessels for both the 2D and 4D techniques (Figures 2 and 4). Finally, the 4D PC acquisition required 11 minutes of scan time. In comparison the series of four 2D PC slices requires ~30 seconds per scan, with a minute of rest between each scan, as well as a five-minute non-contrast angiogram and up to five minutes for prescribing the four slices. Therefore, the four 2D PC slices require 10-15 minutes of scan time. In a time period approximately equivalent to a series of 2D PC slices, the radially undersampled 4D PC acquisition has the ability to provide comparable flow measurements, less error due to slice prescription, no breath holding, a more complete flow waveform via the use of retrospective cardiac gating, a non-contrast-enhanced angiogram, and the potential for deriving additional parameters from the volume data set, such as wall shear stress, pulse wave velocity, and pressure gradients, which benefit from volumetric three-directional velocity information.

There are several limitations to this study. The 2D PC acquisition utilized prospective cardiac gating, whereas the 4D technique employed a retrospective cardiac gating technique. The prospectively gated 2D technique was selected because of its clinical use and the ability to scan within the time of a breath hold. The retrospectively gated 2D PC technique

available on our MR scanner utilized rectilinear k-space sampling and was unfeasible within the time of a breath hold. Therefore, it was the priority of this study to use a clinically available 2D PC technique and one that could be performed within the time of a breath hold. Despite the difference in gating technique used in our 2D and 4D PC methods, we developed a tool to match the 2D and 4D flow waveforms. On another point, the repeatability of flow measurements was only assessed on back-to-back MR examinations. In addition to the study of back-to-back MR examinations, it would be advantageous to investigate the repeatability of flow measurements for MR examinations performed on separate days. As such, physiological variations in flow measurements could be assessed. Ideally such a study would require repeated MR examinations on both the same day as well as on each of two subsequent days so that variations due to the technique could be adjusted for in the evaluation of physiological variations in flow. Furthermore, such a study would require the withholding of food and drink for four hours and for the MR exam to be performed at the same time of day each day to account for diurnal variations in hemodynamics. Finally, it should be noted that it may not be possible to generalize the results of this study to other 4D techniques, as a radially undersampled 4D technique was used in this study. While the 4D technique used respiratory gating with bellows to compensate for respiratory motion, radially sampled sequences are inherently less sensitive to respiratory motion than acquisitions with rectilinear k-space sampling. The fact that each projection traverses the center of k-space mitigates the effects of respiratory motion.

In conclusion, the 2D and 4D PC acquisitions provided a promising means of measuring flow in the renal arteries and pararenal aorta. Both techniques demonstrated repeatability on the order of 14-15% and strong internal consistency of flow measurements. 4D PC flow measurements were significantly lower than 2D PC flow measurements. Further studies comparing the 2D and 4D PC acquisitions are warranted, including studies to assess the effects of prospective and retrospective cardiac gating, to evaluate the 2D and 4D approaches with matching temporal resolution, and to determine the repeatability of flow measurements on inter-day MR examinations. Additionally, the results of this study—in terms of repeatability and internal consistency—give credence to the use of 4D PC in the abdominal vasculature. As a result, 4D PC can be applied in future studies to the evaluation of hemodynamics in the abdominal vasculature, as well as to the computation of various flow-related parameters, including pulse wave velocity and wall shear stress.

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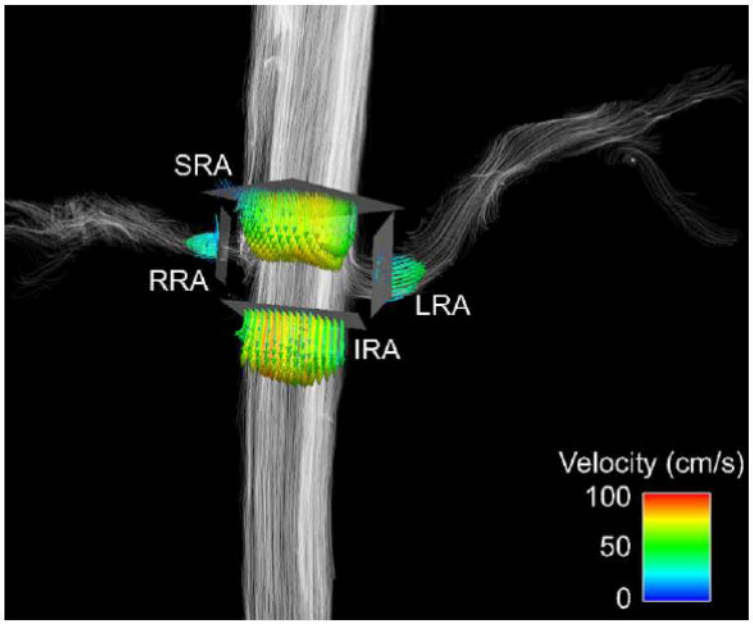

Figure 1.
Vascular geometry and hemodynamics in the abdominal aorta and renal arteries of a healthy volunteer. 3D stream lines depict the systolic blood flow in the abdominal vasculature. Planes demonstrate velocities in the suprarenal aorta (SRA), infrarenal aorta (IRA), and left/right renal arteries (LRA/RRA).

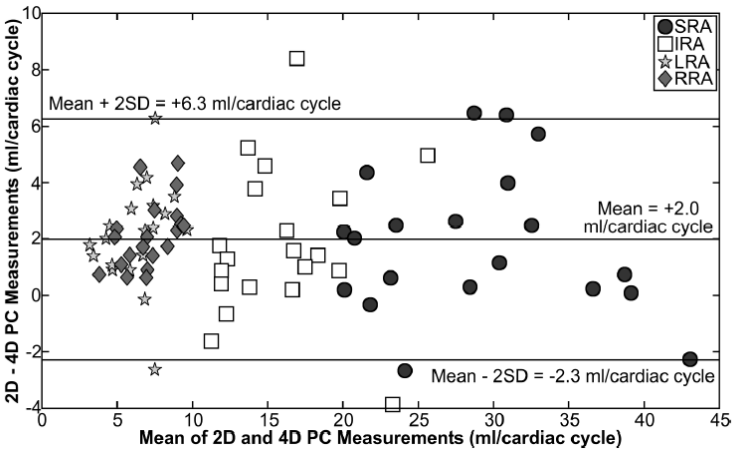

Figure 2.

Bland-Altman analysis of 2D and 4D phase contrast flow measurements (ml/cardiac cycle) in the supra- and infrarenal aorta and the left and right renal arteries via two examinations in each of ten volunteers. The difference in flow measurements between the 2D and 4D techniques is shown on the ordinate, while the mean of the 2D and 4D flow measurements is shown on the abscissa. As represented by the horizontal lines, the mean (±2 SD) of the difference between 2D and 4D flow measurements was +2.0 ± 2.3 ml/cardiac cycle.

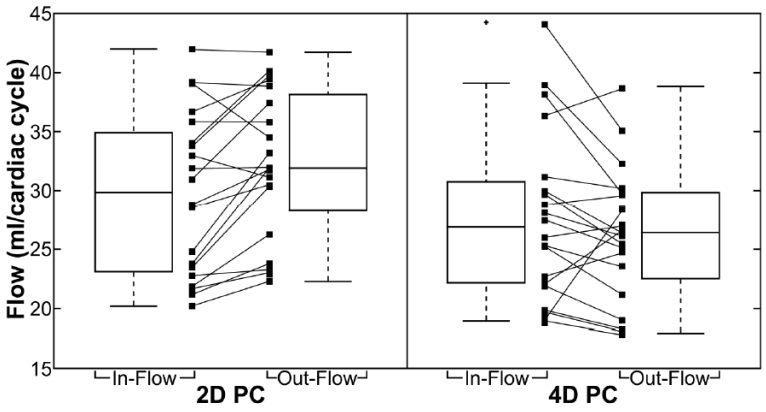

Figure 3.

Box and scatter plots of in-flow (suprarenal aorta [SRA]) and out-flow (infrarenal aorta [IRA] + left renal artery [LRA] + right renal artery [RRA]) in ten volunteers as measured with 2D and 4D phase contrast techniques. Data shown are from both first and second exams in each subject.

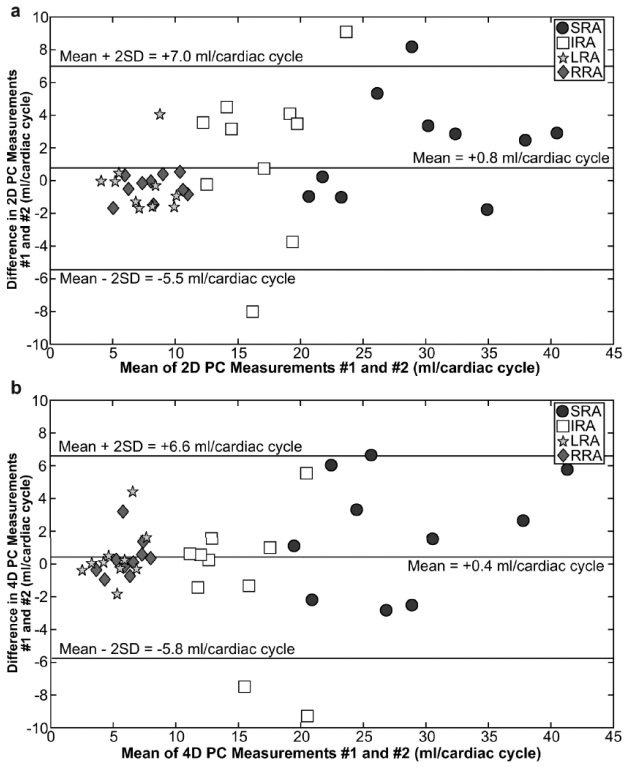

Figure 4.

Bland-Altman analysis of the repeatability of 2D (**a**) and 4D (**b**) phase contrast flow measurements (ml/cardiac cycle) in the supra- and infrarenal aorta and the left and right renal arteries of ten volunteers. The difference in flow measurements between the first and second examinations is shown on the ordinate, while the mean of the first and second flow measurements is shown on the abscissa. As represented by the horizontal lines, the mean (±2 SD) of the difference between repeated 2D flow measurements was +0.8 ± 6.2 ml/cardiac cycle and for repeated 4D flow measurements was +0.4 ± 6.2 ml/cardiac cycle.