Phase contrast MRI in intracranial aneurysms

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Complex flow patterns in a real-size intracranial aneurysm phantom: phase contrast magnetic resonance imaging compared with particle image velocimetry and computational fluid dynamics

Pim van Ooij, Annetje Guédon, Christian Poelma, Joppe Schneiders, Marcel Rutten, Henk Marquering, Charles Majoie, Ed van Bavel, Aart Nederveen

Abstract

To validate flow patterns as measured by high resolution time-resolved 3D phase contrast MRI (PC-MRI) in a real-size intracranial aneurysm phantom, retrospectively gated PC-MRI was performed in an intracranial aneurysm phantom at a resolution of 0.2 x 0.2 x 0.3 mm³ in a solenoid rat coil. Both steady and pulsatile flows were applied. The PC-MRI measurements were compared with Particle Image Velocimetry (PIV) measurements and Computational Fluid Dynamics (CFD) simulations. A quantitative comparison was performed by calculating differences between the magnitude of velocity vectors and angles between velocity vectors in corresponding voxels. Qualitative analysis of the results was executed by visual inspection and comparison of the flow patterns.

The root mean square error (RMSE) of the velocity magnitude in the comparison between PC-MRI and CFD was 5% and 4% of the maximum PC-MRI velocity and the median of the angle distribution between corresponding velocity vectors was 16° and 14° for the steady and pulsatile measurements respectively. In the PC-MRI and PIV comparison the RMSE was
12% and 10% of the maximum PC-MRI velocity and the median of the angle distribution between corresponding velocity vectors was 19° and 15° for the steady and pulsatile measurements respectively. Good agreement was found in the qualitative comparison of flow patterns between the PC-MRI measurements and both PIV measurements and CFD simulations. High resolution time-resolved PC-MRI can accurately measure complex flow patterns in an intracranial aneurysm phantom.
Blood flow velocity measurement using phase contrast MRI (PC-MRI) is performed since the advent of MRI in the early eighties [1]. At present the technique has become more mature by incorporating benefits from several technological advancements in MRI, e.g. parallel imaging, increased signal to noise ratio (SNR) of multichannel coils and increased gradient and field strength. Time-resolved measurement of blood flow velocity in three directions using cardiac gated PC-MRI [2] for the assessment of hemodynamic properties in cardiovascular diseases, such as atherosclerosis and intracranial aneurysms, is gaining interest for clinical use. PC-MRI has been extensively validated in the aortic arch [3-5] and the carotid arteries [6-8]; however, in small structures such as the cerebral arteries [9-10] or intracranial aneurysms [11-13], accurate velocity measurements are more challenging due to higher resolution demands and accompanying SNR loss.

Intracranial aneurysms are found in between 1 and 5 percent of the population [11]. The morbidity and mortality rates after rupture of intracranial aneurysms are high [12] and patients are therefore monitored with extreme caution. The decision to treat an incidentally found unruptured aneurysm is based on the rupture risk and the risks related to treatment with 3-6% morbidity and 1.5% mortality rates for coiling [13]. It is believed that additional value of hemodynamics such as inflow jet size, impingement zone size and wall shear stress can substantially improve rupture risk assessment [14].

At present, computational fluid dynamics (CFD) provides estimations of hemodynamic flow behaviour in intracranial aneurysms. The above mentioned hemodynamic risk factors for aneurysm rupture can be derived from these simulations [15-20]. However, straightforward clinical implementation of this method is hampered by the extensive computational time which is in the order of hours or days, or even weeks.

Hemodynamic information from rapid PC-MRI scans would therefore be preferable to CFD simulations for rupture risk assessment, especially in cases where quick treatment decisions need to be made. Unfortunately, the accuracy of PC-MRI in cerebral arteries and aneurysms remains uncertain. Previous studies showed promising results, but were carried out at relatively low resolutions [21-23], in thick slices through the aneurysm [24-26] or in up-scaled phantoms [27-28]. The goal of this study is the validation of a time-resolved three-dimensional PC-MRI sequence at high resolution in a real-size patient-specific phantom of an intracranial aneurysm by compar-
son with particle image velocimetry (PIV) and computational fluid dynamics (CFD).

2.2 Materials and Methods

2.2.1 Phantom

A glass reproduction was manually created based on a high-resolution 3D Rotational Angiography (3D-RA) dataset of an unruptured aneurysm located in the anterior communicating artery of a patient who supplied informed consent. The phantom is displayed in figure 2.1a. The inflow vessel is slightly curved, as is displayed in figure 2.1b, where a top view of the phantom is displayed. The inner diameter of the in- and outflow vessels was 2.1 mm, and the maximum dimensions of the lumen of the aneurysm were approximately 6 x 4 x 9 mm in x, y and z directions respectively. Wall thickness was 0.2-0.6 mm in the inflow vessel, 0.4-0.6 mm in the outflow vessels and 0.8 mm in the phantom itself.

2.2.2 Flow loop setup and pump setting

The aneurysm phantom was connected to a flow loop consisting of a reservoir, a centrifugal pump, a computer-controlled piston pump (pulse generator) and PVC tubes, as displayed in figure 2.1c. The pumps were placed outside the MRI room. Measurements were performed under steady as well as pulsatile flow. Pulsatile flow was created by the combination of steady action of the centrifugal pump, creating the mean flow, and pulsatile action of the computer-controlled piston pump. As input for the pulse generator, a flow signal was used that was obtained from the same patient. This flow was based on the velocity profile, given in figure 2.1d, as measured in the internal carotid artery of the same patient to ensure sufficient in-plane pixels [29] using a time resolved PC-MRI sequence with a resolution of 0.8 x 0.8 x 0.8 mm³. In the PC-MRI measurements, the pump generated an artificial electrocardiogram signal, which was used by the MRI scanner to synchronize the acquisition with the flow pulses.
2.2.3 Particle image velocimetry

PIV was chosen as an independent experimental modality to measure velocity in high resolution. PIV is an optical flow measurement technique that uses the displacement of small tracer particles to obtain instantaneous velocity fields [30]. The characteristics of the tracer particles (size, density and their concentration) are chosen such that the flow field is not influenced by the tracers.

For the PIV measurements, the phantom was fixed in a transparent plastic box and submerged in fluid of the same refraction index (1.471) as the glass of the model, so that optical distortion due to refraction at the curved surfaces was minimized, which is a requirement for accurate PIV measurements. This surrounding fluid was the same as the actual medium (i.e. blood mimicking fluid) and consisted of a 40% glycerol in water solution to match the kinematic viscosity of blood, taken as 2.95 mm$^2$/s. To further equalize the refraction index of the fluid, a concentration of 1075 g/L Sodium Iodide (NaI) was added to the water/glycerol solution. As tracer material, 12 micrometer hollow glass spheres (“Sphericel”, Potters) were added in a small amount.

Using a pulsed Nd:YLF laser (New Wave Pegasus XR), a thin light sheet was created to illuminate the tracer particles (and thus forming the measurement volume). The images of the tracers were recorded by means of a high-speed camera (Photron APX RS, 1024x1024 pixels). Using a cross-correlation algorithm the local velocity was estimated (for full details of the implementation used, see e.g. Poelma et al. [31]). This provided an instantaneous snapshot of the two in-plane velocity components. Due to the use of a high-speed camera (used at 300 frames/second), the temporal evolution of the pulsatile flow could be fully captured. Furthermore, the camera was phase-locked with the pump. After obtaining at least 15 cardiac cycles, the light sheet was translated in the vertical (out-of-plane) direction over 0.21
mm, so that the next slice could be measured. This was repeated 20-25 times to obtain velocity data over the entire phantom.

The PIV measurements resulted in datasets describing the velocity fields for both the steady and the pulsatile flow. The spatial resolution for both cases was 0.33 x 0.33 x 0.21 mm³. The in-plane resolution was mainly determined by the concentration of tracer material and the camera resolution and magnification. The out-of-plane resolution was determined by the step size of the translation of the slices, which was chosen to match the expected in-plane resolution. For the pulsatile case, the cardiac cycle was described by 20 phases. Note that standard PIV only provides two out of three velocity components.

While the PIV measurement was relatively fast (a few seconds for one plane), slow data transfer from the high-speed camera to the computer was the limiting factor. The full measurement of all planes therefore took approximately 8 hours. PIV is traditionally an “off-line” method – analysis of the data to obtain velocity fields is done afterwards and can take minutes to days, depending on the complexity of the analysis scheme. Further details of the experimental setup and the measurement time are given in table 2.1.

### 2.2.4 Phase contrast magnetic resonance imaging

A retrospectively gated [32] PC-MRI scan with four points encoding [33] was performed on a 3T MR system (Philips Medical Systems, Best, the Netherlands). A solenoid rat coil (Philips Hamburg, Germany) with a diameter of 7 cm was used to obtain high SNR. Imaging parameters were: TE/TR: 3.86 / 11.13 ms, flip angle: 15°, non-interpolated spatial resolution: 0.2 x 0.2 x 0.33 mm³, 50 coronal slices, FOV: 25 x 25 mm, velocity encoding: 50 x 100 x 50 cm/s in the x, y and z direction respectively (see figure 2.1a). 20 cardiac phases were measured.

To avoid pulsatile flow artifacts [34], water was used with a kinematic viscosity (1 mm²/s at room temperature of 20°C) which led to necessary adjustments in pump amplitude and frequency according to the Reynolds and Womersley number as measured in the PIV experiment. The cardiac cycle was set to 3 seconds, resulting in a temporal resolution of 150 ms. Further details of the experimental setup and the scan time are given in table 2.1. The phantom was placed in a plastic box and was submerged in agar gel. It was placed in the isocenter of the MRI scanner. In every image background
correction was performed by subtracting the mean phase of the stationary surrounding agar gel [35] to minimize influences of concomitant gradient terms [36] and eddy currents. The steady PC-MRI measurement was performed twice in one session to study the reproducibility of the technique. These repeated measurements were performed within 30 minutes.

2.2.5 Computational fluid dynamics

To create a geometry needed for CFD simulations, a 3D-RA dataset was obtained from the phantom filled with a contrast agent. This dataset was segmented using level set algorithms in VMTK [37] and subsequently meshed. For both the steady and pulsatile simulations, the spatial x-, y-, and z-components of the velocity profile of the inflow as measured in the PC-MRI measurements were applied as velocity-inlet boundary conditions. In the pulsatile simulation this was performed for every measured cardiac phase in PC-MRI.

The implementation of the boundary conditions in CFD obtained from PC-MRI was performed as follows: a mask in the PC-MRI data was created by segmenting the phantom with the use of contours created in the FFE images based on level set evolution algorithms [38]. These contours were manually corrected where needed. This mask was registered onto a mask of the CFD mesh using rigid body registration (rotation and translation) in 3DSlicer (http://www.slicer.org). The x-, y-, and z-components of the inlet velocity of the PC-MRI measurement were interpolated onto the faces of the velocity-inlet boundary of the CFD mesh. The velocity-inlet of the CFD geometry was manually clipped in VMTK to match the velocity-inlet of the PC-MRI measurement.

Since the CFD simulations were carried out using Fluent® software (ANSYS, Canonsburg, USA) a user defined function (UDF) was written for the application of the velocity-inlet boundary conditions. As the diameters of the outflow vessels were equal, outflow boundary conditions were applied that prescribed equal outflow for both vessels. The mesh consisted of 742,316 tetrahedral cells with a minimum, average and maximum node spacing of 0.075, 0.14 and 0.24 mm respectively. Further details of the numerical setup and the simulation time are given in table 2.1.
### Table 2.1 Measurement and simulation properties for PC-MRI, PIV and CFD experiments

<table>
<thead>
<tr>
<th></th>
<th>MRI</th>
<th>PIV</th>
<th>CFD</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Velocity components</strong></td>
<td>x, y, z</td>
<td>x, y</td>
<td>x, y, z</td>
</tr>
<tr>
<td><strong>Slice selective direction</strong></td>
<td>y</td>
<td>z</td>
<td>-</td>
</tr>
<tr>
<td><strong>Resolution (mm³)</strong></td>
<td>0.2 x 0.33 x 0.2</td>
<td>0.33 x 0.33 x 0.21</td>
<td>0.1 x 0.1 x 0.1</td>
</tr>
<tr>
<td><strong>Voxels</strong></td>
<td>14695</td>
<td>8314</td>
<td>185324</td>
</tr>
<tr>
<td><strong>MRI to PIV resolution (mm³)</strong></td>
<td>0.33 x 0.33 x 0.21</td>
<td>0.33 x 0.33 x 0.21</td>
<td>-</td>
</tr>
<tr>
<td><strong>CFD to MRI resolution (mm³)</strong></td>
<td>0.2 x 0.33 x 0.2</td>
<td>-</td>
<td>0.2 x 0.33 x 0.2</td>
</tr>
<tr>
<td><strong>Fluid density ρ (kg/m³)</strong></td>
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<td>1625</td>
<td>1000</td>
</tr>
<tr>
<td><strong>Dynamic viscosity μ (10⁻³ kg/m·s)</strong></td>
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<td>4.8</td>
<td>1</td>
</tr>
<tr>
<td><strong>Kinematic viscosity ν (10⁻⁶ m²/s)</strong></td>
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<td>1</td>
</tr>
<tr>
<td><strong>Measurement/Simulation time</strong></td>
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<td>1-2 days</td>
<td>1 hour</td>
</tr>
<tr>
<td></td>
<td>pulse 3 hours</td>
<td>1-2 days</td>
<td>3-5 days</td>
</tr>
</tbody>
</table>

#### 2.2.6 Postprocessing

The contours created in the FFE images were copied to the PC-MRI data to extract the velocity information. To reduce noise, each velocity direction was filtered with a 3D median filter with a kernel of 3 x 3 x 3 voxels.

The PIV image data were analyzed using a three-step iterative algorithm with a final resolution of 32 x 32 pixels using 50% overlap, resulting in velocity vector fields with a spatial resolution of 0.33 x 0.33 mm². These vector fields were validated using the universal outlier detection scheme [39], which removed erroneous vectors efficiently. Removed vectors (1-2% of the total data at most) were replaced by linear interpolation of the 3D data set.

The CFD velocity information in every node was extracted and rewritten in matrix form with a resolution of 0.1 x 0.1 x 0.1 mm³.

To allow for a voxelwise comparison of the data, rigid body registration was performed between PIV and PC-MRI. A mask was created from the velocity magnitude of the PIV measurement. Since the PIV measurement only provided the x and y velocity components of the flow, it was not possible to register the velocities of the PIV measurement onto the PC-MRI measurement. Therefore, the previously created PC-MRI mask was registered onto the PIV mask and the resulting rotation and translation were applied on the PC-MRI velocities. After registration the velocity components of the PC-MRI measurement were linearly interpolated to the PIV grid. The resulting z-ve-
locity component of the registered PC-MRI velocities was discarded since this component was not measured in the PIV measurement.

For the CFD and PC-MRI comparison both modalities provided the full 3D information. Consequently the CFD mask was registered onto the PC-MRI mask and subsequently the velocities were linearly interpolated to the PC-MRI grid. A flow chart summarizing these postprocessing steps is shown in figure 2.2. This flowchart was applied to both steady and pulsatile measurements and simulation.

### 2.2.7 Quantification and Statistics

To compare the different experiments, they need to be dynamically similar. This is established when both Reynolds (Re) numbers and Womersley (\(\alpha\)) numbers are similar. Reynolds numbers (Re) were calculated according to:

\[
Re = \frac{\bar{v} D}{\nu}
\]

and Womersley (\(\alpha\)) numbers according to:

\[
\alpha = D \sqrt{\frac{f}{\nu}}
\]

In these formulas, \(\bar{v}\) is the mean velocity in the inflow vessel, \(D\) the diameter of the inflow vessel, \(\nu\) the kinematic viscosity of the fluid and \(f\) the frequency of the flow pulse. The kinematic viscosity of the fluid used in the PIV measurement was different from the fluids used in the PC-MRI measurements and the CFD simulations (see table 2.1). If the same inflow for the measurements were applied, different Reynolds and Womersley numbers would have been found, according to equations (2.1) and (2.2). Therefore,
the pump settings were adjusted in the PC-MRI measurement by decreasing the amplitude and frequency of the pulse to match as closely as possible the Reynolds and Womersley numbers of the PIV experiment. For steady flow, only the Reynolds number needed to be matched. The Reynolds numbers were determined based on the velocities obtained by measuring the outflow volume during one minute.

Due to practical restrictions, it was not possible to exactly match the Reynolds numbers between PIV and PC-MRI. The flow field is however not expected to change fundamentally if a small discrepancy in Reynolds number is present. If Reynolds numbers are similar and viscosity of the fluid used in the PIV measurements is higher, the resulting velocities will be higher in the PIV measurement as well. To allow for a quantitative comparison between the velocities found in the PIV and PC-MRI experiments, the former need to be scaled. The velocities in x and y directions, as measured in the PIV measurement, were scaled independently to match the velocities in x and y directions as measured in the PC-MRI measurement. The ratio between the mean PIV velocity magnitude and the mean PC-MRI velocity magnitude in a cross-section through the inflow vessel was used as scaling factor.

Consistency of velocity patterns between the various modalities was tested using Bland-Altman plots, i.e. scatter plots over all voxels of differences between velocity magnitudes against their mean value. Direct subtraction of corresponding voxels in PC-MRI and PIV and CFD would overemphasize registration and interpolation errors and differences as a result of averaging due to different voxel sizes. Therefore the difference between a PC-MRI velocity magnitude voxel and a PIV or CFD velocity magnitude in a single voxel was calculated by using the minimum of the differences between the PC-MRI voxel and the corresponding PIV or CFD voxel and its 6 nearest neighbours. In the Bland-Altman analysis of the repeated steady PC-MRI measurements, the difference between corresponding voxels was calculated, since the position and orientation of the measurements was identical.

For each comparison, the mean difference, the standard deviation of the paired differences (SDp), the limits of agreement (equal to the mean difference ± 1.96 times SDp), the root mean square error (RMSE) and the distribution of the angles between vectors was calculated. Since the noise in the PC-MRI measurement is highest for low velocities, the distribution was also plotted for voxels with velocity magnitude higher than 20% of the maximum velocity to illustrate this dependency. Furthermore, the volumetric in-,
and outflow rates of the PC-MRI measurement were calculated. In figure 2.3, the orientation of the slices as displayed in the results section is shown.

2.3 Results

2.3.1 Steady measurements

Reproducibility of PC-MRI

In figure 2.4a the Bland-Altman plot is displayed for the difference of the velocity magnitude between the two PC-MRI measurements. Mean velocity in the total phantom was 10.46 cm/s in the first scan and 10.65 cm/s in the second. RMSE was 1.81 cm/s, which is 5% of the maximum velocity. A small significant difference of 0.19 cm/s (p<0.001) existed between the repeated measurements. In figure 2.4b the distribution of the angles between the velocity vectors in corresponding voxels in the phantom is shown in black, the distribution after discarding the angles at voxels where the velocity magnitude was lower than 20% of the maximum velocity magnitude is shown in gray. The mean and median for difference in direction were 14° and 10° (black dotted line), 8° and 6° (gray dotted line) after discarding voxels with velocity magnitudes of less than 20% of the maximum velocity.
PC-MRI versus PIV

Reynolds numbers as measured in the inflow tube were 284 and 261 for PIV and PC-MRI respectively. The $x$ and $y$ velocities of the PIV measurement were scaled accordingly to be able to compare the PIV and PC-MRI measurements. From figure 2.5a it can be seen that the error was largest at intermediate velocities, where the PC-MRI velocities were higher than the scaled PIV velocities. A small significant difference of $0.32 \text{ cm/s (p<0.001)}$ existed between the PC-MRI and PIV measurements. Mean velocities were $7.80 \text{ cm/s}$ and $7.65 \text{ cm/s}$ for PC-MRI and the scaled PIV respectively. Note that these mean velocities were lower than the mean velocities in the repeated steady PC-MRI measurement since the $z$-component was not measured in the PIV measurement and discarded in the PC-MRI postprocessing (see flowchart in figure 2.2). RMSE was $4.18 \text{ cm/s}$, which is 12% of the maximum PC-MRI velocity. The mean and median for difference in direction were $35^\circ$ and $19^\circ$ (black line in figure 2.5b), $11^\circ$ and $9^\circ$ (gray line) after discarding vectors with a velocity magnitude less than 20% of the maximum velocity magnitude.
In figure 2.6a and b the x and y velocity vectors are shown in a slice through the aneurysm. The location of this slice is displayed in figure 2.3. It can be seen that the inflow jet of the scaled PIV measurement was skewed slightly to the right (arrow 1) with respect to the inflow jet of the PC-MRI measurement. Furthermore, a vortex exists at arrow 2, which was not found in the PC-MRI measurement. In figure 2.6g and h similar flow patterns are found but in the PIV measurements the velocity magnitude was higher in the middle of the phantom (arrow 3) while in the PC-MRI measurements the velocity magnitude was higher at the edges. This can also be seen in figure 2.6i where velocity difference in the middle of the phantom was negative, indicating that PIV-velocities were higher here, in contrast to velocity differences at the edges which are positive, indicating that PC-MRI velocities are higher here. Note that these figures are displayed at the resolution of the PIV measurement.

Validation
PC-MRI versus CFD

The Bland-Altman plot in figure 2.7a shows that differences between steady CFD and PC-MRI are close to zero, though a small systematic difference was found (0.27 cm/s, p<0.001). The error was largest in voxels with a velocity magnitude around 10 cm/s. Mean velocities were 10.50 cm/s for MRI and 9.38 cm/s for CFD. RMSE was 2.01 cm/s, 5% of the maximum PC-MRI velocity. The inflow measured from the steady PC-MRI data was 0.38 mL/s, the sum of the two outflows was 0.38 mL/s as well. The mean and median for difference in direction were 22° and 16° (black line in figure 2.7b) respectively, 14° and 10° (gray line) after discarding velocities lower than 20% of the maximum velocity. Figures 2.6d and e show similar flow patterns for PC-MRI and CFD. In figure 2.6k and l the velocity at the top is higher for CFD than for PC-MRI (arrow 4). Directions of velocity vectors were similar in these images, except in the middle of the phantom with low velocity in PC-MRI (arrow 5). Note that these figures are displayed at the resolution of the PC-MRI measurement.

2.3.2 Pulsatile measurements

PC-MRI versus PIV

The Womersley number in the PIV measurement was 1.2 and set accordingly for MRI by reducing the frequency of the pulsatile pump from 1 to 0.33 Hz. The Reynolds numbers for PIV and PC-MRI in the inflow vessel are displayed in figure 2.8a. The scaling factor averaged over time was calculated and the PIV measurement was scaled accordingly. The mean velocity in the total phantom for both measurements is displayed in figure 2.8b. A small significant difference of 0.25 cm/s (p<0.001) between PIV and PC-MRI was found. The Bland-Altman plot in figure 2.9a displays that the
largest errors were found in the velocity range near 20 cm/s. At higher mean velocities the PIV velocities were predominantly higher than the PC-MRI velocities. In the separate Bland-Altman plots for systole (at cardiac phase 5) and diastole (at cardiac phase 20) in the insets of figure 2.10a it can be appreciated that the errors (both mean and SDp) in diastole were smaller than in systole. RMSE averaged over time is 3.31 cm/s, 10% of the time-averaged PC-MRI maximum velocity. The mean and median for difference in direction were 30° and 15° respectively, 7° and 6° after discarding velocities below 20% of the maximum velocity. In figure 2.10b, where flow patterns in systole are shown, the inflow of the scaled PIV is slightly skewed to the right compared to PC-MRI measurements as was observed in the steady measurement. This also holds for figures 2.10g and h. Furthermore, a discontinuity of flow was found at arrow 6 in figure 2.10b. In figures 2.11a and b, the velocity was higher at the edges of the PC-MRI measurement, whereas the velocity was higher in the middle of the phantom in the scaled PIV measurement. In diastole (figures 2.11g and h) this is not seen, locations of relatively high velocities of the PC-MRI and PIV measurement corresponded better, especially at the edges (see figure 2.11i).

Figure 2.8 (a) Reynolds numbers in the inflow vessel for the PIV and PC-MRI experiments. (b) Mean velocities in the total phantom in cm/s.

Figure 2.9 (a) Bland-Altman plot of the velocity magnitude difference between PC-MRI and PIV in the pulsatile measurement: mean ± SDp = 0.25 ± 3.30 cm/s, inset up: Bland-Altman plot at systole, cardiac phase 5, with mean difference and SDp, inset down: Bland-Altman plot at diastole, cardiac phase 20, with mean difference and SDp. (b) Distribution of the angles between the 2D velocity vectors.

Validation
Figure 2.10: Top row: peak systolic MRI (a) and PIV (b) velocity vectors and velocity magnitude difference (c). Second row: peak systolic MRI (d) and CFD (e) in-plane velocity vectors and velocity magnitude difference (f) images in a similar slice. Third row and fourth row: same slices at end diastole. Velocities are in cm/s. See for slice orientation figure 2.3.
Figure 2.11 Top row: peak systolic MRI (a) and PIV (b) velocity vectors and velocity magnitude difference (c). Second row: peak systolic MRI (d) and CFD (e) in plane velocity vectors and velocity magnitude difference (f) images in a similar slice. Third row and fourth row: same slices at end diastole. Velocities are in cm/s. See for slice orientation figure 2.3.
PC-MRI versus CFD

The Reynolds numbers in the inflow vessel for PC-MRI and CFD are displayed in figure 2.12a. The mean velocity in the total phantom for both measurements is displayed in figure 2.12b. It appears that both Reynolds numbers and mean velocity were lower for CFD than PC-MRI in systole. The Bland-Altman plot in figure 2.13a displays that the largest errors were found in the intermediate velocity range, whereas the highest velocities were more accurate. Here again a small significant difference of 0.20 cm/s (p<0.001) was present, whereas similar to PIV the errors were larger in systole than in diastole (see insets). RMSE averaged over time was 1.19 cm/s, 4% of the time-averaged maximum PC-MRI velocity. The mean inflow in the pulsatile PC-MRI measurement was 0.25 mL/s, the total mean outflow was 0.23 mL/s, resulting in a difference of 6%. The outflow was predominantly lower in systole. The mean and median for difference in direction were 20° and 14° respectively, 9° and 6° after discarding the velocities below 20% of the maximum velocity, (see figure 2.13b). The inflow jet of the PC-MRI measurement and CFD simulation corresponded nicely for both systole (figures 2.10d and e) and diastole (figures 2.10j and k). In figures 2.11d and e higher velocities are found at the edges of the phantom for both PC-MRI and CFD except at the top of the image, where the CFD velocity was slightly higher.

In the middle of the phantom the PC-MRI shows colliding flow (arrow 7). In diastole (figures 2.11j and k) flow patterns were similar.

In figures 2.14a, b, e and f a small vortex in the tip and a large vortex in the middle of the phantom can be distinguished for both modalities, as well as a small vortex at the bottom of the phantom in diastole (e and f). In figures 2.14c, d, g and h, the vortex and the inflow jet are similar as well. In figure 2.15 similar flow details can be discerned such as the small vortex at the base of the inflow jet (all images) and the complex flow pattern in the tip of the phantom (c, d, g and h) in slice on the right.

Figure 2.12 (a) Reynolds numbers in the inflow vessel for the CFD and PC-MRI experiments. (b) Mean velocities in the total phantom in cm/s.
Figure 2.14 Top row: peak systolic MRI (a,c) and CFD (b,d) in plane velocity vectors in two sagittal cross-sections. Second row: end diastolic MRI (e,g) and CFD (f,h) in two sagittal cross-sections. Velocities are in cm/s. See for slice orientation figure 2.3.

Figure 2.13 (a) Bland-Altman plot of the velocity magnitude difference between PC-MRI and CFD in the pulsatile measurement: mean ± SDp = 0.20 ± 1.41 cm/s, inset up: Bland-Altman plot at systole, cardiac phase 5, with mean difference and SDp, inset down: Bland-Altman plot at diastole, cardiac phase 20, with mean difference and SDp. (b) Distribution of the angles between the 3D velocity vectors.

Validation
In this study we have shown that a good qualitative and quantitative agreement exists between PC-MRI measurements, CFD simulations and PIV measurements of flow patterns in a real-size intracranial aneurysm. We demonstrated this agreement for both steady and pulsatile measurements. The difference between CFD simulations and PC-MRI measurements (RMSE 4-5 %) was smaller than that between PIV measurements and PC-MRI measurements (10-12 %). Velocity directions (median deviation less than 10° for velocities higher than 20% of the maximum) were comparable between the modalities.

Previous studies have shown that PC-MRI can measure flow patterns in intracranial aneurysms [21-23, 40] in patients, though the accuracy of the velocity fields remains uncertain. PC-MRI data provides valuable information on the severity of the disease and may subsequently aid in therapeutic decision making. PC-MRI is however not yet fully incorporated in the clinical setting. One of the reasons may be that, to fully and convincingly capture complex flow patterns in intracranial aneurysms, high resolution scans are mandatory. Since high resolution scans increase scan time and can be hampered by low SNR, the technique is mostly applied at relatively low resolutions (around 1 mm³), leading to loss of flow information due to averaging of velocity in a voxel, increased intravoxel dephasing and inaccurate vessel wall definition as a result of partial volume effects. To avoid scan time limitations and resulting flow artifacts, the accuracy of PC-MRI has been tested in phantoms. Several phantom experiments were carried out in upscaled phantoms [27-28]. Real-size phantoms were used as well, but in these studies PC-MRI was performed in a single cross-sectional slice [24-26] instead of a 3D volume with isotropic resolution. Furthermore, velocity comparisons on a voxel-by-voxel basis are rarely found in literature and are generally limited to a qualitative comparison.

Our study provides assessment of the accuracy of high resolution PC-MRI using two independent modalities in a real size aneurysm phantom under both steady and pulsatile flow conditions and presents a quantitative comparison between the modalities.

The steady flow measurement showed good reproducibility, indicating the precision of the PC-MRI measurement itself. The minor systematic error could have been caused by small differences in the speed of the pump that generated the mean flow. Interestingly, variation between PC-MRI and CFD
was comparable to that between repeated PC-MRI measurements, illustrating the good agreement between both modalities. This is supported qualitatively by figures 2.6d, e, k and l.

For both CFD and PIV, the mean difference, standard deviation, RMSE, mean and median angle for the pulsatile experiment were smaller than for the steady experiments, suggesting better correspondence between the pulsatile measurements than between the steady measurements. However, considering the Bland-Altman plots of systole and diastole in figure 2.9a and 2.13a, the differences and standard deviations in systole were larger, whereas the differences and standard deviations in diastole were smaller than those of the steady measurements. This indicates that the error scales with the input velocity. Since the duration of systole is shorter than the duration of diastole, more cardiac phases will produce a relatively small error compared to the steady measurements. When the error is subsequently averaged over the heart cycle, the error will be smallest in the pulsatile measurement.

In all cases small significant velocity differences remained between PC-MRI and CFD and PIV. In systole the systematic deviations were largest indicating that the discrepancies between the modalities depend on the velocity magnitude. These discrepancies can be attributed to several limitations of the present study. The fact that the geometry of the phantom for CFD was measured with 3D-RA, whereas the geometry for the PC-MRI was obtained by segmentation of the FFE images, may have introduced a small bias. A second limitation is that small inaccuracies in the measured PC-MRI velocity in the inflow vessel used for the inflow boundary conditions propagates in the velocity values simulated by CFD in the phantom. This may explain the lower mean velocity of CFD during systole in the pulsatile simulation.

The quantitative agreement between PIV and PC-MRI was somewhat less than that between CFD and PC-MRI. The Bland-Altman plot in figure 2.5a shows that differences can be as large as 30 cm/s when PC-MRI is compared with the scaled PIV velocities. This was mainly caused by the skewed inflow jet, as shown in figure 2.6b. Spatial restraints and slightly modified angles of inlet and outlet ports may have caused this difference. The skewed inflow jet led to differences in velocity magnitude and caused flow properties to develop slightly different, as can be seen by the earlier development of the small vortex in figure 2.6b at arrow 2 and the higher velocity in the middle of the phantom in figure 2.6b at arrow 3, in contrast to the low PC-MRI velocity at arrow 3 in figure 2.6g. When vortices occurred at different locations in the
phantom for PIV and PC-MRI, relatively large velocity vector angle differences were found as well. This explains the wide distribution of the velocity vector angle difference in figure 2.5b.

Another limitation in the PIV setup was that blood mimicking fluid was used, whereas water was used in the PC-MRI measurement. The blood mimicking fluid was also tested in the PC-MRI measurement but led to ghosting artifacts, possibly due to the high velocities and the accompanying imperfect synchronization of the PC-MRI acquisition with the pulses of the pump. Therefore, scaling of the results measured with PIV was necessary which may have introduced bias. A third limitation of the PIV study was discussed by Ford et al. [41] who showed that flow is difficult to measure close to the wall of the phantom. The discontinuity in the flow field as seen in 2.10b at arrow 6 is the result of a non-perfect refractive index match. In that region, one of the outflow vessels was attached to the lumen during fabrication. Cooling of the glass induced stress and a non-uniform refractive index. A thin reflection remained visible in the PIV images at the joint, which invalidated flow measurements locally.

Our results cannot be straightforwardly extrapolated to the clinic since our MRI setup is not suited for patients. The steady measurement has however a scan time that is acceptable in the clinic and if adequate MRI hardware is available this measurement can be translated to the in vivo situation. Furthermore, PC-MRI measurements of lower spatial and temporal resolutions and lower SNR can still provide valuable information about flow patterns in intracranial aneurysms. We indeed noticed that the in vivo PC-MRI measurement performed in the same patient showed similar flow patterns as observed in the phantom, see Chapter 5. Patient-specific CFD is needed to further validate these measurements, see Chapter 4.

In conclusion, these results show that high resolution time-resolved 3D PC-MRI can accurately capture complex flow patterns in an intracranial aneurysm phantom. Remaining differences between PC-MRI and other modalities are mainly attributed to small differences in the inflow conditions that are difficult to avoid in experimental setups.

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### 2.6 References


Complex flow patterns in a real-size intracranial aneurysm phantom: phase contrast magnetic resonance imaging compared with particle image velocimetry and computational fluid dynamics.


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