Phase contrast MRI in intracranial aneurysms
van Ooij, P.

Citation for published version (APA):
van Ooij, P. (2012). Phase contrast MRI in intracranial aneurysms
Three-dimensional phase contrast MRI at 3T in intracranial aneurysms compared with patient-specific computational fluid dynamics

Pim van Ooij, Joppe Schneiders, Henk Marquering, Charles Majoie, Ed van Bavel, Aart Nederveen

Submitted for AJNR American Journal of Neuroradiology
chapter 4

Abstract

Background and Purpose

CFD has been proven valuable for assessing blood flow in intracranial aneurysms, which may add to better rupture risk assessment. However, this technique suffers from several drawbacks such as long computation times, which may hinder its clinical implementation. 3D PC-MRI is an alternative technique that enables fast measurements of blood flow. The purpose of this study was to compare flow patterns based on 3D PC-MRI with CFD estimates.

Methods

Eight intracranial aneurysms were studied. 3D PC-MRI data was acquired at 3T with 0.8 mm isotropic resolution for 10 cardiac phases. Patient-specific inflow boundaries for CFD were measured with a separate 2D PC-MRI sequence at high temporal and spatial resolution. 3D PC-MRI and CFD were quantitatively compared by calculation of differences between velocity vector magnitudes and angles. Differences in flow patterns expressed
as the presence and strengths of vortices were determined by calculation of singular flow energy.

**Results**

In peak systole, flow features such as vortex patterns were similar. In end diastole, 3D PC-MRI measurements appeared inconsistent due to low velocity-to-noise ratios. The average relative difference in velocity magnitude was 73.6±56.7% in systole and 35.6±26.2% in diastole. For singular energy this was reduced to 21.9±16.3% and 21.2±19.7%, indicating better agreement between 3D PC-MRI and CFD when flow patterns are considered instead of velocity magnitude.

**Conclusion**

In systole, a good agreement between 3D PC-MRI and CFD on flow pattern visualization and singular energy calculation was found. However, in diastole flow patterns of 3D PC-MRI differed from those obtained from CFD due to low velocity-noise ratios.
Despite a decrease of case fatality of subarachnoid haemorrhage as a result of intracranial aneurysm rupture in recent years [1], this devastating event is lethal in one-third [2] to fifty percent [3] of the patients. Moreover, one-third of the surviving patients are disabled and need recovery treatment [2]. Treatment of incidentally found unruptured aneurysms consist of endovascular coiling or surgical clipping, with procedure-related morbidity and mortality rates slightly in favor of the former [4]. Since the risks of treatment potentially outweigh the risk of rupture [5], treatment decision should be based on as much available information on the individual aneurysm as possible. It is widely believed that intra-aneurysmal hemodynamics contribute substantially to rupture risk assessment and treatment planning assistance [6]. Many studies showed promising results when conducting assessment of risk factors such as intra-aneurysmal flow patterns and wall shear stress using patient-specific CFD [6-17]. A drawback of performing CFD is the difficulty in converting large numbers of patient-specific data into workable models [18]. Without patient-specific data for inflow and outflow boundary conditions, assumptions have to be made regarding heart rate and blood flow, the shape of the inlet velocity profile and flow division ratios in the outflow branches [19]. Further drawbacks are the need for large computational power and extensive calculation time. Despite these drawbacks, CFD has recently been used to associate intra-aneurysmal hemodynamics with rupture [7, 15, 18, 20].

The enormous advancements in MRI technology in the past decade now allow direct measurement of intra-aneurysmal flow, using time-resolved 3D PC-MRI (3D PC-MRI) [21-23]. This technique has been proven useful in large vessels such as the aorta [24-28] and the carotid arteries [29-30]. 3D PC-MRI was also used in intracranial aneurysms [31-36] with promising results. Moreover, the technique was validated against CFD in an up-scaled model at 1.5T [37] and at 3T in a real-size phantom [38]. However, clinical application of 3D PC-MRI in intracranial aneurysms is complicated by the requirements for high resolution, high SNR and realistic scanning times. In this study, a 3D PC-MRI sequence with a scan duration of approximately 10 minutes, and therefore clinically feasible, was applied to eight intracranial aneurysms. The results were compared with patient-specific CFD in which spatial and temporal boundary conditions obtained from a separate time-resolved 2D PC-MRI (2D PC-MRI) acquisition were applied. The purpose of
this study was to assess if the results of 3D PC-MRI and patient-specific CFD are comparable and if 3D PC-MRI is able to measure important quantitative and qualitative features of intra-aneurysmal flow.

4.2 Materials & Methods

4.2.1 Population

The study was approved by the local medical ethics committee. All patients supplied written informed consent. Age of the patients ranged between 44-65 years. Five patients were female, 3 patients were male. Locations and size of the aneurysms were determined on a 3D TOF MRA sequence and are listed in table 4.1.

4.2.2 MR imaging

The protocol consisted of three MRI sequences that were conducted on a 3T scanner (Intera, Philips Healthcare, Best, The Netherlands) using an 8-channel head coil.

First, a high resolution 3D TOF MRA sequence was performed with a scan resolution of 0.39 mm x 0.6 mm x 1 mm, interpolated to 0.39 mm x 0.39 mm x 0.5 mm. Imaging parameters were: TE / TR / FA: 4.2 ms / 21.4 ms / 20°; Field of view: 200 mm x 200 mm x 92 mm; parallel imaging factor: 2.5; scan time: 6.16 min.

Second, to acquire 2D PC-MRI data that served as inflow boundary conditions for CFD, a slice was placed perpendicular to the parent artery proximal to the aneurysm. The acquisition was retrospectively gated using

<table>
<thead>
<tr>
<th>Aneurysm Location</th>
<th>Size (mm, length x width x height)</th>
<th>Isotropic voxel size 3DRA (mm³)</th>
<th>Mesh volume (mm³)</th>
<th>Number of mesh Elements</th>
<th>Element density (elements / mm³)</th>
<th>Input flow (mL/s)</th>
<th>2D PC-MRI</th>
<th>3D PC-MRI</th>
</tr>
</thead>
<tbody>
<tr>
<td>1 Left MCA</td>
<td>13.1 x 7.6 x 8.1</td>
<td>0.22</td>
<td>554</td>
<td>1,765,310</td>
<td>1.6</td>
<td>3.0</td>
<td></td>
<td></td>
</tr>
<tr>
<td>2 BA</td>
<td>8.7 x 6.3 x 7.4</td>
<td>0.22</td>
<td>272</td>
<td>1,422,476</td>
<td>2.2</td>
<td>2.4</td>
<td></td>
<td></td>
</tr>
<tr>
<td>3 Right MCA</td>
<td>14.7 x 8.1 x 9.6</td>
<td>0.25</td>
<td>732</td>
<td>2,608,270</td>
<td>3.1</td>
<td>4.3</td>
<td></td>
<td></td>
</tr>
<tr>
<td>4 Right MCA</td>
<td>7.2 x 5.4 x 6.3</td>
<td>0.10</td>
<td>261</td>
<td>1,467,689</td>
<td>2.0</td>
<td>2.7</td>
<td></td>
<td></td>
</tr>
<tr>
<td>5 Right MCA</td>
<td>10.3 x 5.5 x 6.1</td>
<td>0.17</td>
<td>260</td>
<td>1,168,002</td>
<td>1.9</td>
<td>3.2</td>
<td></td>
<td></td>
</tr>
<tr>
<td>6 BA</td>
<td>9.8 x 8.6 x 12.5</td>
<td>0.22</td>
<td>588</td>
<td>2,315,099</td>
<td>2.0</td>
<td>2.7</td>
<td></td>
<td></td>
</tr>
<tr>
<td>7 Left MCA</td>
<td>12.1 x 9.3 x 10.1</td>
<td>0.22</td>
<td>674</td>
<td>2,238,552</td>
<td>3.3</td>
<td>2.9</td>
<td></td>
<td></td>
</tr>
<tr>
<td>8 BA</td>
<td>9.4 x 9.0 x 11.5</td>
<td>0.22</td>
<td>687</td>
<td>2,559,296</td>
<td>2.6</td>
<td>3.6</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Table 4.1 Locations and size of the aneurysms; voxel size of the 3D-RA datasets; volumes, number of elements, element density of the meshes and input flows measured by 2D and 3D PC-MRI.
either ECG or PPU. Scan resolution was 0.64 mm x 0.65 mm x 3 mm. Further imaging parameters: TE / TR / FA: 5.7 ms / 8.5 ms / 10°; Field of view: 200 mm x 200 mm x 3 mm in one slice; parallel imaging factor: 2; for aneurysm 5 the VENC was 70 cm/s in all directions, for the others 100 cm/s in all directions. To keep the scan time close to 3 minutes and 30 seconds, the number of measured cardiac phases, i.e. temporal resolution, depended on heart rate and ranged between 23-36 cardiac phases. The view sharing factor for the retrospective sorting of acquired k-lines was set to 1.8 [39].

Third, the 3D PC-MRI acquisition was retrospectively gated using either ECG or PPU at an acquired resolution of 0.8 mm x 0.8 mm x 0.8 mm. Further imaging parameters: TE / TR / FA: 3.0 ms/ 5.8 ms/ 15°; Field of view: 200 mm x 200 mm x 20 mm in 25 transversal slices; parallel imaging factor of 3; the velocity encoding was 70 cm/s in all directions for aneurysm 5 and 100 cm/s in all directions for the others; scan time: 10.22 min at 60 beats/min. The number of acquired cardiac phases was 10.

For aneurysm 1, the 2D PC-MRI measurement was performed 9 months later than the 3D PC-MRI measurement, due to a failed initial attempt to acquire the 2D PC-MRI sequence.

### 4.2.3 MRI Postprocessing

Phase images were corrected for background phase offset errors by subtracting the average phase in a static region of interest near the aneurysm. Phase correction was performed for every velocity encoding direction and cardiac phase individually [40]. The segmentation of the vessel and aneurysms was performed with the use of a level set evolution algorithm [41] applied in the magnitude images of one of the complex phase contrast datasets, further referred to as the phase contrast magnitude images. This was done for every cardiac phase separately. Velocity values in pixels that were located outside the segmentation or suffered from partial voluming were set to zero. Pixels in the regions of interest that suffered from velocity aliasing were manually corrected in all three directions. The cardiac cycles were reordered such that the systolic phase occurred at the end of the cardiac cycle. These post-processing steps were performed with custom-built software in Matlab (Mathworks, Natick, MA, USA) and took about 4 hours to conduct. To calculate the flow ratios of the outflow branches, the data was imported into GTFlow (Gyrotools, Zürich, Switzerland).
The geometric vascular models used for CFD simulations were created from 3D-RA. Images were acquired with a single-plane angiographic unit (Integris Allura Neuro, Philips Healthcare, Best, The Netherlands). Contrast agent consisting of 320 mg I/mL of iodixanol (Visipaque, GE Healthcare, Cork, Ireland) was injected through a 6F catheter positioned in the ICA or VA. One hundred images were acquired during a 240° rotational run in 8 seconds with 15-21 mL of contrast agent at 3 mL/s. A 256 x 256 x 256 matrix image of the region of interest was reconstructed on a dedicated workstation. The resolution of the images of the individual aneurysms is given in table 4.1.

These images were imported into VMTK [42]. With the use of a level set algorithm, isosurfaces were created which were subsequently meshed using an average edge length of 0.1 mm, with a minimum of 0.1 μm and maximum 0.4 mm.

Meshes were created consisting of 1.168.002 to 2.608.270 tetrahedral elements with a mesh density of at least 3000 elements per cubic millimeter, in accordance with other studies [6, 43]. The sizes of the meshes are listed in table 4.1. All CFD simulations were performed in FLUENT 6.3 (ANSYS, Canonsburg, PA, USA). Blood density was set to 1060 kg/m$^3$, dynamic viscosity to 0.004 kg/m/s. The pipeline for imposing velocity inlet boundary conditions in the CFD simulations is visualized in figure 4.1. First, the aneurysm in the TOF MRA measurement and the proximal vessel in the 2D PC-MRI slice were manually selected (figure 4.1a). Subsequently, the 2D PC-MRI data was positioned on the TOF MRA data using rotation and translation matrices extracted from DICOM headers (figure 4.1b). The CFD mesh was constructed (figure. 4.1c) and a rigid registration of the TOF MRA measurement on the CFD mesh was conducted in FLIRT [44] (figure 4.1d). The velocities measured with 2D PC-MRI were rotated and translated likewise and interpolated onto the nodes of the CFD inflow boundary (figure 4.1e). The interpolated velocity vectors are shown in figure 4.1f. The velocity at the nodes at the edge of the vessel was set to zero. Steps E and F were performed for every measured cardiac phase in 2D PC-MRI. These steps were performed with custom-built software in Matlab (Mathworks, Natick, MA, USA).

CFD iterations were continued until the residual of the continuity equation was below 0.001. The CFD estimates were resolved at fixed time intervals equal to the measured RR interval divided by the number of cardiac phases used for the 2D PC-MRI measurement. Three heart cycles were sim-
ulated to eliminate transient effects. The third of these cycles was used in the comparison with the 3D PC-MRI results.

Flow through the outflow vessels of the CFD model was prescribed according to outflow measurements at every cardiac phase of the 3D PC-MRI data averaged over time. If an outflow vessel was too small to quantify flow, a combination of measured flow and Murray’s law [45] was applied. The average simulation time was 36 hours per aneurysm.

4.2.5 Data quantification and visualization

Calculations of the SNR of the phase contrast magnitude images at peak systole and end diastole of the 3D PC-MRI measurements were performed as described by Plein et al. [46], see Chapter 5 or Chapter 6. As region of interest for the SNR calculation, the total aneurysm with inflow and outflow vessels was taken. VNR equals the product of SNR and velocity divided by VENC. VNR is not calculated separately.

During postprocessing, the number of cardiac phases of CFD was reduced to equal the number of cardiac phases of the 3D PC-MRI measurement.

To quantify differences between 3D PC-MRI and CFD, the CFD data were registered and linearly interpolated to the 3D PC-MRI data. To take aneurysm pulsatility in the 3D PC-MRI data into account, registration was conducted for every cardiac phase separately. Peak systole and end diastole were defined as the cardiac phase where the spatially averaged velocity magnitude was maximal and minimal, respectively.

Further comparison consisted of visualization of the location and quantification of magnitude of vortices, by calculation of singular energy of the intra-aneurysmal flow [47], see Chapter 7. The technique used in the current study extends the original 2D approach to 3D by including the singular energy for the transverse, sagittal and coronal 2D slices. The singular energy was calculated according to:

$$E_x(x, \sigma) = \lambda^1(x, \sigma) + \lambda^2(x, \sigma)$$  \hspace{1cm} (4.1)
where \( x \) is the location in the flow field, \( \sigma \) is the scale, \( \hat{A}_v \) and \( \hat{A}_s \) are the normalized dimensionless projection coefficients describing vortices and sinks and sources respectively:

\[
\hat{A}_v(x, \sigma) = \frac{F(x) \otimes \phi_v(x, \sigma)}{\hat{A}(x, \sigma)}
\]

(4.2)

and

\[
\hat{A}_s(x, \sigma) = \frac{F(x) \otimes \phi_s(x, \sigma)}{\hat{A}(x, \sigma)}
\]

(4.3)

where \( F \) is the flow-field, \( \phi_v \) and \( \phi_s \) are basis flow functions representing regional and scale dependent vortex flow and sinks and sources respectively [48]. \( \hat{A} \) represents the magnitude of the laminar flow and is determined by:

\[
\hat{A}(x, \sigma) = F(x) \otimes \phi(x, \sigma)
\]

(4.4)

A scale \( \sigma \) of 4 voxels (3.2 mm) was used. All quantification and visualization was performed with custom-built software in Matlab (Mathworks, Natick, MA, USA). Pathline images were created and flow quantification in the inflow vessel of the 2D and 3D PC-MRI was performed in GTFlow (Gyrotools, Zurich, Switzerland). The input flow values for the aneurysms are given in table 4.1.

### 4.2.6 Statistics

The difference in velocity magnitude and singular energy between CFD and 3D PC-MRI was determined for every voxel and subsequently averaged over space to yield a mean paired difference (MDif) at every cardiac phase:

\[
MDif = \frac{\sum_{i=1}^{N} (MRI_{i} - CFD_{i})}{N}
\]

(4.5)

where \( N \) is the number of voxels. The standard deviation of the paired difference (SDif) was calculated as well. Its significance was tested with a paired t-test; \( p < 0.05 \) was considered statistically significantly different. A relative difference in velocity magnitude between both methods was based on the mean CFD velocity magnitude per subject:
Differences in flow direction were calculated from the angle difference between corresponding velocity vectors. Since these differences are positive by definition, median rather than mean values were calculated. Bland-Altman plots for the velocity magnitude and singular energy at systole and diastole were created.

\[ RD_{if} = \frac{MD_{if}}{\sum_{CFD_i}} \]  \hspace{1cm} (4.6)

4.3 Results

The averaged SNR of the 3D PC-MRI velocity measurements of all aneurysms was 13.5±2.2 in peak systole and 10.6±1.9 in end diastole.

Figure 4.2 shows intra-aneurysmal flow patterns in the aneurysms. In systole, the circular motion in the vortices and the direction of inflow jets was qualitatively similar for both methods. This can further be appreciated from the pathlines in figure 4.3. In figure 4.2, in systole the maximum inflow jet velocity magnitude of aneurysm 1 and 4 was almost two times lower in CFD than in 3D PC-MRI. In diastole, the vortices of the 3D PC-MRI measurement appeared disrupted and irregular in most aneurysms.

For most aneurysms, the 3D PC-MRI measurements resulted in higher velocity magnitude values than CFD (MDif in table 4.2). This is a result of the higher velocities in the inflow vessel in 3D PC-MRI than in 2D PC-MRI (table 4.1). These differences were most prominent in systole, as can be seen in the spatially averaged velocity magnitude curve displayed in 4.4. In most cases, the SDif and the RDif were higher in systole than in diastole and differences in estimated local flow direction were found primarily in diastole, see table 4.2.
Three-dimensional phase contrast MRI at 3T in intracranial aneurysms compared with patient-specific computational fluid dynamics.
In figure 4.5, the locations with singular energy magnitude higher than half the maximum are displayed for four aneurysms. For aneurysm 2 and 3 the locations and magnitudes of the maximum singular energy were similar. For aneurysms 8, the vortex center location was different for 3D PC-MRI and CFD, in agreement with the different intra-aneurysmal flow patterns that were shown in figure 4.2. For aneurysm 6 and 8, the magnitude of the singular energy was twice as low for CFD.

RDif averaged over all aneurysms in systole was a factor three smaller for singular energy than for velocity magnitude. Better correspondence in singular energy than in velocity magnitude in systole can also be observed in the Bland-Altman plots in figure 4.6.

<table>
<thead>
<tr>
<th>Aneurysm</th>
<th>MDif (cm/s)</th>
<th>SDif (cm/s)</th>
<th>RDif (%)</th>
<th>Median angle (°)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Diastole</td>
<td>Diastole</td>
<td>Systole</td>
<td>Systole</td>
</tr>
<tr>
<td>1</td>
<td>21.1*</td>
<td>2.0*</td>
<td>12.7</td>
<td>6.3</td>
</tr>
<tr>
<td>2</td>
<td>0.2</td>
<td>0.0</td>
<td>17.1</td>
<td>8.5</td>
</tr>
<tr>
<td>3</td>
<td>9.2*</td>
<td>5.2*</td>
<td>18.0</td>
<td>9.6</td>
</tr>
<tr>
<td>4</td>
<td>19.5*</td>
<td>4.9*</td>
<td>17.9</td>
<td>10.2</td>
</tr>
<tr>
<td>5</td>
<td>10.4*</td>
<td>2.8*</td>
<td>20.0</td>
<td>11.9</td>
</tr>
<tr>
<td>6</td>
<td>4.8*</td>
<td>4.8*</td>
<td>14.2</td>
<td>12.2</td>
</tr>
<tr>
<td>7</td>
<td>14.7*</td>
<td>7.4*</td>
<td>13.1</td>
<td>11.1</td>
</tr>
<tr>
<td>8</td>
<td>10.9*</td>
<td>5.0*</td>
<td>19.8</td>
<td>13.0</td>
</tr>
<tr>
<td>Average</td>
<td>11.4±7.0</td>
<td>4.0±2.3</td>
<td>16.6±2.9</td>
<td>10.4±2.2</td>
</tr>
</tbody>
</table>

Table 4.2 Differences between velocity fields as determined with 3D PC-MRI and CFD. Indicated are MDif and SDif, RDif and the median angle, as determined on a voxel basis and averaged over the whole aneurysm and connecting vessels, between 3D PC-MRI and CFD. * indicates significant difference.

Validation
Table 4.3 Differences between singular energy fields as determined with 3D PC-MRI and CFD. Indicated are MDif, SDif, and RDif as determined on a voxel basis and averaged over the whole aneurysm and connecting vessels, between 3D PC-MRI and CFD. * indicates significant difference.

<table>
<thead>
<tr>
<th>Aneurysm</th>
<th>MDif</th>
<th>SDif</th>
<th>RDif (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Systole</td>
<td>Diastole</td>
<td>Systole</td>
</tr>
<tr>
<td>1</td>
<td>0.02</td>
<td>-0.05*</td>
<td>0.66</td>
</tr>
<tr>
<td>2</td>
<td>0.02</td>
<td>0.01</td>
<td>0.64</td>
</tr>
<tr>
<td>3</td>
<td>-0.08*</td>
<td>-0.11*</td>
<td>0.83</td>
</tr>
<tr>
<td>4</td>
<td>0.16*</td>
<td>0.30*</td>
<td>0.60</td>
</tr>
<tr>
<td>5</td>
<td>-0.39*</td>
<td>-0.13*</td>
<td>1.43</td>
</tr>
<tr>
<td>6</td>
<td>-0.31*</td>
<td>0.08*</td>
<td>0.97</td>
</tr>
<tr>
<td>7</td>
<td>0.33*</td>
<td>0.41*</td>
<td>0.85</td>
</tr>
<tr>
<td>8</td>
<td>0.33*</td>
<td>0.26*</td>
<td>1.13</td>
</tr>
<tr>
<td>avg</td>
<td>0.01±0.27</td>
<td>0.10±0.20</td>
<td>0.89±0.28</td>
</tr>
</tbody>
</table>
4.4 Discussion

In this study, both 3D PC-MRI and CFD were applied in eight intracranial aneurysms. In systole, the results showed good qualitative agreement for complex flow properties such as inflow jet behavior and vortical flow patterns. In diastole the estimated intra-aneurysmal flow patterns were irregular due to decreased velocity to noise ratio in the 3D PC-MRI measurements. Quantitative differences in velocity magnitude were observed in both systole and diastole. Vortex quantification based on singular energy calculation demonstrated similar vortical flow behavior in flow patterns measured with 3D PC-MRI and simulated with CFD. In systole the vortex-related singular energy showed better quantitative agreement than the velocity magnitude and directions.

Studies comparing 3D PC-MRI with CFD on a voxel-by-voxel basis in aneurysms at 3T are not available in the literature. One study compared 3D PC-MRI with CFD in the aorta [49], and one study in five intracranial aneurysms on 1.5T at relatively low spatial resolution [35]. Both studies found a good qualitative agreement between both techniques and a moderate quantitative agreement.

The need for reliable patient-specific CFD simulations has been described by many authors. However, the prescription of inflow boundary conditions that produce accurate CFD results is still a matter of debate. Several studies used flow rates that were measured with 2D PC-MRI in separate volunteers as inflow boundary conditions in CFD. Based on these reference data and using the Womersley solution, fully developed velocity profiles are then created and subsequently scaled by the area of the inflow vessel to obtain a mean wall shear stress of 15 dyne/cm² [15, 20, 50]. Other studies applied uniform velocities on extended inflow vessels [36, 51]. Spatial and temporal velocity vector values as measured with 3D PC-MRI at each node of the inflow boundary have been applied at low resolution in only two studies [35, 49]. These last two studies used inflow boundary conditions obtained from the same imaging sequence that they wish to validate. Furthermore, 3D PC-MRI needs to cover the entire head in anterior-posterior and right-left direction to avoid fold-over and thus has limited spatial and temporal resolution compared to a 2D acquisition. Therefore, in the current study, spatial and temporal velocity vectors from a separate 2D PC-MRI acquisition were applied as inflow boundary conditions for the CFD simulations.
The singular energy measure as presented in this study is introduced to facilitate the comparison between 3D PC-MRI and CFD. Singular energy provides a quantitative measure of flow patterns. It is unclear if it may lead to more insight in the nature of the aneurysm with respect to rupture, as has been discussed in the literature recently [52-53]. While this is an intriguing possibility, it was not the purpose of the current work to address the predictive value of this quantity.

While flow patterns between 3D PC-MRI and CFD agreed qualitatively, a mismatch in velocity magnitude between CFD and 3D PC-MRI was encountered. This mismatch can mainly be attributed to a discrepancy between the total inflows measured by 3D and 2D PC-MRI, where boundary conditions were based on the latter. On average the 3D PC-MRI measurements resulted in 50% higher flow estimates than the 2D PC-MRI ones. Discrepancies between flow measurements from 2D and 3D PC-MRI (±18%) [24] or 2D and endovascular sonography (±15%) [54] have been reported in the literature earlier. Wentland et al. concluded that flow measurements in healthy volunteers in the renal vasculature revealed that 3D measurements tended to be more internally consistent than 2D measurements [55]. This difference may increase when small intracranial arteries are considered. One cause of the difference may be variation of the actual flows between the scans. The 3D PC-MRI was always performed first, followed by the 2D PC-MRI, and some adaptation of flow might have occurred during the scanning session. Yet, cerebral flow is strongly autoregulated and it seems therefore rather unlikely that such flow variations would lead to 50% differences. Alternatively, the calculated inflows for either 2D or 3D PC-MRI might systematically deviate from the true one. Without a ground truth, it is difficult to deduct which of the two methods causes this systematic difference. Possibly, the relatively large thickness (3 mm) of the 2D PC-MRI slice compared to the 3D measurement (0.8 mm) induces averaging of measured velocities resulting in underestimation of flow.

The inflow boundary of the angiographic mesh used for CFD contains more points than the vessel area of the 2D PC-MRI contains pixels. The required upsampling of the measured velocity information to the inflow boundary could result in lower velocity inflow boundary conditions.

To study the influence of the inflow boundary conditions, a second series of simulations was performed with inflow boundary conditions obtained from 3D rather than 2D PC-MRI. Six simulations were performed, in two
cases the inflow of the CFD mesh was located outside the FOV of the 3D PC-MRI sequence. We have included these results in the supplement. This reduces the systematic differences in local velocity 5-fold for MDif and a factor 2.5 for RDif. Random differences (SDif) were similar for both inflow boundary conditions. The results for the singular energy and the median angle did not change significantly. We therefore conclude that different inflow boundary conditions have a large influence on magnitude of velocity values. However, velocity vector directions and locations and magnitude of vortices are fairly independent on inflow boundary conditions.

Another limitation is the semi-automatic segmentation of the 3D-RA dataset, resulting in possible under- or overestimation of neck width [56]. Also limitations with regard to the 3D PC-MRI setup may contribute to the found discrepancies between both techniques. In our study SNR values within aneurysms were relatively low due to small voxel sizes and the use of parallel imaging [57]. Therefore, at low velocities during diastole, the velocity may be overestimated due to noise. It is clear that more accurate estimation of intracranial aneurysm hemodynamics from 3D PC-MRI requires improved technology. With improvements in acquisition techniques such as varying velocity [58] or dual VENC encoding [59], sufficient velocity-to-noise ratio may be obtained in diastole. Furthermore, with acceleration techniques such as radial undersampling [31] and compressed sensing [60], scan times of 3D PC-MRI may be shortened in the near future. Higher field strengths can improve SNR [61]. One last recently developed promising technique to improve 3D PC-MRI measurement is divergence-reduction processing [62].

4.5 Conclusion

In this study, high resolution 3D PC-MRI was compared with patient-specific CFD on a voxel-by-voxel basis in eight aneurysms. In peak systole, qualitative similarities in flow features such as vortical flow patterns and inflow behavior were evident. In end diastole, the flow patterns of the 3D PC-MRI measurements were different compared to those generated with CFD due to low velocity-to-noise ratio of the 3D PC-MRI measurements. Singular energy calculation revealed quantitative agreement between 3D PC-MRI and CFD in systole.
4.6 Acknowledgements

This work was supported by a grant from the Nuts Ohra Foundation, the Netherlands. A research grant for research into the role of hemodynamics in the rupture risk assessment of intracranial aneurysms.

4.7 References


Three-dimensional phase contrast MRI at 3T in intracranial aneurysms compared with patient-specific computational fluid dynamics.


In this supplement we present the results of the CFD simulations in six aneurysms with spatial inflow boundary conditions obtained from 3D PC-MRI. In Table 4.S1 the differences between velocity fields are given. In Table 4.S2 the differences between singular energy are given. In Figure 4.S1 the velocity vector fields are displayed, in Figure 4.S2 the singular energy in three aneurysms.

### Table 4.S1 Differences between velocity fields as determined with 3D PC-MRI and CFD. Indicated are MDif and SDif, RDif and the median angle, as determined on a voxel basis and averaged over the whole aneurysm and connecting vessels, between 3D PC-MRI and CFD. * indicates significant difference.

<table>
<thead>
<tr>
<th>Aneurysm</th>
<th>MDif (cm/s) Systole</th>
<th>Diastole</th>
<th>SDif (cm/s) Systole</th>
<th>Diastole</th>
<th>RDif (%) Systole</th>
<th>Diastole</th>
<th>Median angle (°) Systole</th>
<th>Diastole</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>1.9*</td>
<td>-4.2*</td>
<td>17.0</td>
<td>8.1</td>
<td>6.0</td>
<td>23.9</td>
<td>20.8</td>
<td>27.8</td>
</tr>
<tr>
<td>2</td>
<td>-7.8*</td>
<td>-4.3*</td>
<td>16.5</td>
<td>9.9</td>
<td>18.7</td>
<td>20.8</td>
<td>17.8</td>
<td>25.5</td>
</tr>
<tr>
<td>3</td>
<td>9.2*</td>
<td>1.6*</td>
<td>17.8</td>
<td>12.0</td>
<td>61.4</td>
<td>13.7</td>
<td>33.3</td>
<td>50.7</td>
</tr>
<tr>
<td>4</td>
<td>-3.7*</td>
<td>-2.6*</td>
<td>26.3</td>
<td>12.8</td>
<td>8.7</td>
<td>11.5</td>
<td>24.0</td>
<td>31.0</td>
</tr>
<tr>
<td>5</td>
<td>3.5*</td>
<td>0.7*</td>
<td>19.3</td>
<td>11.9</td>
<td>10.8</td>
<td>3.5</td>
<td>22.0</td>
<td>27.5</td>
</tr>
<tr>
<td>6</td>
<td>-</td>
<td>-</td>
<td>-</td>
<td>-</td>
<td>-</td>
<td>-</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td>7</td>
<td>9.1*</td>
<td>4.0*</td>
<td>16.9</td>
<td>13.4</td>
<td>56.0</td>
<td>32.2</td>
<td>37.3</td>
<td>49.1</td>
</tr>
<tr>
<td>8</td>
<td>-</td>
<td>-</td>
<td>-</td>
<td>-</td>
<td>-</td>
<td>-</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td>average</td>
<td>2.0±6.8</td>
<td>-0.8±3.4</td>
<td>19.0±3.7</td>
<td>11.4±2.0</td>
<td>26.9±25.0</td>
<td>17.6±10.1</td>
<td>25.9±7.7</td>
<td>35.3±11.5</td>
</tr>
</tbody>
</table>

### Table 4.S2 Differences between singular energy fields as determined with 3D PC-MRI and CFD. Indicated are MDif, SDif and RDif as determined on a voxel basis and averaged over the whole aneurysm and connecting vessels, between 3D PC-MRI and CFD. * indicates significant difference.

<table>
<thead>
<tr>
<th>Aneurysm</th>
<th>MDif (cm/s) Systole</th>
<th>Diastole</th>
<th>SDif (cm/s) Systole</th>
<th>Diastole</th>
<th>RDif (%) Systole</th>
<th>Diastole</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>0.00</td>
<td>-0.09*</td>
<td>0.67</td>
<td>0.74</td>
<td>0.1</td>
<td>7.2</td>
</tr>
<tr>
<td>2</td>
<td>-0.34*</td>
<td>-0.06</td>
<td>1.17</td>
<td>0.95</td>
<td>21.1</td>
<td>4.9</td>
</tr>
<tr>
<td>3</td>
<td>-0.17*</td>
<td>-0.22*</td>
<td>0.93</td>
<td>1.41</td>
<td>15.3</td>
<td>18.2</td>
</tr>
<tr>
<td>4</td>
<td>0.18*</td>
<td>0.32*</td>
<td>0.51</td>
<td>1.38</td>
<td>29.6</td>
<td>47.6</td>
</tr>
<tr>
<td>5</td>
<td>-0.32*</td>
<td>-0.18*</td>
<td>0.94</td>
<td>0.97</td>
<td>28.5</td>
<td>17.4</td>
</tr>
<tr>
<td>6</td>
<td>-</td>
<td>-</td>
<td>-</td>
<td>-</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td>7</td>
<td>0.24*</td>
<td>0.35*</td>
<td>0.86</td>
<td>1.11</td>
<td>20.2</td>
<td>39.6</td>
</tr>
<tr>
<td>8</td>
<td>-</td>
<td>-</td>
<td>-</td>
<td>-</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td>average</td>
<td>-0.07±0.25</td>
<td>0.02±0.25</td>
<td>0.85±0.23</td>
<td>1.06±0.23</td>
<td>20.6±11.5</td>
<td>22.5±17.4</td>
</tr>
</tbody>
</table>
Figure 4.S1 Velocity vector images in a characteristic slice depicting the main vortex in the six aneurysms and inflow jet in most aneurysms. The images depict the aneurysms at peak systole and diastole in isosurfaces (gray) for 3D PC-MRI and CFD with inflow boundary conditions obtained from 3D PC-MRI.

Figure 4.S2 Singular energy magnitude and location at peak systole in aneurysm volumes (gray) of aneurysm 1, 2, and 3 for 3D PC-MRI (top row) and CFD with inflow boundary conditions obtained from 3D PC-MRI (bottom row). For visualization purposes only the areas with singular energy above half the maximum value are indicated.