Phase contrast MRI in intracranial aneurysms
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General Introduction
Intracranial aneurysms

Intracranial or cerebral aneurysms are outpouchings of intracranial arteries that occur mainly on bifurcations in the vicinity of the Circle of Willis, a ring-like vessel structure at the base of the brain. The majority of intracranial aneurysms occur on the posterior communicating artery, anterior communicating artery and the middle cerebral artery, see figure 1.1. Rupture of intracranial aneurysms causes subarachnoid hemorrhage, which has a high case fatality rate. Since the majority of unruptured aneurysms do not inflict any symptoms on patients, patients are mostly treated after rupture. As the use of MRI and other imaging techniques increases, unruptured aneurysms are discovered more frequently.

Treatment of ruptured and unruptured aneurysms consists of clipping and coiling. In the clipping procedure, craniotomy is performed to access the aneurysm and a clip is permanently placed across the neck of the aneurysm, excluding it from circulation, see figure 1.2a. During coiling, a microcatheter is inserted in the femoral artery and, with the use of angiographic monitoring, advanced into the aneurysm. Detachable coils are then deployed to decrease the amount of blood flowing into the aneurysm and to induce thrombus formation, see figure 1.2b. Morbidity and mortality rates for clipping range from 4.0 to 10.9 percent and 1.1 to 3.0 percent respectively.
Morbidity and mortality rates for coiling range from 3.7 to 5.3 percent and 1.1 to 1.5 percent respectively [1]. Coiling is therefore preferred to clipping.

For both aforementioned interventions, the risk of treatment of incidentally detected unruptured aneurysms may outweigh the risk of rupture of the aneurysm, and therefore careful consideration whether to treat the aneurysm...
must be made. At the moment the consensus is that aneurysms of the ante-
rior circulation of more than 7 mm in size and those located in the posterior
circulation need treatment [2]. Unfortunately, aneurysms excluded from
potential treatment with these guidelines may be subject to rupture as well.
A better risk assessment would therefore allow a more optimal decision to
treat, potentially leading to lower morbidity and mortality and more efficient
health care.

There are several possibilities for improving rupture risk assessment.
Amongst these, assessment based on local hemodynamics is of particular
interest. This is based on the sensitivity of vascular cells for wall shear stress.
Such sensitivity is well documented for atherosclerosis, where high non-re-
versing flow is atheroprotective and low flow in combination with spatial
and temporal gradients is atheroprone [3-4]. For intracranial aneurysm
progression, hemodynamics have been suggested to have similar relevance.
In addition to wall shear stress distribution, information on several coupled
hemodynamic factors could help risk assessment. These include flow com-
plexity and stability, inflow jet concentration and impingement of flow on
the aneurysmal wall [5-6]. Other more recently developed flow character-
istics are kinetic energy, strain rate and viscous dissipation [7-8]. Yet, firm
evidence for their predictive value awaits improved methodology for their
measurement at sufficient temporal and spatial resolution in intracranial
aneurysms.

### 12 Blood Flow measurements in Intracranial arteries and aneurysms

Several techniques exist for measurement of intracranial vascular hemody-
namics. Transcranial Doppler (TCD) [9], a technique based on ultrasound,
is, depending on the experience of the clinician, an easy to use, quick and
inexpensive modality to measure the blood velocity in the intracranial
arteries located in the Circle of Willis. However, TCD merely measures the
maximal velocity of blood flow, and without knowledge of the diameter of the
vessels, the actual blood flow can not be determined. Furthermore, spatial
velocity profiles are not resolved in TCD. TCD is therefore well-suited for the
diagnosis of stenosis, but for hemodynamic measurements in intracranial
aneurysms TCD would not be helpful.
Another relatively recent developed technique based on ultrasound combining flow measurements and imaging of intracranial vessels is transcranial colour-coded duplex sonography (TCCS) [10]. TCCS allows 2-dimensional imaging of brain parenchyma and color-coded imaging of the vessels [11]. TCCS is well-suited for detecting intracerebral hemorrhages and vessel occlusions. However, the technique is not able to resolve three-dimensional flow patterns.

Ultrasound can also be used based on intravascular techniques. A few studies have applied this in intracranial vessels and aneurysms, using either flow wires [12] or combowires with combined Doppler and pressure sensors [13] [14]. A drawback of using a Doppler wire is that it, again, merely measures the maximal velocity of the blood flow in vessel field of interest and that spatial velocity profiles are not resolved. They could however serve to provide information on flow in the entrance and exit vessels.

With magnetic resonance imaging (MRI) it is possible to measure spatial velocity profiles and quantify blood flow in the intracranial arteries and aneurysms. This thesis will focus on time-resolved three-dimensional phase contrast MRI (PC-MRI).

1.3 Phase Contrast MRI

Phase contrast MRI is based on the phenomenon that the velocity of hydrogen nuclei (protons, hereafter called spins) in blood moving along a magnetic field gradient translates in the phase of the image. To this end, a velocity-encoding gradient, which comprises two lobes of equal area and opposite polarity, a so-called bipolar gradient [15], is added to a gradient echo sequence. Because the net area of the bipolar gradient is zero, it produces no net phase accumulation for stationary spins [16]. The bipolar gradient is shown in figure 1.3. Since the phase of gradient echo images is sensitive to $B_0$ inhomogeneities, a second acquisition is performed with an inverted bipolar gradient (toggling). By subtraction of the two images phase errors are minimized.
The phase difference obtained after subtraction of the two images is proportional to the velocity with which the blood is flowing:

$$\Delta \varphi = 2 \gamma G v \tau$$  \hspace{1cm} (1.1)$$

Where $\gamma$ is the gyromagnetic ratio, $G$ is the gradient strength, $\tau$ is the gradient duration and $v$ is the velocity. The combination of $G$ and $\tau$ determines the amount of velocity encoding; $2G\tau$ is often rewritten as $\Delta m$, the change in the gradient first moment between consecutive bipolar gradients. By increasing $\Delta m$ of the velocity encoding gradients i.e. lowering the velocity encoding settings (VENC), the sensitivity for low velocities can be increased. However, since phase can only be measured between $-\pi$ (corresponding to $-\text{VENC}$) and $\pi$ (corresponding to $+\text{VENC}$) velocities higher than VENC will fold into the image (phase wrapping or aliasing). It is therefore necessary to choose VENC carefully.

By adding bipolar gradients to the slice-selective, phase and read-out directions, a three-dimensional velocity vector can be measured in one slice (2D PC-MRI). By adding a second phase encoding to the slice-selective direction, velocity measurements can be performed in a three-dimensional volume. This sequence is called three-dimensional phase contrast, which will be referred to as PC-MRI throughout the thesis, except in Chapter 4 where it will be referred to as 3D PC-MRI to prevent confusion with 2D PC-MRI.

Since each of the velocity encoding gradients is toggled to compensate for $B_0$ inhomogeneities, PC-MRI comprises six acquisitions, called six-point encoding. However, six-point encoding can be simplified to four-point encoding if one common reference image is used for all directions. Still, scanning time of phase contrast MRI remains inherently long. The majority of
data in this thesis is acquired using a two-sided four point encoding scheme, which is schematically displayed in table 1.1. Some pilot data in the early stage of the project was acquired using an enhanced four point or Hadamard encoding scheme, as displayed in table 1.2.

### Table 1.1 Gradient first moments for two-sided four point encoding.

<table>
<thead>
<tr>
<th>scan nr.</th>
<th>x</th>
<th>y</th>
<th>z</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>Δm/2</td>
<td>Δm/2</td>
<td>Δm/2</td>
</tr>
<tr>
<td>2</td>
<td>-Δm/2</td>
<td>Δm/2</td>
<td>Δm/2</td>
</tr>
<tr>
<td>3</td>
<td>Δm/2</td>
<td>-Δm/2</td>
<td>Δm/2</td>
</tr>
<tr>
<td>4</td>
<td>Δm/2</td>
<td>Δm/2</td>
<td>-Δm/2</td>
</tr>
</tbody>
</table>

### Table 1.2 Gradient first moments for enhanced four point encoding.

<table>
<thead>
<tr>
<th>scan nr.</th>
<th>x</th>
<th>y</th>
<th>z</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>Δm/2</td>
<td>Δm/2</td>
<td>Δm/2</td>
</tr>
<tr>
<td>2</td>
<td>-Δm/2</td>
<td>-Δm/2</td>
<td>Δm/2</td>
</tr>
<tr>
<td>3</td>
<td>-Δm/2</td>
<td>Δm/2</td>
<td>-Δm/2</td>
</tr>
<tr>
<td>4</td>
<td>Δm/2</td>
<td>-Δm/2</td>
<td>-Δm/2</td>
</tr>
</tbody>
</table>

The Hadamard velocities are resolved using:

\[
2\varphi_x = (\rho_2 + \rho_1) - (\rho_1 + \rho_3) \quad (1.2a)
\]
\[
2\varphi_y = (\rho_2 + \rho_3) - (\rho_1 + \rho_3) \quad (1.2b)
\]
\[
2\varphi_z = (\rho_3 + \rho_1) - (\rho_1 + \rho_2) \quad (1.2c)
\]

where \(\rho_i\) denotes the accumulated phase in the \(i\)th acquisition. The advantage of Hadamard velocity encoding is slightly increased signal to noise ratio (SNR). However, phase wrapping occurs for velocities lower than VENC and affects other flow directions [17], making it difficult to resolve the phase wraps.

To be able to acquire temporal information, synchronization with the cardiac cycle is carried out by either prospectively or retrospectively gating the phase contrast measurement with an electrocardiogram (ECG) or a peripheral pulse unit (PPU).

A typical PC-MRI acquisition results in a series of magnitude and phase images, as shown in figure 1.4 for one slice and one cardiac phase.
In this thesis several aspects and applications of PC-MRI are studied. This thesis is divided in three parts: validation of PC-MRI, improvements of PC-MRI and estimation of wall shear stress based on PC-MRI.

1.3.1 Part I: Validation

To test if PC-MRI in intracranial aneurysms meets its requirements and performs well in a clinical setting, in vitro and vivo verification and validation is needed. In this thesis, PC-MRI is performed in vitro and compared with Particle Image Velocimetry (PIV) and Computational Fluid Dynamics (CFD). In vivo PC-MRI is compared with CFD.

Particle Image Velocimetry

PIV is an optical method used to measure instantaneous velocity fields of in vitro flow seeded with particles. These particles should be small enough to follow the fluid acceleration but large enough to scatter light sufficient to form bright images. In order to illuminate the flowing particles of micrometer size, a pulsed laser source is used. An optical camera rapidly records images of the illuminated particles which provide the measurements of the particle displacement [18]. Since PIV requires a transparent reproduction of an intracranial aneurysm it can not be applied directly to in vivo aneurysms.

Computational Fluid Dynamics

The current method of choice for estimation of flow patterns in individual aneurysms is CFD [19]. CFD is a technique that numerically solves the Navier-Stokes equation, which for incompressible fluid and constant viscosity is:

$$\frac{\partial \mathbf{u}}{\partial t} + (\mathbf{u} \cdot \nabla) \mathbf{u} = -\frac{1}{\rho} \nabla p + \nu \nabla^2 \mathbf{u} + \mathbf{g}$$  \hspace{1cm} (1.3)
where \( \mathbf{v} \) is the velocity, \( t \) is the time, \( \rho \) is the density, \( p \) is the pressure, \( \nu \) is the kinematic viscosity and \( g \) represents the gravitational acceleration constant. To perform such an approach in aneurysms, a few requirements need to be fulfilled. First, a patient-specific geometry of the aneurysm must be created. The geometry can be obtained from high resolution imaging data, e.g. three-dimensional rotational angiography (3D-RA), CT Angiography or contrast-enhanced magnetic resonance angiography (CE-MRA). Second, inflow boundary conditions are needed. In the majority of studies, these are not personalized but rather based on PC-MRI measurements in slices of intracranial vessels obtained in a few volunteers without aneurysms. Two ways of using these data have been described. First, based on these reference data and using the Womersley solution, fully developed velocity profiles are created and subsequently scaled by the area of the inflow vessel to obtain a mean wall shear stress of 15 dyne/cm\(^2\) [5, 7, 20]. Alternatively, uniform velocities on extended inflow vessels are applied [21-22]. These different inflow prescriptions in CFD would result in slightly different outcomes. However, in either case the non-personalized boundary flows may cause deviations from the true velocity profiles that may well be substantial. Disadvantages of CFD are that CFD requires mesh generation, which is often strenuous manual labor, and CFD suffers from long computation times. Another drawback is the need for assumptions such as rigid walls and non-Newtonian fluid properties. An important advantage of CFD is the ability to simulate blood flow patterns at high spatial and temporal resolution. Therefore, CFD could allow estimation of the hemodynamic factors mentioned above and help unraveling their role in rupture risk.

1.3.2 Part II: Improvements

In PC-MRI different velocity values of flowing blood in one voxel are averaged. Therefore, the spatial resolution of PC-MRI in intracranial aneurysms needs to be as high as possible. Generally in MRI, increasing spatial resolution lowers SNR and increases scan time. Furthermore, since PC-MRI captures flow information over the heart cycle, the temporal resolution needs to be as high as possible to measure flow close to peak systole.

Our in vivo PC-MRI measurements in intracranial aneurysms are performed with a resolution of 0.8 x 0.8 x 0.8 mm, measuring 10 cardiac
phases. Normally such an acquisition would take around 30 minutes, which would be too long since other imaging sequences are played out as well and the total scan time is limited to 45 minutes per patient. Therefore, a parallel imaging (SENSE [23]) acceleration factor of 3 is applied, with the disadvantage of SNR degradation. In this thesis other possibilities to shorten scan time or acquire images with more SNR are described.

1.3.3 Part III: Wall shear stress

The current consensus in literature is that wall shear stress, the tangential force that blood exerts on the vessel wall, is an important marker for aneurysm formation, growth [24] and rupture [25].

As stated above, wall shear stress can be calculated using CFD. However, due to aforementioned drawbacks of CFD, alternative wall shear stress estimation methods can considerably contribute to aneurysm rupture risk assessment. In this thesis a novel method to calculate wall shear stress is presented and applied to PC-MRI data measured in an in vitro and in vivo aneurysm.

1.4 Outline of the thesis

Since PC-MRI is a relatively new technique for velocity mapping in intracranial aneurysms, extensive validation is needed. The general aim of this thesis is to validate and optimize PC-MRI. Validation of PC-MRI is described in Part I, optimization in Part II. Furthermore, the validation of wall shear stress calculated from PC-MRI data is described in Part III. In Chapter 2 PC-MRI is applied in a rigid intracranial aneurysm phantom with a size similar to in vivo aneurysms. These data are then compared with PIV in the same phantom and with CFD in a geometry of the phantom. In Chapter 3 a new technique to describe flow patterns, based on multi-scale algorithms, is presented and applied to PC-MRI data. In Chapter 4 a second validation study is described that compared in vivo PC-MRI in eight intracranial aneurysms with CFD. As previously noted, PC-MRI suffers from fairly long scan times. Therefore, in Chapter 5, two acceleration techniques to speed up the PC-MRI sequence are compared. In Chapter 6 the influence of higher field strengths on PC-MRI in intracranial aneurysms is described. A novel method to calculate wall shear stress PC-MRI data is described and validated in Chapter 7. This method is applied to the aneu-
rysm phantom and an in vivo aneurysm; the results are presented in Chapter 8. Finally, the findings of the studies and possible future work are discussed in Chapter 9.

1.5 References


