Automatic Segmentation of Intracranial Arteries in 4-Dimensional Phase Contrast Magnetic Resonance Angiography

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Abstract

The development of a highly effective phase-contrast magnetic resonance imaging (PC-MRI) technique named phase-contrast vastly undersampled isotropic projection reconstruction (PC-VIPR) has improved the ability to image blood flow in the brain. The technique allows for the acquisition of temporally resolved volume images with high spatial resolution. Utilizing these improvements is of importance for diagnostic and research applications. The aim in this project was to investigate and implement PC-VIPR suitable segmentation techniques for blood flow quantification and labeling of blood vessels. The aim was to construct an automatic segmentation tool being able to accurately quantify blood flow and to label a few key arteries in the Circle of Willis.

A vascular tree construction was performed in which the vascular tree was separated into individual branches. Four different methods of boundary detection of blood vessels were implemented and evaluated on their performance in quantifying blood flow based on conservation of mass principles and internal error. A labeling algorithm was constructed in which labels of a few key arteries were assigned. A total of ten subjects were analyzed to provide evaluation of the segmentation tool.

The segmentation tool was constructed with complete automaticity. The best method for boundary detection showed an average mass conservation error of $-0.9 \pm 6.5\%$ where the internal carotid artery splits into the middle cerebral artery, the anterior cerebral artery and the posterior communicating artery. A labeling accuracy of 83% was acquired. The results of the blood flow quantifications and the labeling of arteries were partly a result of the vascular tree construction, which were considered effective.

Keywords. 4D PC-VIPR, segmentation, intracranial arteries, flow quantification, artery labeling
Sammanfattning

Automatisk segmentering av intrakraniella artärer i 4-dimensionell faskontrast-magnetresonansangiografi. Utvecklingen av en effektiv teknik för faskontrast-magnetresonansavbildning (forkortad PC-VIPR) har förbättrat möjligheten att avbilda blodflöden i hjärnan. Tekniken har gjort det möjligt att producera tidsupplösta volymbilder med hög rumslev upplösning. Att dra nytta av dessa framsteg är viktigt för kliniska och forskningsrelaterade tillämpningar. Syftet med detta projekt var att undersöka och implementera segmenterings tekniker för bestämning av blodflöde i och namngivning av artärer. Målet var att konstruera ett automatiskt segmenteringsverktyg med noggrann flödesbestämning och namngivning av en antal artärer i Williscirkeln.


Segmenteringsverktyget konstruerades med total automatik. Den bästa metoden för bestämning av blodflöde visade ett medelfel på $-0.9 \pm 6.5\%$ i för greningen där halspulsådern förgränar sig i den mellersta och främre storhjärnsartären samt den bakre sammanbindningsartären. En noggrannhet på $83\%$ uppnåddes i namngivningen av artärer. Resulten från bestämningen av blodflöde och namngivningen av artärer var till del påverkade av resultatet av kärlträdkonstruktionen, vilken ansågs effektiv.

Nyckelord. 4D PC-VIPR, segmentering, intrakraniella artärer, flödesbestämning, namngivning av artärer
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List of Abbreviations

ACA    anterior cerebral artery
ACoA   anterior communicating artery
BA     basilar artery
CD     complex difference
CHT    circular hough transform
CV     coefficient of variation
ICA    internal carotid artery
LPC    local phase coherence
LPC-HT  local phase coherence hough transform
MCA    middle cerebral artery
MRI    magnetic resonance imaging
PCA    posterior cerebral artery
PCoA   posterior communicating artery
PC-MRA  phase contrast magnetic resonance angiography
PC-VIPR phase contrast vastly undersampled isotropic projection reconstruction
Prin-Comp principal component analysis
tMIP   time maximum intensity projection
VA     vertebral artery
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1 Introduction

Studying blood flow in the brain is motivated by the huge impact on public health from blood flow deficiencies, including stroke (Donnan et al., 2008) and dementia (Román et al., 2002). A few key arteries in the brain account for a major part of blood supply of the brain, and are of special importance. Vascular disease in general, including heart disease are listed as the leading causes of death (World Health Organization (WHO), 2008). Magnetic resonance imaging (MRI) is commonly used for imaging and studying of blood flow, and is one of the most useful measuring modalities in studying stroke disease (Donnan et al., 2008). Extracting useful information from magnetic resonance images demands efficient and reliable segmentation techniques, a topic that is subject to a large amount of research, which is partly motivated by a vast spread in magnetic resonance imaging techniques (Lesage et al., 2009). This report is the result of a project in collaboration with the Department of Biomedical Engineering and Informatics at the University Hospital in Umeå. The department conducts research and development in the field of biomedical engineering and is involved with studying intracranial blood flow using magnetic resonance imaging (Wåhlin et al., 2012).

1.1 Motivation

A new magnetic resonance technique, phase-contrast vastly undersampled isotropic projection reconstruction (PC-VIPR), allows for the acquisition of highly resolved magnetic resonance images with short imaging times (Gu et al., 2005). PC-VIPR allows for temporally resolved imaging of velocities within an imaging volume with high spatial resolution. The 4-dimensional images are useful in the analysis of non-stationary processes in the human body such as blood flow, which varies over the cardiac cycle. The large volumetric and temporal coverage of the technique offers opportunities for comprehensive evaluation of blood flow and geometry of blood vessels. Since the technique is new, techniques of analyzing this kind of data are lacking, and images acquired by the PC-VIPR has so far been analyzed with a certain degree of manual effort. It is therefore desired to develop segmentation techniques for the analysis of this kind of data. Ideally, a segmentation technique should be accurate, robust and work automatically. Such a technique could provide accurate evaluation of blood flow and geometry of blood vessels in an efficient way. While being time saving for a user, it also has the potential of reducing the amount of inter- and intra-observer variability by being completely systematic in it’s execution. Such a technique could aid in both research and diagnosis of vascular disease. A simple tool for this was developed by Wåhlin et al. (2012).

Much effort has been made to segment medical images in general and magnetic resonance images in particular. Advances in magnetic resonance imaging motivates ongoing research in this field. Segmentation techniques range from low-level methods with much user interaction to high-level automated methods.
Most traditional techniques rely on morphological information for segmentation. Hoogeveen and Bakker (1998) showed limitations in traditional magnetic resonance methods to provide useful velocity data for segmentation purposes. The PC-VIPR technique is highly efficient and was shown to be able to produce 3D images with comparable accuracy to conventional 2D images for blood flow quantification (Gu et al., 2005).

1.2 Objectives

The objective in this project was to develop a segmentation tool for the analysis of PC-VIPR data. The goal was set to develop a tool that would work automatically to accurately assess blood flow in a set of large intracranial arteries. Emphasis was put on utilizing as much as possible of the data gathered in the PC-VIPR measurements in the segmentation process. Four different methods for blood vessel boundary detection were implemented, to investigate the potential and performance of using velocity and/or temporal information in the segmentation process. A few subgoals where set up to build the tool. First, finding an efficient way of separating the large amount of blood vessels in the brain from each other. The first goal was mainly put up to facilitate the enabling of the second and third goal, and was only indirectly evaluated. Second, to implement a few promising methods for boundary detection of blood vessels and determine their accuracy in assessing blood flow in the large arteries. Third, to automatically identify a few of the large arteries and label them according to anatomy. The tools ability to perform these tasks were evaluated on a set of nine arteries composed of the left and right internal carotid artery (ICA), the left and right middle cerebral artery (MCA), the left and right anterior cerebral artery (ACA), the basilar artery (BA) as well as the left and right posterior cerebral artery (PCA). The tool was evaluated on data from 10 healthy subjects, of which 7 were male and 3 were female.

1.3 Report Outline

This section has presented an introduction to this report, describing the motivation behind and the aim of this work. The theory section provides anatomical and MRI theory that could be useful to the reader to get a good background in these topics. In the methodology section, the Section 3.2 on segmentation is the main section since this is the main focus of the project. Section 3.4 describes how the segmentations were evaluated. Results, discussion and conclusions are presented at the end of the report.
2 Theory

Here theory relevant to the report is presented. Section 2.1 on anatomy is useful to be able to follow the rest of the report in which structures of blood vessels as well as specific blood vessels will be referred to. Section 2.2 provides theoretical background on MRI in general and specifically on phase-contrast MR angiography (PC-MRA). The section serves the purpose of making the reader familiar with MRI.

2.1 Anatomy

Purves et al. (2004) describe how the blood vessels in the brain form a complex structure. The structure resembles the structure of a tree, with a few large blood vessels splitting into several smaller ones at several levels. The notion of vascular tree is common and will be used extensively in this report. The blood vessels in the brain could be divided into arteries and veins, where arteries supply the brain with oxygen-rich blood and veins drain the brain of oxygen-poor blood. The blood supply of the brain is composed of the supply through two sets of arteries. One of the sets is the vertebral arteries (VA) and the other set is the internal carotid arteries (ICA). The vertebral arteries come together to form the basilar artery (BA). The basilar artery and the internal carotid arteries joins at the base of the brain in an arterial circle called the Circle of Willis. The basilar artery splits into the posterior cerebral arteries, forming the posterior part of the Circle of Willis. The internal carotid arteries split into the middle cerebral arteries (MCA) and the anterior cerebral arteries (ACA), and forms the anterior part of the Circle of Willis. The anterior and posterior part of the Circle of Willis are connected with a couple of communicating arteries. The anterior communicating artery (ACoA) bridge the two anterior cerebral arteries, and the posterior communicating arteries (PCoA) bridge the posterior cerebral arteries with the internal carotid arteries. Figure 2.1 shows a schematic view of the arteries in the Circle of Willis. The MCA and ACA form the anterior circulation and spread and branch off to supply the forebrain with blood. The basilar and posterior cerebral arteries form the posterior circulation and supply the posterior cerebral cortex, the midbrain, and the brainstem.

The above description of the Circle of Willis and as shown in Figure 2.1 describe the complete circle. However, morphological variations exist between subjects. Several variations in both the anterior and posterior part of the Circle of Willis are described by Krabbe-Hartkamp et al. (1998). It is common that single or multiple branches in the Circle of Willis are missing, as inborn traits, or obstructed, for example as a result of stroke. The circle provides a backup, should for example one or more major arteries be occluded or missing. With it, blood is able to flow in a few alternate routes to supply the same areas of the brain. As an example it has been shown, that the existence of the anterior communicating arteries in subjects with carotid occlusion, helps prevent brain damage as a result of blood deprivation (Bisschops et al., 2003). The morphological variations will have implications for a segmentation algorithm.
Figure 2.1: Circle of Willis (Gray, 1918).
An automatic labeling process will not only have to be adaptable to varying geometry and location of vessels, it will also need to recognize the existence or non-existence of vessels, since the Circle of Willis appear in several configurations.

A blood vessel being far out in the vascular tree is said to be distal, while a blood vessel being close to the root of the tree is said to be proximal. The branches ACA, MCA and PCA can be divided into subsegments according to Krabbe-Hartkamp et al. (1998). In the ACA, the A1 segment is the part of the ACA between the bifurcations at the ICA and the ACoA. The A2 segment is the segment distal to the bifurcation between A1 and the ACoA. In the MCA, the M1 segment is the segment distal to the bifurcation of the ICA into the MCA and ACA. In the PCA, the P1 segment is the segment between the end of the BA and the bifurcation of the PCA with the PCoA. The P2 segment is the segment distal from the bifurcation of the PCA and the PCoA.

2.2 Phase-Contrast MR Angiography

Angiography is a technique to image the inside, the lumen, of blood vessels. Magnetic resonance angiography (MRA) is a group of techniques based on MRI, which uses the intrinsic magnetic spin of atomic nuclei to image different kinds of matter. To understand how PC-MRA works, it is useful to first understand the basics of MRI. According to Bernstein et al. (2004), MRI is based on the physical phenomenon of nuclear magnetic resonance. Atomic nuclei have angular momentum, or spin, and therefore possess small magnetic fields. In a small sample positioned spatially at \( r \), the bulk magnetization will be time-dependent and related to the bulk angular momentum,

\[
M(r, t) = \gamma J(r, t),
\]

where \( \gamma \) is the gyromagnetic ratio. Applying a static magnetic field \( B_0 \) will cause these magnetizations to align with it. Applying a radio frequency (RF) pulse will cause the magnetization vector to dis-align briefly from the direction of the static magnetic field, and will cause it to precess around the static field at a frequency,

\[
\omega_L = \gamma B_0,
\]

where \( \omega_L \) is the Larmor frequency. The Larmor frequency is dependent on the angular momentum of atomic nuclei, and will be different for different kinds of substances. The magnetization vector will eventually re-align with the static field after that the RF pulse has been applied. It is during this period of time that the MR signal is measured. An MR camera is usually built with one main magnet and a few gradient coils. The gradient coils add a gradient field, \( G(r, t) \), to the total magnetic field,

\[
B = (B_0 + G_x x + G_y y + G_z z)\hat{z},
\]

or

\[
B = (B_0 + G \cdot r)\hat{z},
\]

With the addition of the gradient field, the total magnetic field varies with spatial location. A substance will in addition to being encoded by its bulk
angular momentum therefore also be encoded spatially. With the addition of the gradient field, the Larmor frequency is

$$\omega_L(r) = \gamma (B_0 + G \cdot r). \quad (2.5)$$

The Larmor frequency is demodulated with respect to the Larmor frequency in the static field $B_0$,

$$\omega(r) = \omega_L(r) - \gamma B_0. \quad (2.6)$$

The precessing magnetization vectors induced by the RF pulse will in turn induce a signal in a receiver coil,

$$s(t) = e^{-i\omega(r)t} \int_{-\infty}^{\infty} \int_{-\infty}^{\infty} \int_{-\infty}^{\infty} f(x,y,z) \, dx \, dy \, dz, \quad (2.7)$$

where $f(x,y,z)$ is the MR image of the imaged volume. The measurement of the signal takes place in $k$-space. The signal acquired can be interpreted as scans of Fourier space,

$$s(k) = e^{-i2\pi k \cdot r} \int_{-\infty}^{\infty} \int_{-\infty}^{\infty} \int_{-\infty}^{\infty} f(x,y,z) \, dx \, dy \, dz, \quad (2.8)$$

and the image reconstruction is performed taking the inverse Fourier transform of the signal,

$$f(x,y,z) = \mathcal{F}^{-1}(s(k)) \quad (2.9)$$

So far, spatial encoding has been achieved by applying a gradient magnetic field, $G(t)$. For moving substances, the MR signal will also be velocity-dependent. This may produce artifacts in an MR image, but can also be exploited to image the moving substance exclusively, and is done in PC-MRI. Considering the demodulated Larmor frequency, spins will accumulate phase over time,

$$\phi(r,t) = \gamma \int_0^t G(t') \cdot r \, dt' \quad (2.10)$$

A Taylor expansion of Equation (2.10) reveals that

$$\phi(r,t) = \phi_0 + \gamma r_0 \int_0^t G(t') \, dt' + \gamma v \int_0^t G(t') t \, dt' + \ldots \quad (2.11)$$

The second term in Equation (2.11) is the contribution to the accumulated phase from static spins, and the third term is the contribution from moving spins. The third term can be found by making two image acquisitions. In the first acquisition, a bipolar gradient is applied as shown in Figure 2.2. It will add no phase to stationary spins, but add to moving spins. In the second acquisition, the bipolar gradient is reversed. Subtraction of the two acquisitions results in a $\Delta\phi$-image which is directly proportional to velocity. A reference scan plus three additional scans, can provide velocity information in the $x$-, $y$- and $z$-direction. PC-MRA applies this technique to image the lumen of blood vessels. The velocity data is used to depict and calculate blood flow. Velocity encoding is dependent on how the gradient field is applied. Too large velocities accumulate phase in Equation 2.11 so that phase wraps will occur. The velocity encoding, $v_{enc}$, is set in a measurement to determine the highest measurable velocities.
Figure 2.2: The bipolar gradient adds differently to stationary and moving spins. By reversing the bipolar gradient between two acquisitions, it is possible to subtract the resulting images to produce a velocity image.

Higher velocities then the $v_{enc}$ will cause aliasing in the image. Setting the velocity encoding as low as possible is useful to receive a velocity image with as strong signal as possible.

A few effects MRI have on the images it produces are worth mentioning, as they can provide challenges when assessing blood flow and other quantities. Partial volume effects result from imaging objects that are too small. In PC-MRI, a voxel containing both moving and stationary substance will be averaged to show intensity and velocity values somewhere in between the stationary and moving substance. Partial volume effects can produce errors in flow measurements if too few voxels occupy a blood vessel (Wåhlin et al., 2011). Blurring also occur in MRI images (Bernstein et al., 2004). Further, image noise can be spatially correlated in MR images (Stobbe and Beaulieu, 2011).
3 Methodology

This section describes the methods used to achieve the goals set out in the introduction. Section 3.1 describes what imaging protocol and hardware was used to acquire the data analyzed in this report, and which images constituted this data. Section 3.2 is the main part of the methodology section and describes how the segmentation was performed. It starts with a synoptic description of the segmentation process and proceeds with describing in more detail the methods used in all steps of the segmentation process. Section 3.3 presents how the segmentations were visualized and how a simple interface was created. The focus in this report is on the technical aspects of segmentation, and therefore this section is kept short. However, its relevance is motivated by the need to validate what has been segmented and how it has been segmented. Section 3.4 describes the methods used to validate the segmentation and comes with two subsections, one describing the segmentations ability to quantify blood flow, and the other describing the segmentations ability to label a few key arteries correctly.

3.1 Data Acquisition

Recent advances in MRI protocols has spawned a technique named phase-contrast very undersampled isotropic projection reconstruction (PC-VIPR). The technique acquire images by undersampling $k$-space in radial projections. The PC-VIPR protocol allows for short acquisition times with a large volume coverage and high isotropic resolution. It can cut the imaging time by a factor of 30 compared to a conventional 3D MR scan with the same spatial resolution (Gu et al., 2005).

Data in this report were acquired by a 4D PC-VIPR sequence, resulting in detailed time-resolved MR images. Retrospective gating was used to be able to asses blood flow over the cardiac cycle. For improved signal-to-noise-ratio, a five-point PC-VIPR method was used (Johnson and Markl, 2010). The imaging protocol produced a set of 100 images per subject, where 5 images were reconstructed at each of 20 isotropically spaced time-frames over one cardiac cycle. For each time-frame three velocity images, $v_x$, $v_y$ and $v_z$, were produced. Complex difference (CD) images were constructed showing anatomical details of the vascular system. Also, anatomical images showing the entire brain anatomy were acquired. For the sake of notation, let $I$ denote the set of images produced for a subject, so that $I = \{anat_j, CD_j, v_{xj}, v_{yj}, v_{zj}\}$, where $j = 1, 2, \ldots, 20$, $anat_j$ are the anatomical images and $CD_j$ are the complex difference images.

Scans were conducted using a clinical 3-Tesla GE Discovery MR 750 scanner. A resolution of $320 \times 320 \times 320$ voxels was used over a field-of-view (FOV) of $220 \times 220 \times 220$ mm resulting in a voxel size of $0.69 \times 0.69 \times 0.69$ mm. 20 frames/heart cycle were reconstructed. The velocity sensitivity was set to $v_{enc} = 110$ cm/s.
3.2 Segmentation

Image segmentation is the process of dividing an image into multiple segments. Dividing an image into segments is used to separate them from each other and to be able to analyze parts in the image separately. A segment can be analyzed for example by its geometry, location or intensity. Segmentation can be used to calculate properties of the objects. In this project, the most important property to be able to calculate was blood flow. Finding the geometry of blood vessels is also interesting, and was used in the labeling process in this project. By separating the vascular tree into segments corresponding to individual blood vessels, blood flow calculations can be performed separately in separate vessels. Segmentation also allows for analysis of geometry and the ability to highlight specific segments in the image which could be used for efficient visualization and interaction.

This report deals with time-resolved 3D images, that is, 4D images. In this project, four different methods for detecting the boundary between blood vessel and other brain structure were implemented and compared in their performance in quantifying blood flow. The segmentations that were produced were static (the same for all images over the cardiac cycle). Section 2.1 made the distinction of the lumen (the inside) of blood vessels and blood vessels as a whole. When the notion of blood vessel is used below, it refers to the lumen if not otherwise stated.

A few key problems were identified to be able to achieve the goals set out in the beginning of this report and are outlined below.

1. Separate foreground from background, that is, determine which voxels that correspond to blood vessels and which do not. The result is a binary image, where ones and zeros are representing foreground and background respectively.

2. Separate the vascular tree into separate branches for further analysis.

3. Calculate flow in a few branches of interest to be able to validate the segmentation. Automatically identify the branch classes ICA (left and right), MCA (left and right), ACA (left and right), BA and PCA (left and right).

The first point is important for the assessment of quantitative parameters, including blood flow and geometric parameters such as diameter and length of blood vessels. An over- or under-segmentation will produce values of these parameters that are too large and too small, respectively. The second point is important for the studying of individual branches and branch classes. The separation of the vascular tree into branches is essential for the task of quantifying blood flow and geometry for specific vessels and for finding and labeling of the key branches, which is performed under the third point.

A background on blood vessel segmentation will be given in Section 3.2.1. The distinction between extraction scheme, models and features will be made and further elaborated in Sections 3.2.2, 3.2.3 and 3.2.4, respectively. Image features used in this report will be explained in Section 3.2.4 and details on how the features were used is explained in Section 3.2.5. The problem of finding the boundary between the vascular tree and surrounding brain structure will be
addressed in Section 3.2.5, where four different methods of boundary detection will be presented and evaluated. The problem of separating the vascular tree into separate branches is accomplished in Section 3.2.6, by the use of a thinning operation and the development of an indexing algorithm. The results of this section produce a simple representation of the vascular tree, which simplifies greatly the evaluation of blood flow and geometry of vessels. Section 3.2.7 describes in detail how blood flow was calculated in the segments. Section 3.2.8 describes an algorithm for labeling a few specific vessels in the vascular tree.

3.2.1 Background

In a review article by Lesage et al. (2009), it is established that much effort has been made to develop techniques for blood vessel lumen segmentation in medical images, notably in computed tomography angiography (CTA) and magnetic resonance angiography (MRA). There are many different MRA techniques, each producing images with certain characteristics. The techniques vary in how many dimensions they image, resolution, contrast and level of noise. This motivates the large amount of segmentation techniques that exist. Some techniques could be considered general while some highly specific to a certain kind of data. The success of a segmentation technique is highly dependent on the characteristics of the data being segmented. The choice of segmentation technique will have implications on robustness and computational efficiency. The choice should also be influenced by what prior knowledge of the data exist, and ideally exploit this as much as possible. Many segmentation techniques include a centerline extraction or a vascular tree construction along with a boundary extraction. A centerline is a curve representation of an object and is an useful feature in blood vessel segmentation. In a blood vessel branch, a centerline is a curve centered in the propagation direction of the vessel and is a one-voxel thick representation of the vessel. This representation is useful and efficient in the separation of the vascular tree into branches and can be used for subsequent surface extraction at a local scale in the vicinity of the centerline. The representation provides structural information about the blood vascular tree and aids in computational efficiency since it allows for computation in the vicinity of it, therefore avoiding processing the entire data volume. Boundary extraction is key in a successful segmentation for accurate evaluation of blood flow and geometry. While a vascular tree construction provides structural information and indexing of branches, it does not provide any useful information about what voxels to include in flow and geometry calculations. Boundary extraction decides what voxels are considered blood vessel and non-blood vessel. Boundary extraction is typically performed analyzing various image features, including morphology and gradient images.

Lesage et al. (2009) further make the distinction between models and features in a segmentation approach. An extraction scheme describes the overall process of a segmentation technique. Modeling can be used to exploit prior knowledge of the characteristics of the image. Geometric models include constraints on the geometry of objects, blood vessels for example can be modeled as elongated objects with circular cross sections. Appearance models include the analysis of intensity distributions, voxels may be separated into background and foreground, by analyzing intensity histograms. A set of data can be filtered to display certain features of the data. These features can be used on their own or together with model assumptions to produce segmentations. An extraction
scheme is a description of the way to initiate and conduct the segmentation process. Some extraction schemes include both or either of pre-processing and post-processing. An automatic segmentation algorithm needs an extraction scheme that requires no user interaction to produce the final segmentation. Extraction schemes range from completely automatic to highly manual, in the latter a user often both selects a vessel of interest and specifies the boundary manually by deciding what pixels or voxels to include.

The segmentation tool developed by Wahlin et al. (2012) could be considered semi-automatic. Here a user selected a region of interest (the location of a blood vessel), which was used as input in a region-growing algorithm including voxels in a foreground-background separated Time Maximum Intensity Projection image.

In an article by Chung et al. (2004), the notion of local phase coherence was introduced. Local phase coherence is a measure of a voxel's similarity in velocity direction to that of its neighbors. The local phase coherence image was used together with statistical modeling on speed data, where a Maxwell-Gaussian-uniform mixture model was fitted to the image data to choose appropriate thresholds. Schmidt et al. (2009) used a combination of 3D and 4D information to segment the large thoracic arteries. Local phase coherence was calculated in a similar fashion as by Chung et al. (2004), and was found to be a good indicator for vessels. Due to pulsatility of blood flow, vessel voxels could be distinguished by looking for temporal variations in velocity. Temporal flow variance was defined as the variance of flow over time in each voxel. The significance of temporal flow variance could be reduced in noisy data and in the segmentation of smaller vessels as well as vessels with low pulsatility. A variation of the method of using temporal variance was evaluated in this report, and is presented in Section 3.2.5.

A segmentation based on temporal information was evaluated by Alperin and Lee (2003). Segmentations were evaluated on flow measurements conducted with cine phase-contrast MRI and on phantom data. Here, the segmentation was performed by choosing a reference waveform (flow speed over time) by manually selecting a pixel inside a vessel and calculating correlation coefficients with all pixels in the image. High correlation of pixels with the reference pixel was an indicator of those pixels belonging to the same vessel. Zöllner et al. (2009) implemented another segmentation method based on temporal information. Here, k-means clustering was performed on the temporal data in 2D cine phase-contrast MRI. This was shown to work well in segmentation of the renal arteries in the 2D cine PC-MRI.

### 3.2.2 Extraction Scheme

The aim of this project was to create a completely automatic segmentation tool. The extraction scheme presented here facilitated this by including several required components, including accurate boundary detection, on both a global and a local scale, efficient vascular tree construction, and a way to classify a few key arteries. A schematic view of the extraction is shown in Figure 3.1. Data acquisition is followed by extraction of global features, which results in two images, a time maximum intensity projection (tMIP) and a local phase coherence (LPC) image. These images are further described in Section 3.2.4, and are used to create a global foreground-background segmentation that is
used in the skeletonization process. The skeletonization produces a one voxel thick representation of the vascular tree, which is processed in the vascular tree construction step which constructs the vascular tree from the skeleton, dividing the skeleton into branches and removing spurious skeleton objects. The branches are indexed so that they are separated from each other. The branches in the vascular tree construction are used as potential objects for the vessels of interest in the labeling step. For a subset of the branches, blood flow and geometry is evaluated which aids in the labeling process. To evaluate blood flow and geometry, the foreground-background separation is repeated on a local scale. At the local scale, four different methods for boundary detection are implemented and compared. Finally, a labeled segmentation including hemodynamics and geometry evaluation is produced.

3.2.3 Models

Modeling can be used to exploit prior knowledge of the data and to induce constraints and adaptation in a segmentation process. Two kinds of modeling relevant to blood vessel segmentation are considered here. The first one is appearance modeling, the other is geometrical modeling. An appearance model express prior knowledge on the intensity distribution of the vascular tree. The challenge is to separate the foreground from a noisy background. Given an image, the separation is usually performed by applying a threshold for which intensities above (or below) are considered foreground, and intensities below (or above) are considered background. The threshold can be determined manually or automatically. An appearance model is used for determining the threshold in a specific image. In an article by Chung et al. (2004), gaussian mixture modeling was used to decide on suitable thresholding. In an article by Wåhlin et al. (2012), a simpler method showing good agreement with manually segmented 2D PC-MRI data was used, where a threshold was set at 18% of the maximum intensity in a time maximum intensity projection (tMIP) image. Statistical mixture modeling has the benefit of adapting for variations in the relationship between foreground and background signal resulting for example from variations in the data acquisition protocol. Thresholding based on maximum intensities or absolute values has the advantage of being simple to implement. In Section 3.2.5, thresholding was based on maximum intensities and absolute values. Examples of histograms of a tMIP image and an LPC image are shown Figure 3.3 and Figure 3.5, respectively. By analyzing histograms one can find suitable thresholds for image segmentation. Geometrical modeling can be used to induce geometrical constraints in the segmentation process. The notion of vascular tree was introduced in Section 2.1 for the reason that the system of blood vessels resembles a tree in structure. In the vascular tree, the system of blood vessels is made up of several branches, with smaller branches originating from larger branches at bifurcations, or junctions. A short segment of a branch could be considered cylindrical in shape, a branch could be considered an elongated object with circular cross sections. For one of the methods in Section 3.2.5, blood vessels were modeled as being circular in shape in cross sections perpendicular to the propagation direction of the vessels.
Figure 3.1: Extraction scheme. Foreground-background separation is performed at two stages in the extraction scheme. First, a foreground-background separation is performed on a global scale to be able to produce the vascular tree construction. Second, foreground-background separations are performed locally in the vicinity of vessels to evaluate blood flow and geometry. On the local scale, four different methods are implemented and compared.
3.2.4 Features

*Features* is used as a general term to describe a set of images \( I \) in different ways. Various features can be calculated using the same set of data, but show different characteristics which all could be used in segmentation. The features are calculated either globally or locally. The features described in this section are the time maximum intensity projection (tMIP), the local phase coherence (LPC), gradient features and principal component analysis (PCA) features. In Section 3.2.5, several methods of boundary detection are considered. In that section, one or more features described in this section are used alone or in combination to extract information from the data. This section describes qualitatively the features, while Section 3.2.5 presents the details on how the features were used to extract useful information.

**Time Maximum Intensity Projection**

A time maximum intensity projection (tMIP) image is the maximum complex difference over the cardiac cycle. A tMIP image is a 3D image and provides a good morphological representation of the vascular tree. Bright voxels in the tMIP correspond to high velocity of blood flow, making the large arteries prominent, while veins and smaller arteries show less brightness. An axial projection (looking from the neck upwards in the brain) of a tMIP image is shown in Figure 3.2. A histogram of the data in Figure 3.2 is shown in Figure 3.3, where two thresholds used in this report are plotted. A log scale is used to be able to distinguish the foreground (to the right in the image) from the background (to the left in the image).

**Local Phase Coherence**

Local phase coherence (LPC) was introduced by Chung et al. (2004) and was found to be a good indicator of blood vessels in MRI. Here, an LPC image was constructed according to Schmidt et al. (2009), which offers a small variation to the original definition. The LPC is constructed from the mean velocity over the cardiac cycle, \( \vec{v}(r) \),

\[
LPC(r) = \frac{1}{27} \sum_{i=-1}^{1} \sum_{j=-1}^{1} \sum_{k=-1}^{1} \arccos \left( \frac{\vec{v}(r) \cdot \vec{v}(r_{i,j,k})}{||\vec{v}(r)|| ||\vec{v}(r_{i,j,k})||} \right),
\]

(3.1)

where

\[
r_{i,j,k} = r + \Delta(i,j,k), \quad i,j,k = \{-1,0,1\},
\]

(3.2)

\( \Delta \) is the resolution in the data and \( r \) is the \((x,y,z)\)-coordinate in the image. An LPC image of the same data featured in the tMIP in Figure 3.2, is shown in Figure 3.4. A histogram of the data in Figure 3.4 is shown in Figure 3.5, where the threshold used in this report is plotted. A log scale is used to fit both the foreground (left peak) and the background (right peak) into the graph. The LPC image is calculated locally, resulting in an image appearing to show similar intensities for all vessels, including small arteries and veins. Mainly the largest arteries in the vascular tree were considered in this report however. In comparison, the LPC image appears to have more contrast than the tMIP image, which is shown in Figure 3.6.
Figure 3.2: A tMIP axial projection.

Figure 3.3: Intensity histogram of a tMIP image. The frequency is plotted in log scale to be able to distinguish the foreground (right of thresholds) from the background (left of thresholds). The 15 % threshold is used in the vascular tree construction, and the 18 % threshold is used for blood flow and geometry quantifications.
Figure 3.4: LPC axial projection in inverse grayscale.

Figure 3.5: Intensity histogram of an LPC image. The frequency is plotted in log scale to be able to distinguish foreground (left of threshold) from background (right of threshold). A threshold of 0.75 is used to distinguish foreground from background in the LPC image.
Gradient Features

Gradient filtering is a common technique to find edges in images. An edge could be defined as points in an image where image brightness change at or above a certain rate relative to spatial location. In a 2D image $H(r)$, a gradient intensity image $F(r)$ could be defined as

$$F(r) = |\nabla H(r)| = \sqrt{\left( \frac{\delta H(r)}{\delta x} \right)^2 + \left( \frac{\delta H(r)}{\delta y} \right)^2}. \quad (3.3)$$

By thresholding the gradient intensity image, an image defining edge points can be produced. How the threshold is set will determine how strong indicators of edges will be found. Setting this threshold high will produce edges not always enclosing objects entirely, setting it low can produce edges with no meaning in the underlying image. In a small cross section to a blood vessel, one major edge should exist, the edge between blood vessel and background. Locating this edge using gradient features is addressed in Section 3.2.5, where a model assumption about circular cross sections deals with un-enclosing boundaries. Figure 3.6 shows an example of a cross section at a point in an ICA vessel of gradient intensity images of the tMIP and the LPC image.

![Gradient intensity images](image)

(a) tMIP gradient intensity in a cross section to an ICA. (b) LPC gradient intensity in a cross section to an ICA.

Figure 3.6: Gradient intensity images.

Principal Component Analysis

Principal component analysis (Prin-Comp) was applied to the temporal data with the aim of using temporal variation of blood flow as an indicator of blood vessels. A feature was defined based on a principal component analysis of the variation of speed in a subset of voxels in the imaged volume. As stated by Johnson and Wichern (2007), principal component analysis is an orthogonal linear transform that transform a set of data to a new coordinate system in which the maximum amount of variance is along the first dimension, the second maximum amount of variance along the second dimension etc., so that as much as possible of the total variance is in the first dimension. In this application,
no other than the first principal component was thought to provide any useful information, but could be a way to separate irrelevant principal components that might be arising from factors such as correlated noise. It has the advantage over an approach such as in the article by Alperin and Lee (2003) in that no reference waveform is needed, and was thought to provide a more noise resistant segmentation. In this application, it had the disadvantage of being numerically heavy, extracting much useless information along with the useful information. To perform principal component analysis based on correlations, the variables were standardized. For a set of temporally resolved speed data, 20 observations where made in \( p \) standardized variables.

\[
X' = [X_1, X_2, \ldots, X_p], \tag{3.4}
\]

where rows of \( X' \) corresponds to observations in time and columns to voxels. Let \( X' \) have the covariance matrix \( \Sigma \) and consider the linear combinations

\[
Y_1 = a'_1X = a_{11}X_1 + a_{12}X_2 + \ldots + a_{1p}X_p \\
Y_2 = a'_2X = a_{21}X_1 + a_{22}X_2 + \ldots + a_{2p}X_p \\
\vdots \\
Y_p = a'_pX = a_{p1}X_1 + a_{p2}X_2 + \ldots + a_{pp}X_p \tag{3.5}
\]

Further,

\[
\text{Var}(Y_i) = a'_i\Sigma a_i, \quad i = 1, 2, \ldots, p \tag{3.6}
\]

\[
\text{Cov}(Y_i, Y_k) = a'_i\Sigma a_k, \quad i, k = 1, 2, \ldots, p \tag{3.7}
\]

The first principal component is the linear combination \( a'_1X \) that maximizes \( \text{Var}(a'_1X) \) subject to \( a'_1a_1 = 1 \). In the first principal component, the larger the size of the coefficients \( a'_1 \), the more likely these voxels are to belong to a blood vessel.

### 3.2.5 Boundary Detection

The boundary between foreground and background could be represented by a binary image, with ones and zeros representing foreground and background, respectively. An example of a binarization of the product of the images in Figures 3.2 and 3.4 is shown in Figure 3.7. Boundary detection is performed at two stages in this report, serving two different purposes. First, by finding the boundary between the vascular tree and the background at a global scale (considering the whole image volume), it is possible to find the structure in the vascular tree by vascular tree construction, as described in Section 3.2.6. Second, the boundary is used in order to produce quantitative data, including blood flow and geometry of vessels, and is performed at a local scale in cross sections to the vessels. Section 3.2.7 describes how flow was calculated in cross sections along the vessels. The cross sections were limited in size to a grid of 17 by 17 pixels. Bilinear interpolation was used to create cross sections of the same resolution as the original data. Interpolation was performed in two steps, rotating a volume of 17 by 17 by 17 voxels in the xy-plane, followed by a rotation in the xz-plane.

For the purpose of finding the structure in the vascular tree, a foreground-background representation of the tMIP, \( B_{tMIP} \), image was created by applying an intensity threshold of 15 % of the maximum voxel intensity value. A
Figure 3.7: A binary vascular tree.
foreground-background representation was also made of the LPC image, \( B_{LPC} \), by applying an intensity threshold of 0.75. The intersection of the two binary images, \( B_{tMIP} \cap B_{LPC} \), were used as input in the vascular tree construction. The LPC image was used due to its apparent high contrast and tendency to display small arteries clearly, and intersected with the thresholded tMIP image to remove noise and artifacts. The validity of this approach was not evaluated directly, but had implications for the resulting vascular tree construction, which was evaluated by its ability to divide the blood vascular tree into quantifiable and classifiable segments as described in Section 3.4.

Four different methods for boundary detection were compared for flow quantifications and are presented in detail below in this section. In these methods, the boundary was detected at a local level, that is in cross sections perpendicular to the propagation direction of the vessels. In the first method, the boundary was defined as by Wahlin et al. (2012). This method was chosen to provide a reference segmentation, and was expected to perform similarly as in that work. Although the same boundary definition was used, calculation of blood flow was not performed in the same way. In the second method, an intensity threshold was applied to the LPC image. The third method combined gradient information in the LPC image with modeling of a circular boundary in cross sections perpendicular to the propagation direction of the blood vessels. In the fourth method, temporal variance of speed data was analyzed using principal component analysis. For the second (LPC), third (LPC-HT) and fourth (Prin-Comp) methods, image thresholds were calibrated to produce accurate segmentations. Histograms produced from features of the PC-VIPR data do not typically show a clear separation between foreground and background, which is apparent in Figures 3.3 and 3.5. Therefore, a range of thresholds for the LPC, LPC-HT and Prin-Comp methods were evaluated. The evaluation was based on blood flows showing a high level of consistency at bifurcations as well as a reasonable level of internal consistency. These criteria are thoroughly described in Section 3.4, where they are used to evaluate the methods. To exclude any other vessels occurring other than the one of interest in a cross section, a region growing algorithm was used to incorporate only those foreground pixels in connection with a centerline point.

**tMIP**

In this method, a threshold was defined at a global scale. Voxels were separated by a threshold at 18% of the intensity of the brightest voxel, \( tMIP_{max} \), in the image. The threshold was set relative to the image intensity distribution to compensate for varying absolute values of the intensity between images. The binary image was

\[
B_{tMIP}(\mathbf{r}) = \begin{cases} 
1, & \forall tMIP(\mathbf{r}) > 0.18tMIP_{max} \\
0, & \forall tMIP(\mathbf{r}) < 0.18tMIP_{max}
\end{cases}
\]

**Local Phase Coherence**

In this method, a threshold was defined at a global scale as well. Thresholds between 0.25 and 1 were considered in increments of 0.05, and a threshold of 0.75 was found to be the most accurate in separating voxels in the LPC image. The threshold was set at an absolute value since the LPC image features
coherence between voxels rather than intensities related to the magnitude of blood flow. Voxels with a certain level of coherence to their neighbors were considered foreground.

\[ B_{LPC}(r) = 1, \quad \forall \text{LPC}(r) < 0.75 \]
\[ B_{LPC}(r) = 0, \quad \forall \text{LPC}(r) > 0.75 \]  (3.9)

Local Phase Coherence with Geometrical Modeling

Blood vessels are commonly modeled as tubular objects (Mohan et al., 2010), or as having circular cross sections (Schmidt et al., 2009). In this report, the possibility of improving flow quantification by using geometric constraints was explored using an approach in which circular objects where fitted to a gradient intensity feature in the cross sectional images. Gradient intensity images were constructed in cross sections according to Equation (3.3). These images where thresholded to produce an edge map, \( E(r) \)

\[ E(r) = 1, \quad \forall F(r) > 0.25 \]
\[ E(r) = 0, \quad \forall F(r) < 0.25 \]  (3.10)

with ones defining edges and zeros non-edges. Thresholds between 0.025 and 0.275 were considered in increments of 0.025, and a threshold of 0.25 in the edge map was found to produce the most accurate segmentations. The edge map could be used directly with a region growing algorithm to include all pixels inside a boundary in a foreground-background representation. Noisy edge maps or edge maps with weak indicators of edges can however disturb this inclusion. To avoid this problem, circular resembling objects were detected in the edge map using the Circular Hough Transform as described by Yuen et al. (1990). The Circular Hough Transform takes a set of coordinates in \((x,y)\)-space and transforms them into a parametric \((r,a,b)\)-space, where

\[ r^2 = (x - a)^2 + (y - b)^2. \]  (3.11)

The coordinates in \((x,y)\)-space defined by the edgemap in Equation (3.10) are transformed into \((r,a,b)\)-space. For each point in the edgemap, cones are drawn in the \((r,a,b)\)-space. The cones are accumulated into an accumulation array, so that bright spots in \((r,a,b)\)-space correspond to intersecting cones. These spots \((r,a,b)\)-coordinates describe circles in \((x,y)\)-space via Equation (3.11). The most prominent circle is found by finding the maxima in the accumulation array, and is defined as the boundary of the blood vessel in the cross section. A region growing algorithm was used to include the pixels inside the boundary.

The method is referred to as the LPC-HT (local phase coherence Hough transform) method.

Principal Component Analysis

In the Prin-Comp method, a threshold was defined globally. Thresholds between 0.04 and 0.14 were considered in increments of 0.01, and a threshold of 0.07 was found to be the most accurate in separating voxels in the Prin-Comp images. The threshold was used on the absolute value of the coefficients (pixels) in the first principal component.

\[ B_{\text{Prin-Comp}}(r) = 1, \quad \forall |\text{Prin-Comp}(r)| > 0.07 \]
\[ B_{\text{Prin-Comp}}(r) = 0, \quad \forall |\text{Prin-Comp}(r)| < 0.07 \]  (3.12)
A principal component analysis was made in each cross section separately for computational efficiency.

3.2.6 Vascular Tree Construction

A vascular tree construction is a representation of the vascular tree that contains explicit structural information about the vascular tree which is not apparent in the raw images. The construction is performed by finding the skeleton of the vascular tree by a process called skeletonization. The skeleton allows for separation and indexing of branches by detecting bifurcations. The vascular tree construction represents each branch in the vascular tree as a one voxel thick curve in 3D space. The construction also allows for the calculation of parameters such as blood flow and geometry separately for each branch. Further, these parameters can be evaluated within a branch along the curve. In this report, the vascular tree construction is used extensively for flow and geometry quantifications, as described in Section 3.2.7 and for labeling of arteries, as described in Section 3.2.8.

For a complex structure such as the vascular tree in the brain, the skeletonization produces a skeleton containing several anomalies, including spurs and isolated sticks (Chen and Molloi, 2003). This was dealt with by an iterative algorithm, where the vascular tree construction was modified and updated by deleting objects of certain characteristics until it converged to the final construction. The vascular tree construction could together with quantification of blood flow and geometry be considered a full vascular tree reconstruction of the relevant parts in the vascular tree. The algorithm is described in Algorithm 1 and the steps in the algorithm are described further below.

Vascular tree construction algorithm

Skeletonization

while branches are being removed do
    separate skeleton into branches
    calculate length of branches
    for all branches do
        if branch too short then
            remove branch
            update branch removal counter
        end
    end
end

Algorithm 1: Vascular tree construction algorithm.

Skeletonization

Skeletonization is the process of finding the skeleton of an object in an image. A skeleton is a representation of the shape of a binary image and represents the basic structure of the object in a topology conserving way. An approximation to a topology conserving skeleton can be produced using thinning techniques. Thinning is a technique that works iteratively to reduce an object in size, peeling of layer by layer until only an approximation to the skeleton remains. The thinning technique used here is described by Palágyi et al. (2001) and is suitable
for elongated objects such as blood vessels.

Let $X$ be a discrete binary 3D image. Each element in $X$ will have a value of 1 or 0 assigned to it, representing either a vessel point or a background point, respectively. The set of points $V \subseteq X$ is the set of all vessel points in the image. The set of points $X \setminus V$ is the set of all background points. Adjacency is the notion of a point being adjacent to a set of neighboring points in a certain way. Figure 3.8 shows the set of points $N_j(p)$, $j = 6, 18, 26$ being $j$-adjacent to a point $p$. Point $p$ is 6-adjacent to the points marked U, D, N, S, E, and W. Point $p$ is 18-adjacent to the points marked U, D, N, S, E, W and •. Point $p$ is 26-adjacent to the points marked U, D, N, S, E, W, • and ○. A set of vessel or background points in $N_j(p)$ is $j$-connected if a continuous path can be drawn through the entire set of points using $j$-adjacencies. In other words, in any subset of points smaller than that entire set, at least one of those points needs to be $j$-adjacent to a point not included in that subset. Deleting points in the image $X$ is the process of morphing vessel points into background points. A vessel point is a simple point, if its deletion does not change the topology of the image. Simple points are deleted to produce the skeleton, and are found by investigating the connectivity between vessel and background points in a $3 \times 3 \times 3$ voxel neighborhood to a vessel point $p$. A vessel point $p$ is a simple point if and only if the following four conditions hold.

![Figure 3.8: Cube of adjacencies. $N_6(p)$ is the set of $p$ and the points marked U, D, N, S, E, and W. $N_{18}(p)$ is the set of points $N_6(p)$ plus the points marked •. $N_{26}(p)$ is the set of points $N_{18}(p)$ plus the points marked ○, that is, all points except the point $p$.](image)
1. The set $N_{26}(p) \cap V \setminus \{p\}$ is not empty.
2. The set $N_{26}(p) \cap V \setminus \{p\}$ is 26-connected in itself.
3. The set $X \setminus V \cap N_{6}(p)$ is not empty.
4. The set $X \setminus V \cap N_{6}(p)$ is 6-connected in the set $X \setminus V \cap N_{18}(p)$.

The first condition makes sure that the point $p$ is not isolated; if it is isolated, it should not be deleted. The third condition tests if the point $p$ is a border point; if it is not, it should not be deleted. Conditions 2 and 4 test the connectivity of vessel and background points, and are required to hold to produce the skeleton in a topology conserving way. The third condition is evaluated in the U, D, N, S, E, and W directions sequentially according to Algorithm 2. This means that vessel points being border points in the U direction will be deleted first, vessel points being border points in the D direction will be deleted second etc. The algorithm is sequential, first marking points for deletion in one direction at a time, followed by a re-test of the four conditions to delete simple points. The algorithm works iteratively, deleting one layer of border points at a time until no simple points remain to be deleted. The final output is the thinned skeleton, $Y$. Considering that simple points are deleted sequentially in the U, D, N, S, E, and W directions, skeletons can be produced with some variation depending on which order in direction the conditions are tested. A skeleton produced with this thinning algorithm is therefore an approximation.

**Branch Separation**

The skeleton produced by the method described above is a one-voxel thick representation of the vascular tree. This representation makes it easy separating branches from each other, by identifying *end points* and *junction points*. This report follows the same notations described by Klette (2006).

**Definition 1.** A skeleton point $p$ will have a branching index $m$ depending on how many other skeleton points there are in the neighborhood $N_{26}(p)$.

- $p$ is a singular point if $m = 0$
- $p$ is an endpoint if $m = 1$
- $p$ is a middle point if $m = 2$
- $p$ is a junction point if $m \geq 3$

Further, a 26-connected set of middle points, will be referred to as a *branch* in the vascular tree construction. A 26-connected set of junction points, will be referred to as a *junction*. A 2D representation of this definition is shown in Figure 3.9b.

**Pruning**

An undesired effect of the thinning algorithm is that it creates *spurs* (Chen and Molloi, 2003). A spur is a spurious part of the skeleton that does not represent a real branch, rather it is a short object originating from the true skeleton, stretching out towards the wall of a blood vessel. A spur is an undesirable
**Thinning algorithm**

\[ Y = X \]

**while** vessel points are being deleted **do**

- delete simple(\( Y, U \))
- delete simple(\( Y, D \))
- delete simple(\( Y, N \))
- delete simple(\( Y, S \))
- delete simple(\( Y, E \))
- delete simple(\( Y, W \))

**end**

**function** delete simple(\( Y, \text{dir} \))

**for** all points \( p \) in \( Y \) **do**

- test the four conditions

  **if** point \( p \) is simple in the \( \text{dir} \) direction **then**
  - mark point \( p \) as deletable

**end**

**for** all deletable points **do**

- re-test the four conditions

  **if** simple **then**
  - delete point

**end**

**Algorithm 2:** Thinning algorithm. Inside the while loop, the four conditions stated above are tested. One layer of border points is deleted for each iteration of the while loop. The **delete simple** function is sequential in that it first marks simple points for deletion and then deletes the marked points one by one if the conditions still hold.

![Diagram](image_url)

(a) The thinning algorithm applied to a small 2D object. (b) Labeling of branch points to distinguish between end points (light gray), middle points (gray), and junction points (black).

**Figure 3.9:** The skeleton of a blood vessel-resembling object and its categorization of skeleton points.
feature, and should be removed. This process is called pruning. The pruning criteria used here also removes any isolated sticks, that is short skeleton segments not connected to a larger skeleton object. Based on the fact that the objects segmented here are elongated objects with a limited diameter, a simple criteria for identifying spurs was used.

**Definition 2.** A branch is a spur if

1. it is shorter than 8 voxels
2. the branch ends in at least one end point.

The first criteria was designed to remove any possible spurs, but could also remove some possibly true peripheral branches. The second criteria made sure not to remove any short intermediate branches.

**Final Representation**

In the final representation, each branch, or each segment, was indexed with numbers ranging from \( i = 1, \ldots, N_{\text{segments}} \), where \( N_{\text{segments}} \) was the total number of segments in the vascular tree construction. The points in a segment were further indexed so that for a branch, \( b_i \), consisting of points \( b_i = \{ p_{i,1}, \ldots, p_{i,N_{\text{points}}} \} \), the points \( p_{i,1} \) and \( p_{i,N_{\text{points}}} \) were the start and end points of the segment, respectively. Start to end direction was defined as the direction of the flow in the segment. A vascular tree construction of the subject shown in Figure 3.2 is shown in Figure 3.10.

### 3.2.7 Quantifications

This section deals in detail with how values for blood flow and geometry parameters were calculated. Blood flow and diameter were calculated in cross sections perpendicular to the propagation direction of blood vessels. For each segment of interest in the vascular tree construction, that is for each \( b_i = \{ p_{i,1}, \ldots, p_{i,N_{\text{points}}} \} \), blood flow and diameter were evaluated along the segment. The direction of the normal to the cross section was defined, for a point \( p_{i,j} \), as

\[
\mathbf{n} = p_{i,j+3} - p_{i,j-3} \quad \text{for} \quad j = 4, \ldots, N_{\text{points}} - 3. \tag{3.13}
\]

A schematic view of a placement of a cross section in a vessel is shown in Figure 3.11. Apart from being an efficient way of estimating vessel direction, it excluded the first and last points in the segments, and so avoiding measuring too close to (potentially inside) a bifurcation between vessels. From the velocity images flow was calculated as the mean flow over the cardiac cycle,

\[
Q = \frac{1}{20} \int \int A \sum_{i=1}^{20} \mathbf{v}_i \cdot \mathbf{n} dA, \tag{3.14}
\]

where \( \mathbf{n} \) is the propagation direction of a blood vessel as defined in Equation (3.13). The area in Equation (3.14) over which flow was calculated was determined by the local boundary detection in the segmentation process. Blood flow and geometry quantifications were repeated for the four local boundary detection methods described in Section 3.2.5. The cross sections were limited in size
Figure 3.10: A pruned and indexed vascular tree construction. Different colors show different segments.

Figure 3.11: Placement of a crosssection in a vessel. The skeleton points are used to estimate the normal to the cross section.
to a grid of 17 by 17 pixels, or about 11.7 by 11.7 mm. Bilinear interpolation was used to create cross sections of the same resolution as the original data. Interpolation was performed in two steps, rotating a volume of 17 by 17 by 17 voxels in the xy-plane, followed by a rotation in the xz-plane.

This approach quantified blood flow and diameter as a function of location along a vessel. This could be compared an to approach such as the one by Wåhlin et al. (2012), where blood flow were averaged over a short segment in a relatively straight part in a vessel. Both approaches are viable and both have advantages and disadvantages. Blood flow evaluation could be less accurate in vessels where they have a high degree of curvature, causing perhaps turbulent flows. The approach by Wåhlin et al. (2012), deals with these potential problems, by allowing the user to decide where in a vessel to measure blood flow. However, measuring only over a short segment, could mean noisier measurements and could be prone to suffer from intra- and inter-user variability. The approach used in this report, where blood flow is evaluated along an entire vessel, produces additional information. By sampling at several points along a branch in a segment in the vascular tree construction, many more measurements are made, likely resulting in a more robust measurement. It becomes possible to investigate internal consistency in a branch, by examining the spread of the measurements, and potential trends. The approach is also systematic, minimizing inter- and intra-user variability. Diameter and length of branches were evaluated to produce nominal values for classes of branches, and was used in the labeling process. Nominal geometric values for the major arteries in the Circle of Willis are presented in Table 3.1. The length of a branch (in voxels) was defined as the number of voxels in that branch.

Table 3.1: Nominal values for the vessel classes. The nominal values are obtained using the LPC method.

<table>
<thead>
<tr>
<th></th>
<th>ICA</th>
<th>MCA</th>
<th>ACA</th>
<th>BA</th>
<th>PCA</th>
</tr>
</thead>
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<td>flow (ml/s)</td>
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<td>2.42</td>
<td>1.41</td>
<td>2.11</td>
<td>1.00</td>
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<td>3.1</td>
<td>2.7</td>
<td>3.4</td>
<td>2.4</td>
</tr>
<tr>
<td>length (voxels)</td>
<td>121</td>
<td>14</td>
<td>23</td>
<td>38</td>
<td>42</td>
</tr>
</tbody>
</table>

Section 3.4 describes how the blood flow quantifications were validated. For the purpose of validation, blood flow was calculated as the mean over subsegments in the branches. As large subsegments as possible were used to minimize the effect of noisy measurements. However, to minimize the incorrectness that could occur from small undetected vessels connected to the MCAs, the ACAs, the BAs and the VAs, blood flow was calculated as the mean over a part in each of the segments belonging to each of these classes. Blood flow in the MCA, ACA and BA was calculated as the mean over the first 10 cross sections, while blood flow in the vertebral arteries was calculated over the last 10 cross sections. To avoid an error in blood flow quantification resulting from a build-up of signal strength close to the neck in the acquired images, blood flow in the ICA was calculated as the mean over the 31st to the last cross sections.
3.2.8 Artery Labeling

An artery labeling algorithm was developed to detect the existence or non-existence of and to automatically label a total of nine vessels, the left and right ICA, the left and right MCA, the left and right ACA, the BA and the left and right PCA. The algorithm was constructed so that the segments in the vascular tree construction were considered candidates to each of the nine vessel classes. Each of the segments probability to belong to each of the classes were determined by the comparison to an atlas and to nominal values of geometry and blood flow of that class. The segments were combined into various configurations, allowing a few vessels to be missing. Spatial requirements between segments and a flow summation criteria were used to exclude and penalize configurations which were not intrinsically aligned correctly or showing large deviations in summation of blood flow.

Atlas construction has been used to label brain tissue in MRI (Fischl et al., 2002). Here, voxels were assigned to brain tissue classes based on probabilistic information. The labeling was enhanced by setting spatial requirements between brain tissue classes.

A set of atlases were created from the data analyzed in this report. A probabilistic framework was set up as described briefly above and in detail below to produce the labelings. The developed algorithm is described in Algorithm 3 and further explained below.

Atlas Construction

An atlas is a construction that relates spatial location in an image with probabilities of occurrences of objects. Brain anatomy is bound by certain restrictions and display certain patterns, as was described in Section 2.1, and motivates the construction of an atlas. Atlas construction is however made difficult by anatomical variations. Anatomical variations include variations not only in geometry and location, but also in occurrences of objects. Another issue is how to relate spatial coordinates in an image to those in an atlas, a subject’s brain MR angiogram needs to be aligned with the atlas for a good comparison. During data acquisition, good alignment between subjects were observed, including location and rotation inside the imaging volume. This was exploited in a rather simple atlas construction, where an atlas was constructed by stacking segmentations of classes of blood vessels on top of each other.

For each of the ten subjects, \( i = 1, 2, \ldots, 10 \), an atlas function \( f_{i,j}(r) \), was calculated from the remaining nine subjects to avoid comparing each of the subjects to itself. For each subject a set of nine sub-functions were created to be able to analyze classes of vessels separately, \( j = 1, 2, \ldots, 9 \). The atlas functions were constructed by assigning labels manually to the nine vessel classes in the vascular tree construction. For each vessel class, the manually labeled vascular tree construction segments were added to produce a binary image, \( C \), as shown in Figure 3.12. The image was then dilated,

\[
D = C \oplus B = \{(p + q) | p \in C, q \in B\}, \tag{3.15}
\]

where \( B \) is a ball shaped structuring element with radius 7 voxel units. The dilation operation effectively expands and merges the vascular tree construction...
segments in Figure 3.12. The dilated image \( D \) was smoothed by a gaussian filter to produce the final atlas functions \( f_j(r) \), where \( 0 \leq f_j(r) \leq 1, \forall r \).

Figure 3.12: A set of nine (excluding the tenth branch) ICA branches used to construct an atlas.

**Probabilistic Framework**

A probabilistic framework was set up in which first single branches in the vascular tree construction was rated on how probable they were to belong to either of the nine classes of vessels. Second, the most probable branches for each vessel class were combined into configurations which in turn were rated on a whole as being probable configurations of branches. The process was set up separately for the anterior and posterior part of the Circle of Willis, apart from that no overlap was allowed (no branch could be labeled more than once).

Given a subject with the set of images \( I \) and atlases \( f_j(r) \), the labeling was performed in a number of steps. Each segment in the vascular tree construction that overlapped a class in the atlas was assigned a probable candidate to this class. Segments assigned to the classes ICA and BA were excluded if they did not propagate upwards in the brain. Segments assigned to the classes MCA and PCA were excluded if they did not propagate outwards from the circle of Willis. The initial probability of each assigned segment to belong to the respective assigned class was expressed as a score \( \omega_{\text{initial}} \) based on prior knowledge of the
vessel class.

\[
\omega_{i,j} = 6 \left( \frac{\int b_i f_j(r)}{l_{\text{nominal},j}} - 1 \right) + \left| \frac{l}{l_{\text{nominal},j}} - 1 \right| + \left| \frac{d}{d_{\text{nominal},j}} - 1 \right| + \left| \frac{Q}{Q_{\text{nominal},j}} - 1 \right| \tag{3.16}
\]

\(b_i\) is the \(i\):th branch segment and \(l_{\text{nominal},j}\), \(d_{\text{nominal},j}\) and \(Q_{\text{nominal},j}\) are the average length, diameter and flow of the 10 subject’s segmentations. The nominal values are presented in Table 3.1. The first term in Equation (3.16) captures the agreement of a branch to the atlas. The second term penalizes long segments occurring as potentials for a vessel class normally consisting of a short vessel. The third and fourth term captures the agreement in diameter and flow to nominal values. Flow and diameter are correlated, in that large vessels generally carry high flow, but the correlation is non-linear, which motivates the inclusion of both terms. In Equation (3.16), a low score indicated a good match for a segment to a vessel class. The five best scoring segments for each class were considered probable enough to be combined into a number of configurations for subsequent evaluation.

Configuration probabilities were calculated separately for the anterior and posterior part of the Circle of Willis, dividing the nine classes of vessels into two subgroups of classes. For both the anterior and posterior part of the Circle of Willis, a maximum number of two vessels, \(N_{\text{missing}} = 2\), were allowed to be missing. This was motivated by morphological variation between subjects, where branches can be missing (Krabbe-Hartkamp et al., 1998). The number of vessel classes in each subgroup was \(N_{\text{sub}} = 6\) and \(N_{\text{sub}} = 3\) for the anterior and posterior part, respectively. The number of potential vessels for each class from the initial screening was set to \(N_{\text{pot}} = 5\). This resulted in a number of configurations,

\[
N_{\text{configs}} = \left( \frac{N_{\text{sub}}}{N_{\text{sub}}} \right)^{N_{\text{pot}}} + \left( \frac{N_{\text{sub}}}{N_{\text{sub}} - 1} \right)^{N_{\text{pot}}^{N_{\text{sub}} - 1}} + \ldots + \left( \frac{N_{\text{sub}}}{N_{\text{sub}} - N_{\text{missing}}} \right)^{N_{\text{pot}}^{N_{\text{sub}} - N_{\text{missing}}}}. \tag{3.17}
\]

For the anterior part \(N_{\text{configs}} = 43750\), and for the posterior part \(N_{\text{configs}} = 215\). Several configurations could have their probabilities set to zero based on a few exclusion criteria. First, configurations where more than one label had been assigned to the same segment were excluded. The same segment could be assigned to more than one label because of an overlap in the atlas. For example, a left ICA could be mistaken for a left MCA or left ACA. Second, some vessels should occur in a fixed spatial order. This was implemented by excluding configurations where the two groups of vessels left MCA - left ACA - right ACA - right MCA and left PCA - right PCA did not appear in a left to right order. Third, configurations where the MCA and the ACA were not connected via one junction on the left and right sides respectively were excluded.

The approach in which one or more vessels are allowed to be missing, has the disadvantage of always picking the minimum number of vessels with the best individual scores. A configuration should however make sense out of a conservation of mass perspective. Therefore a score based on flow conservation
An approximative flow conservation score was constructed and defined as, for the left and right part separately for the anterior part of Circle of Willis,

\[
\Delta Q = \hat{Q}_{ICA} - \hat{Q}_{MCA} - \hat{Q}_{ACA} \quad \text{if } \hat{Q}_{ICA} \text{ exist}
\]

\[
\Delta Q = \frac{\hat{Q}_{MCA} - \hat{Q}_{ACA}}{(\hat{Q}_{MCA} + \hat{Q}_{ACA})/2} \quad \text{if } \hat{Q}_{ICA} \text{ does not exist}
\]

(3.18)

and as

\[
\Delta Q = \frac{\hat{Q}_{BA} - \hat{Q}_{PCA_L} - \hat{Q}_{PCA_R}}{(\hat{Q}_{PCA_L} + \hat{Q}_{PCA_R})/2} \quad \text{if } \hat{Q}_{BA} \text{ exist}
\]

\[
\Delta Q = \frac{\hat{Q}_{PCA_L} - \hat{Q}_{PCA_R}}{(\hat{Q}_{PCA_L} + \hat{Q}_{PCA_R})/2} \quad \text{if } \hat{Q}_{BA} \text{ does not exist}
\]

(3.19)

for the posterior part. Let \( k \) be the remaining configurations, so that \( k = 1, \ldots, N_{\text{remain}} \) and \( N_{\text{remain}} \leq N_{\text{configs}} \). Each branch segment index, \( i \), associated to a label \( j \) in a configuration \( k \), is denoted \( i(j,k) \). In each configuration \( k \), let \( N_k \) denote the number of labeled branches. Then, following this notation, the final score for each of the configurations, \( \Omega_k \), was defined as

\[
\Omega_k = \sum_j \omega_{i(j,k),j} + \Delta Q_j \quad \frac{N_k}{N_k},
\]

(3.20)

where \( j = 1, 2, \ldots, 6 \) for the anterior part and \( j = 7, 8, 9 \) for the posterior part of the Circle of Willis. The configuration with the lowest \( \Omega_k \) for the anterior and posterior part, respectively, were the best scoring configurations, and branches were labeled thereafter.

**Labeling algorithm**

1. find potential branches to all classes
2. for all potential branches do
   1. exclude branches propagating in the wrong direction
3. end
4. combine best matching branches into configurations
5. for all configurations do
   1. if branches are uniquely labeled then
     1. if spatially correct then
       1. if fulfill connectivity criteria then
         1. calculate flow summation score
         2. update total score
       2. else
         1. delete configuration
     2. else
       1. delete configuration
   2. else
     1. delete configuration
   end
6. end
7. Keep configuration with lowest score

**Algorithm 3:** Labeling algorithm
3.3 Visualization

A visualization tool was developed mainly to be able to validate the labeling of arteries. The arteries would appear color-coded in the complex difference image as well as the anatomical image. A scrolling function allowed for the user to scroll axially, sagittally and coronally through the segmentations. The visualization tool also provided a simple interface for relabeling arteries. The interface is shown in Figure 3.13.

Figure 3.13: The visualization tool allowed the user to scroll through the segmentations. The graph shows blood flow over one heart cycle for a selected vessel.

3.4 Validation

The accuracy of the segmentation algorithm was evaluated for its ability to quantify blood flow and to label arteries. In the validation process of blood flow quantification, vessels were labeled manually to ensure that no errors would occur from mislabeled arteries. By evaluating blood flow quantification and labeling of arteries separately, interference between the two processes was eliminated. The ability to quantify blood flow accurately was evaluated based on the concepts of mass conservation and internal consistency, as presented in Section 3.4.1. The ability to correctly recognize a few key arteries in the vascular tree, was judged based on a set of criteria presented in Section 3.4.2.

3.4.1 Blood Flow Quantification

To determine the validity of a segmentation’s ability to quantify blood flow, an approach similar to that by Roldán-Alzate et al. (2012) was taken. The flow quantifications were evaluated indirectly based on two criteria. First, conservation of mass was considered at two set of junctions. The blood flow in the
ICA should be equal to the blood flows in the ACA, the MCA and the PCoA combined,

\[ \vec{Q}_{ICA} = \vec{Q}_{MCA} + \vec{Q}_{ACA} + \vec{Q}_{PCoA}, \]  

(3.21)

and the conservation of mass error at the ICA junction was defined as

\[ \text{Error}_{ICA} = \frac{\vec{Q}_{MCA} + \vec{Q}_{ACA} + \vec{Q}_{PCoA} - \vec{Q}_{ICA}}{\vec{Q}_{ICA} + \vec{Q}_{MCA} + \vec{Q}_{ACA} + \vec{Q}_{PCoA}}. \]  

(3.22)

Also, the blood flow in the BA should be equal to the sum of the blood flows in the left and right vertebral arteries,

\[ \vec{Q}_{BA} = \vec{Q}_{VAl} + \vec{Q}_{VAR}, \]  

(3.23)

and the conservation of mass error at the BA junction was defined as

\[ \text{Error}_{BA} = \frac{\vec{Q}_{BA} - \vec{Q}_{VAl} - \vec{Q}_{VAR}}{\vec{Q}_{BA} + \vec{Q}_{VAl} + \vec{Q}_{VAR}}. \]  

(3.24)

However, a conservation of mass analysis at the BA junction could be subject to error resulting from additional small blood vessels close to it. Second, internal consistency in the ICA was evaluated using the coefficient of variation (CV), which was defined as the standard deviation of the flow divided by the mean flow along the ICA.

### 3.4.2 Artery Labeling

Labeling accuracy was assessed by the consensus of two experts. The observers evaluated the algorithms ability to classify the ICA (left and right), the ACA (left and right), the MCA (left and right), the BA, and the PCA (left and right), based on three criteria. For each of the nine blood vessel classes, the criteria were:

1. Determination of the existence or non-existence of the vessel.
2. Assignment of the right label to the class.
3. Labeling in such a way that efficient flow quantification could be performed. This meant that the MCA-labeled segments should start with the M1 segment, the ACA-labeled segments should start with the A1 segment, and that the PCA-labeled segments should start with the P1 segment, as shown in Figure 2.1.

The first criteria was designed to be able to take into account physiological variations. There are nine potential vessels of interest in each subject, but not all subjects have all these vessels represented. The second criteria was designed to test wether the right labels (ICA left, ICA right, MCA left, etc.) were assigned to the right vessels. The third criteria was designed to label subsegments of the MCA, the ACA and the PCA, rather than necessarily including entire vessels. For example, in the vascular tree construction, depending on the prominence of the ACoA, the A1 and A2 segments could be segmented as separate branches or as one branch. Labeling the A1 segment as ACA, although not including all of ACA, was more relevant from a flow quantification perspective than including the entire ACA or labeling the A2 segment as ACA.
4 Results

The overall goal stated in the introduction to this report was to develop an automatic tool that would accurately quantify blood flow and label the major arteries in the Circle of Willis. Results of the blood flow quantifications and the labeling of arteries are presented separately in Sections 4.1 and 4.2 respectively. In Section 4.1, arteries were manually identified and labeled to eliminate any contribution in error from the labeling process. The overall functionality, including an evaluation of the segmentation tools ability to work automatically, is presented in Section 4.3. The vascular tree construction algorithm was created to be able to quantify blood flow and label arteries. However, several useful side-effects of this reconstruction were produced that adds to the functionality of the tool, and a few examples are described here. These examples are presented qualitatively, since no specific validations on them were performed. The tools ability to separate branches from each other in the vascular tree efficiently and accurately was not directly evaluated, but affected the overall result to a large extent, and is therefore implicitly partly responsible for the results presented here.

4.1 Flow Quantification

The four boundary detection methods were compared by analyzing the means and standard deviations of the conservation of mass error for each method and for each category of junction (ICA and BA). Figure 4.1 shows the comparison for the ICA junction, and Figure 4.2 the comparison for the BA junction. The coefficients of variation in the ICA for the four methods are shown in Figure 4.3. Corresponding numerical values are presented in Table 4.1. In the 10 subjects, 19 junctions of the ICA splitting into the MCA, the ACA and the occasional PCoA were identified. In one subject’s right cerebral hemisphere, no ACA or PCoA were apparent in the segmentation, resulting in the ICA and MCA appearing as one segment and disregarded in the flow quantification analysis. 7 junctions of the left and right VAs coming together into the BA were identified. In the remaining 3 subjects, one of the vertebral arteries were either missing or too small to be detected in the segmentation process. At the ICA junction, the tMIP, LPC and Prin-Comp showed good agreement in

<table>
<thead>
<tr>
<th></th>
<th>tMIP</th>
<th>LPC</th>
<th>LPC-HT</th>
<th>Prin-Comp</th>
</tr>
</thead>
<tbody>
<tr>
<td>Error_{ICA}</td>
<td>3.3 ± 7.7 %</td>
<td>-0.9 ± 6.5 %</td>
<td>-11.7 ± 11.7 %</td>
<td>0.9 ± 7.5 %</td>
</tr>
<tr>
<td>Error_{BA}</td>
<td>-9.0 ± 2.4 %</td>
<td>-13.1 ± 9.6 %</td>
<td>-11.6 ± 11.1 %</td>
<td>-12.2 ± 6.4 %</td>
</tr>
<tr>
<td>CV</td>
<td>7.8 ± 5.6 %</td>
<td>8.1 ± 2.7 %</td>
<td>8.4 ± 2.5 %</td>
<td>17.7 ± 8.1 %</td>
</tr>
</tbody>
</table>

Table 4.1: Conservation of mass errors and coefficients of variation for the four boundary detection methods.
Figure 4.1: Mean conservation of mass errors from 19 ICA junctions. Error bars show one standard deviation. The errors were calculated as $(\tilde{Q}_{MCA} + \tilde{Q}_{ACA} + \tilde{Q}_{PCoA} - \tilde{Q}_{ICA})/((\tilde{Q}_{ICA} + \tilde{Q}_{MCA} + \tilde{Q}_{ACA} + \tilde{Q}_{PCoA})/2)$.

Figure 4.2: Mean conservation of mass errors from 7 BA junctions. Error bars show one standard deviation. The errors were calculated as $(\tilde{Q}_{BA} - \tilde{Q}_{VA_{L}} - \tilde{Q}_{VA_{R}})((\tilde{Q}_{BA} + \tilde{Q}_{VA_{L}} + \tilde{Q}_{VA_{R}})/2)$.
conservation of mass. The LPC method showed the lowest conservation of mass error (−0.9±6.5 %). The LPC-HT method showed the largest error (−11.7±11.7 %). The methods tMIP, LPC and LPC-HT showed similar mean values in coefficient of variation, the Prin-Comp method showed in comparison a large coefficient of variation. With similar mean values of coefficient of variation, but with lower conservation of mass error, the LPC method was considered to outperform the tMIP method at the ICA junction. The LPC-HT method performed poorly considering conservation of mass principles, and the Prin-Comp method resulted in a relatively noisy segmentation, performing poorly in the coefficient of variation comparison. A correlation analysis was performed and produced an $r$ value of 0.88 for the LPC method. Slope of 0.95 and intersect of 0.19 were obtained. A correlation plot is shown in Figure 4.4.

At the BA junction, all methods showed an average negative error (ranging from an average of −9.0 to −13.1 %). A correlation analysis for the LPC method showed a higher correlation statistic compared to the ICA junction, $r = 0.95$, and with slope 1.21 and intersect −0.12. A correlation plot is shown in Figure 4.5. The negative errors in Figure 4.2 indicate a loss of blood flow between the vertebral arteries and the basilar artery.

Average blood flow values for all methods are presented in Table 4.2.

### 4.2 Artery Labeling

The labeling was assessed by a consensus of two experts. The assessment was formulated both quantitatively and qualitatively. For each vessel class in each subject a score of 1, 0.5 or 0 was assigned representing a correct, partly correct
Figure 4.4: Correlation plot for the LPC method at the ICA junction. Blood flow in the ICA branch is correlated to the sum of blood flow in the branching blood vessels. The dashed line shows equal flows.

Figure 4.5: Correlation plot for the LPC method at the BA junction. Blood flow in the BA branch is correlated to the sum of blood flow in the left and right VAs. The dashed line shows equal flows.
Table 4.2: Average blood flow values (ml/s) obtained with the four methods for boundary detection.

<table>
<thead>
<tr>
<th></th>
<th>tMIP</th>
<th>LPC</th>
<th>LPC-HT</th>
<th>PCA</th>
</tr>
</thead>
<tbody>
<tr>
<td>ICA</td>
<td>3.80 ± 0.48</td>
<td>4.02 ± 0.52</td>
<td>3.85 ± 0.49</td>
<td>3.82 ± 0.54</td>
</tr>
<tr>
<td>MCA</td>
<td>2.47 ± 0.27</td>
<td>2.42 ± 0.30</td>
<td>2.08 ± 0.28</td>
<td>2.37 ± 0.43</td>
</tr>
<tr>
<td>ACA</td>
<td>1.36 ± 0.45</td>
<td>1.41 ± 0.38</td>
<td>1.21 ± 0.39</td>
<td>1.34 ± 0.36</td>
</tr>
<tr>
<td>BA</td>
<td>2.28 ± 0.53</td>
<td>2.11 ± 0.52</td>
<td>1.95 ± 0.51</td>
<td>2.33 ± 0.56</td>
</tr>
</tbody>
</table>

or incorrect labeling, respectively. With this notation, a total success rate of 83 % was achieved, with a partial success rate of 93 % for the anterior part and 63 % for the posterior part of the Circle of Willis. A summation of the labeling accuracy is shown in Table 4.3. A full score-board is presented in Table 4.4. For the anterior part of the circle of Willis, labeling was completely correct in 8 of 10 subjects. The discrepancies in Table 4.3 belong to the other 2 subjects. In the right hemisphere of subject 6, neither ACA or ACoA were existent, resulting in the ICA and the MCA being segmented as one object in the vascular tree construction, rather than as two separate vessels. In the right hemisphere of subject 9, a short part of the ICA was segmented as a separate vessel, this segment was incorrectly labeled ACA right, the true ACA right as well as the MCA right were not labeled. The discrepancies in the posterior part of the Circle of Willis were larger than in the anterior part. Two major causes for these errors were apparent, in 4 out of 5 cases where the BA was partly correct or incorrect, one of the vertebral arteries was labeled BA. In 3 out of 8 cases where the PCA was partly correct or incorrect, the PCA started in the P2 segment rather than in the P1 segment. In 3 other cases where the PCA was partly correct or incorrect, the superior cerebellar artery was labeled PCA. An example of a correctly labeled subject is shown in Figure 4.6.

Table 4.3: A summary of the labeling accuracy. The vessels in the anterior part of the Circle of Willis are more often correctly labeled than the vessels in the posterior par.

<table>
<thead>
<tr>
<th></th>
<th>correct</th>
<th>partly correct</th>
<th>incorrect</th>
</tr>
</thead>
<tbody>
<tr>
<td>ICA</td>
<td>18</td>
<td>2</td>
<td>0</td>
</tr>
<tr>
<td>MCA</td>
<td>18</td>
<td>0</td>
<td>2</td>
</tr>
<tr>
<td>ACA</td>
<td>19</td>
<td>0</td>
<td>1</td>
</tr>
<tr>
<td>BA</td>
<td>5</td>
<td>1</td>
<td>4</td>
</tr>
<tr>
<td>PCA</td>
<td>12</td>
<td>3</td>
<td>5</td>
</tr>
</tbody>
</table>
Table 4.4: Detailed labeling accuracy in the 10 subjects. Most subjects (8 of 10) have one or more mislabeled arteries.

<table>
<thead>
<tr>
<th></th>
<th>s1</th>
<th>s2</th>
<th>s3</th>
<th>s4</th>
<th>s5</th>
<th>s6</th>
<th>s7</th>
<th>s8</th>
<th>s9</th>
<th>s10</th>
</tr>
</thead>
<tbody>
<tr>
<td>ICA left</td>
<td>1</td>
<td>1</td>
<td>1</td>
<td>1</td>
<td>1</td>
<td>1</td>
<td>1</td>
<td>1</td>
<td>1</td>
<td>1</td>
</tr>
<tr>
<td>ICA right</td>
<td>1</td>
<td>1</td>
<td>1</td>
<td>1</td>
<td>1</td>
<td>0.5</td>
<td>1</td>
<td>1</td>
<td>0.5</td>
<td>1</td>
</tr>
<tr>
<td>MCA left</td>
<td>1</td>
<td>1</td>
<td>1</td>
<td>1</td>
<td>1</td>
<td>1</td>
<td>1</td>
<td>1</td>
<td>1</td>
<td>1</td>
</tr>
<tr>
<td>MCA right</td>
<td>1</td>
<td>1</td>
<td>1</td>
<td>1</td>
<td>1</td>
<td>0</td>
<td>1</td>
<td>1</td>
<td>0</td>
<td>1</td>
</tr>
<tr>
<td>ACA left</td>
<td>1</td>
<td>1</td>
<td>1</td>
<td>1</td>
<td>1</td>
<td>1</td>
<td>1</td>
<td>1</td>
<td>1</td>
<td>1</td>
</tr>
<tr>
<td>ACA right</td>
<td>1</td>
<td>1</td>
<td>1</td>
<td>1</td>
<td>1</td>
<td>1</td>
<td>1</td>
<td>1</td>
<td>0</td>
<td>1</td>
</tr>
<tr>
<td>BA</td>
<td>1</td>
<td>0.5</td>
<td>0</td>
<td>0</td>
<td>1</td>
<td>1</td>
<td>1</td>
<td>0</td>
<td>0</td>
<td>1</td>
</tr>
<tr>
<td>PCA left</td>
<td>1</td>
<td>1</td>
<td>0.5</td>
<td>1</td>
<td>0.5</td>
<td>1</td>
<td>1</td>
<td>0</td>
<td>0</td>
<td>1</td>
</tr>
<tr>
<td>PCA right</td>
<td>0</td>
<td>1</td>
<td>1</td>
<td>0</td>
<td>1</td>
<td>1</td>
<td>1</td>
<td>0.5</td>
<td>0</td>
<td>1</td>
</tr>
</tbody>
</table>

Figure 4.6: A successfully labeled subject. All existing arteries are correctly labeled, the right PCA is not existent and is not labeled.
4.3 Functionality

The segmentation tool, working through all steps except the data acquisition step in Figure 3.1 worked completely automatic. Starting with the user specifying a search path to a set of images $I$, the segmentation process proceeded extracting global features, which were used to create a binary representation of the vascular tree, enabling the construction of a skeleton which was used to separate branches from each other to create a vascular tree construction. Blood flow and geometry were quantified in these branches, and some branches were labeled based on their alignment to an atlas and comparison to nominal values of blood flow and geometry, ending with a full vascular tree reconstruction. The complete automaticity of the tool came with a few disadvantages. Although partly successful, the labeling process were prone to mislabel one or a few arteries per subject. The full automaticity didn’t come with full labeling accuracy. Some post-processing could therefore be beneficial to correct for any such discrepancies, to relabel the occasional mislabeled arteries.

Much information other than blood flow was obtained in the segmentation process. Geometric information was extracted and used in the labeling algorithm. Geometric information can also be useful on its own and provide valuable information. The vascular tree construction could be used to evaluate tortuosity, which is important to the diagnosis of many diseases (Bullitt et al., 2003). Diameter information along vessels could be useful in stenosis evaluation. An example of where blood flow and diameter of the ICA is plotted from the neck to the Circle of Willis is shown in Figure 4.7. Total computation time on a typical subject was about 6-9 min on an iMac 2.93 GHz Intel Core i7 with 16 GB of RAM.

![Figure 4.7: Plotting of blood flow and diameter along one ICA vessel. In the flow quantification validation process, the first 30 measuring points are cut off due to a build-up of signal strength.](image)
5 Discussion

Of the four methods used to quantify blood flow, the tMIP, the LPC and the Prin-Comp methods were shown to produce the most accurate segmentations based on a conservation of mass evaluation in the ICA junction. The Prin-Comp method showed a much larger coefficient of variation than the three other methods. The LPC method showed less average error and less deviation and could be considered a better candidate for blood flow quantification than the tMIP method. Using velocity data was shown to benefit segmentation of the large thoracic vessels by calculating an LPC image (Schmidt et al., 2009). In this report velocity data was shown to be useful for segmentation in 4D PC-VIPR MRA of the cerebral vascular tree. A conservation of mass evaluation at the ICA junction showed an average error of $-0.9\pm6.5\%$, which could be compared to the conservation of mass errors of $5.9\pm2.5\%$ and $5.8\pm3.1\%$ at two junctions in the liver obtained with 4D flow MRI by Roldán-Alzate et al. (2012). The LPC method appeared to have more contrast and make less difference between large arteries and small arteries and veins, in comparison to the tMIP method. However, blood flow in mainly large arteries (except for the occasional posterior communicating artery) were evaluated in this report. The explicit velocity data in the PC-VIPR acquisition was shown to be useful for segmentation purposes. The Prin-Comp method showed that analyzing temporal variance could also be used to distinguish blood vessels from the brain, however with no addition in accuracy and also producing noisy measurements. The model assumptions about circular blood vessels in the LPC images that were used in the LPC-HT method did not add any accuracy to the segmentations. All methods showed a negative error in the conservation of mass evaluation in the BA junction. The negative error indicate a loss of blood from the vertebral arteries to the basilar artery, and could have been influenced by the complex structure of small arteries originating from the basilar and the vertebral arteries. Many small vessels, such as the cerebellar arteries and the pontine at the basilar artery, or the vessels originating from the middle cerebral artery, often do not show up clearly on the scans due to limited spatial resolution and velocity encoding. This makes blood flow evaluation somewhat complex by introducing a potential inconsistency in a vessel. The results of the flow quantifications at the BA are ambiguous, even though care was taken to quantify blood flow in close vicinity to the junction, there seem to exist a systematic error in the measurements. This view is augmented by the relative high $r^2$ value in the correlation plot for the LPC method in the BA junction compared to the ICA junction. The slope of 1.21 in the correlation plot could indicate a systematic error. Especially the posterior and anterior inferior cerebellar arteries could have been the cause of this error. The ambiguity at the BA junction motivated that the results obtained at the ICA junction be weighted more. Also, a total number of 7 junctions at the BA were analyzed, compared to 19 at the ICA junction, providing comparable less statistical data. Quantifying blood flow is subject to several additional sources of error. Partial volume effects and blurring in MRI images can make it hard to distinguish the boundary between blood vessel and the rest of the
brain. These effects are especially considerable for small vessels, and could have interfered with the blood flow quantifications.

The labeling algorithm performed much better in the anterior part of the Circle of Willis compared to the posterior part. This was likely a cause of the relatively complex anatomy in the posterior part. The existence of the cerebellar arteries including the superior cerebellar artery just below the posterior cerebral arteries made it unfeasible to put constraints on connectivity between vessels. Overall, there were more segments in the posterior part of the Circle of Willis in the vascular tree construction. The construction of an atlas was shown to be very useful to label arteries. Spending more effort in atlas construction would most likely benefit the labeling process. Image registration could also be used to align an atlas with a set of data to improve precision (Fischl et al., 2002). The comparison of values of blood flow, diameter and length for specific branches might be inefficient for subjects with values deviating from the nominal values, this could be especially true for subjects with vascular disease. The labeling algorithm showed adaptability to variations in morphology by using combinatorics to allow for a few vessels to be missing. The analysis of configurations of vessels was found useful to incorporate structural information of the Circle of Willis. This could be improved by introducing more constraints on the configurations, pseudo-connectivity etc. Using an approximate conservation of mass score penalized configurations not making sense out of a flow conservation perspective. The PCoA and the smaller arteries originating at the BA were not considered, since they were not labeled. Labeling more arteries could make the conservation of mass score more effective.

The automaticity of the segmentation tool was to a great extent enabled by the vascular tree construction. By separating the vascular tree into indexed objects, blood flow and geometry could be quantified branch by branch. The vascular tree construction and the separation of branches were not directly evaluated, but was to a great deal influencing the results of the flow quantifications and enabling the labeling. The vascular tree construction used in this report used thinning and pruning techniques similar to those used to automatically construct a vascular tree in computed tomography angiography by Chen and Molloi (2003), and was shown to be efficient in 4D PC-VIPR images of the cerebral vascular tree. The vascular tree construction also enabled extensive evaluation of geometric parameters, which could be useful in future work. The vascular tree construction benefited from complete automaticity, compared to for example the segmentation approach by Schmidt et al. (2009), which required manual corrections of the centerline extraction.

The segmentation tool was constructed to work completely automatic. The complete automaticity suffered in the labeling stage, where the occasional mislabeling would occur. A completely automatic program also being completely accurate in labeling would need to overcome this problem. A few suggestions for improvements were stated here. The automaticity is valuable in that it is systematic, practically eliminating inter- and intra-user variability. The corrections sometimes needed in the labeling stage would also have a user reselect objects rather than selecting the exact location where to quantify blood flow.
6 Conclusions

In this report, methods for segmentation of intracranial arteries suitable for 4D PC-VIPR data were implemented and investigated. The report was limited to the large arteries in the Circle of Willis at the base of the brain. Four methods of boundary detection were implemented and evaluated in their ability to quantify blood flow accurately. The LPC method showed the smallest average relative error where the ICA splits into the MCA, the ACA and the PCoA based on conservation of mass principles. The coefficients of variation for the four methods were similar except for the Prin-Comp method, which showed a relative high error. Based on this analysis, segmentation based on temporal information might not be suitable for 4D PC-VIPR data.

Labeling of the ICAs, the MCAs, the ACAs, the BA and the PCAs showed the feasibility of a labeling algorithm. The anterior part of the Circle of Willis was correctly labeled at a higher degree than the posterior part (93 % in comparison to 63 %, respectively). This was concluded to be a result of more complexity in the anatomy in the posterior part of the Circle of Willis.

Full automaticity was obtained. The main downside of the automatic scheme was the occasional mislabeling. The vascular tree construction was found to be efficient and enabled to a great extent the labeling process. It also provided some extra features not evaluated in this report such as the possibility for geometric evaluations of segments and along-vessel analysis.

Future work could include improving the labeling process. An atlas construction were shown to be effective, but care needs to be taken when designing it. Image registration could possibly improve the accuracy in comparing a subject to an atlas. Further work could also include investigating optional methods for boundary detection to improve on blood flow and geometry quantifications. This could be especially interesting for smaller arteries and veins in the vascular tree, which were not evaluated in this report.
Bibliography


