Implementation and evaluation of motion correction for quantitative MRI

Examensarbete utfört i medicinsk informatik vid Tekniska högskolan i Linköping av

Jonatan Larsson

LiTH-IMT/MI30-A-EX–10/494–SE
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Image registration is the process of aligning two images such that their mutual features overlap. This is of great importance in several medical applications. In 2008 a novel method for simultaneous T1, T2 and proton density quantification was suggested. The method is in the field of quantitative Magnetic Resonance Imaging or qMRI. In qMRI parameters are quantified by a pixel-to-pixel fit of the image intensity as a function of different MR scanner settings. The quantification depends on several volumes of different intensities to be aligned. If a patient moves during the data acquisition the datasets will not be aligned and the results are degraded due to this. Since the quantification takes several minutes there is a considerable risk of patient movements. In this master thesis three image registration methods are presented and a comparison in robustness and speed was made. The phase based algorithm was suited for this problem and limited to finding rigid motion. The other two registration algorithms, originating from the Statistical Parametrical Mapping, SPM, package, were used as references. The result shows that the pixel-to-pixel fit is greatly improved in the datasets with found motion. In the comparison between the different methods the phase based algorithm turned out to be both the fastest and the most robust method.
Abstract

Image registration is the process of aligning two images such that their mutual features overlap. This is of great importance in several medical applications. In 2008 a novel method for simultaneous T1, T2 and proton density quantification was suggested. The method is in the field of quantitative Magnetic Resonance Imaging or qMRI. In qMRI parameters are quantified by a pixel-to-pixel fit of the image intensity as a function of different MR scanner settings. The quantification depends on several volumes of different intensities to be aligned. If a patient moves during the data acquisition the datasets will not be aligned and the results are degraded due to this. Since the quantification takes several minutes there is a considerable risk of patient movements. In this master thesis three image registration methods are presented and a comparison in robustness and speed was made. The phase based algorithm was suited for this problem and limited to finding rigid motion. The other two registration algorithms, originating from the Statistical Parametrical Mapping, SPM, package, were used as references. The result shows that the pixel-to-pixel fit is greatly improved in the datasets with found motion. In the comparison between the different methods the phase based algorithm turned out to be both the fastest and the most robust method.

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Chapter 1

Background

In this chapter the purpose and the problem description of this master thesis is presented. A brief introduction to medical images is presented as well as an introduction to MRI. Finally quantitative MRI is presented together with the problems caused by patient movements.

1.1 Purpose

The purpose of this master thesis is to implement and evaluate registration algorithms that handles the problem of patient movements in quantitative Magnetic Resonance Imaging. The main focus of the evaluation is to investigate how the movement affects the quantification. A comparison between the registration algorithms have also been made.

1.2 Problem

The process of aligning two images is called image registration. When the images are considered to be aligned, mutual features, such as lines and edges, overlap. There are several clinical applications that require image registration. If, for example, one would want to study the development of a tumour over a time period with one before and one after image, image registration will help to emphasize the differences by aligning the images. Another field requiring registration is functional MRI, fMRI. In fMRI brain activity is mapped by comparing brain volumes from activity and rest. Active regions are found by studying the MRI signal over time and this demands a perfect alignment of the volumes.

In 2008 a novel method for a simultaneous $T_1$, $T_2$ and proton density quantification was suggested by Warntjes et al.\cite{1}. The new approach quantifies the properties of interest in one sequence and images of certain echo and repetition times can be reconstructed with postprocessing. The quantification method is based on a curvefitting of the voxel intensities in the datasets.
In some areas the registration algorithm have to handle non-rigid transformations. If the case of study is the development of breast cancer, the deformation of the tissue when doing the screening is non-rigid. In the case of quantitative MRI on the other hand the different scans are done with such short amount of time in between that structural changes inside the brain are extremely unlikely. The datasets are taken at different time points which influences the magnetization of the voxels and thereby the intensity in the volumes. For that reason the registration algorithm cannot depend on intensity information. Image registration of volumes with different intensities have been adressed, for example in the field of qMRI [2].

Since the acquisition takes several minutes to finish it can be hard for the patient to lie perfectly still. Motion during the acquisition creates motion artefacts. When the acquisition is done the voxels from the different volumes might not be aligned. This is problematic since voxels of different tissue types are fitted in a curve assuming that their magnetic properties are the same. The errors can be seen in a quantification of the relaxation rate R1 [2], figure 1.1, or when watching the curve fitting result of one voxel, figure 1.2.

Figure 1.1: Example of quantification of the relaxation rate R1 on an axial slice of the brain on a healthy volunteer. A: Normal measurement without movement. B: Corrupted measurement where the subject rotated his head from right to left. Severe artifacts occur throughout the image. C: Motion corrected image with the phase based algorithm. D: Motion corrected image with mutual information.
1.3 Magnetic Resonance Imaging - MRI

This section will begin with a short summary of the development of medical imaging and then describe MRI in detail.

1.3.1 Medical Imaging

The beginning of medical imaging started when Roentgen discovered the X-rays in 1895. By letting radioactive substances decay and at the same time send energy through the body and register the photons on a screen behind the person, Roentgen could distinguish between tissue and bone. About fifty years later the x-ray technique took further steps when development of the image intensifier was made and about 20 years later the CT was introduced and facilitated a possibility for imaging 3D volumes. In the fifties the ultrasound technique was introduced to medicine. This new modality, originating from the sonar technique used in the second world war, offered something that x-rays could not, it was free from radiation. MRI, or Magnetic Resonance Imaging, is a spinoff from another scientific field, NMR or Nuclear Magnetic Resonance. Although MRI still uses the signals from nuclei the N in the acronym was removed since it gave negative associations to nuclear power. As early as in the fifties J.R. Singer proposed that NMR could be used as a non-invasive tool for measuring bloodflow. In 1971 it was found that signals from tumours in mice had longer relaxation times than those of healthy tissue. This was a big breakthrough for investigations since it offered a higher contrast between cancerous and normal tissue than x-rays and ultrasound could provide. Since MRI is based on picking up signals from the magnetic properties of the body, this technique was also free from ionizing radiation. In 1973, Paul Lauterbur, used magnetic gradients to be able to distinguish between signals from
different location in the body. During the seventies a slice selective technique was born and the first 2D images were produced. After these inventions the development really brisked and today about 35 000 scanners are operational worldwide.

1.3.2 A backward summary of MRI

As in the book of McRobbie et al. [3] a short introduction of MRI will be given, starting with the images. As the authors express it: "you don’t expect to understand how the internal combustion engine works before you learn to drive". A more detailed explanation follows later then starting with the physics. The backward summary will go through the following

1. The contrast of the images
2. Picking up signals
3. What part of the body does the signal come from?

1. The contrast of the images

The contrast of the images exist due to the fact that different tissue have different magnetic properties. The measured signal depends on several magnetic properties of the proton. Depending on what magnetic property we want to study, the scanner settings are altered. Often the settings are set such that different tissue will differ in contrast thanks to their different magnetic properties.

2. Picking up signals

The signals are picked up by coils inside the MR scanner. The signals are not the actual image but the Fourier transform of it, which will be shown later. The Fourier transform of the image tells us what the frequency content of the image looks like. The image is therefore produced by taking the inverse Fourier transform of the signal. What frequencies to collect can be chosen by alternating the scanner settings and when the frequency content of our wish is collected the image can be produced. If higher frequencies are collected finer details will be seen in the image, but the scan time will increase. A brain slice together with its corresponding frequencies is presented in figure 1.3

3. What part of the body does the signal come from?

The protons in the body act as small magnetic spins that are aligned with the main magnetic field of the MR scanner. A Radio Frequent (RF) pulse can push them away from the equilibrium state. The pulse has to match the Larmour equation. The spins then experience a torque perpendicular to the main magnetic field and they will start to precess around its axis. When the RF pulse is turned off, the precession will continue while the spins relax back to the equilibrium state. During
1.3 Magnetic Resonance Imaging - MRI

(a) The image in the spatial domain. (b) The magnitude of the image in the Fourier domain.

Figure 1.3: A image shown in the (a) spatial and (b) Fourier domain. The Fourier domain plot is in log-scale. In (b) the signals picked up by the coils are shown this time a coherent precession of many spins can be picked up by the RF coils as a macroscopic signal. The coils are sensing the alterations in the magnetic field the protons produce. Since the combination of the magnetic field and the radio frequency is important to match the resonance frequency of the protons, one can apply a magnetic field that grows in strength from head to toe. Then it is only a small slice of the body that matches the correct combination of radio frequency and the magnetic field strength. The protons of that slice only will emit the signal which is measured.

1.3.3 MRI In detail

A more detailed explanation of the technique of MRI, starting with the physics and ending with the images, will be given in the following paragraphs.

The physics

Every human being contains a lot of water, and water contains hydrogen ions or protons. These protons have magnetic properties that make them interesting to study. If a magnetic field is applied a force will drive the protons to different energy levels, the so called Zeeman effect. The force is proportional to the magnetic field strength and puts the protons in two different energy levels, depending on their inner spin. The magnetic difference between the groups of protons at the different levels can be expressed as a magnetic vector. By applying a radio frequency, it will be showed that these are the matching frequencies, the protons will move from the
lower energy level to the higher and alter the net magnetization. The potential energy produced by the magnetic field is given by

\[ U = -\mu B \]  

(1.1)

and the difference between the energy levels is given by

\[ \Delta U = 2\mu B \]  

(1.2)

By using the energy of the photons at the radio frequency \( E = hf \), where \( h \) is Planck’s constant, we get a matching criterion for the frequency

\[ hf = 2\mu B \]  

(1.3)

Typical clinical usage is magnetic field of strength 1-3 T which gives us frequencies in the radio frequency domain. Equation 1.3 can be rewritten into

\[ \omega = \gamma B \]  

(1.4)

where \( \gamma \) is called the gyromagnetic ratio and equation 1.4 is called the Larmour equation. The total magnetization of the protons can be replaced by a resulting magnetic moment. A vector can visualize the axis the protons are spinning around and the length the strength of the magnetization. When applying an external magnetic field the vector will align with the field. Therefore the alternating magnetic field caused by the protons cannot be separated from the magnetic field by the surrounding coils. The coils are rather designed to find magnetism orthogonal to the external magnetic field. To be able to see the signal from the protons it is therefore necessary to flip the the magnetization vector into the orthogonal plane of the external field. This is done by applying a second magnetic field directed in the xy-plane. This gradient have to rotate with the Larmour frequency since the protons needs to be influenced by the resonance frequency. The movement of the magnetization \( M \) is given by

\[ \left( \frac{\delta M}{\delta t} \right)_{fix} = \gamma M \times B \]  

(1.5)

and an example can be seen in figure 1.4. Since the gradient in the transverse plane is rotating with the Larmour frequency it is convenient to switch to a rotating frame such that

\[ \left( \frac{\delta M}{\delta t} \right)_{rot} = \left( \frac{\delta M}{\delta t} \right)_{fix} - \omega \times M = \gamma M \times B - \omega \times M = \gamma M \times (B + \frac{\omega}{\gamma}) \]  

(1.6)

If the Larmour frequency is choosen to be the angular moment of the rotating frame, \( \omega = -\omega_0 \) and \( B = B_0 = \gamma \omega_0 \), then the magnetization, \( M \), will be considered to be static. By using the rotating frame and inserting the applied gradient, \( B_1 \), the equation will be

\[ \left( \frac{\delta M}{\delta t} \right)_{rot} = \gamma M \times \left( B_0 + \frac{\omega}{\gamma} + B_1 \right) = \gamma M \times B_1 \]  

(1.7)
Figure 1.4: If looked upon in a static frame, the magnetic vector will rotate down to the transverse plane.

if the rotating frame is rotating with the Larmour frequency.

The cross product gives a vector orthogonal to the two vectors. This means that the motion caused by the $B_1$ field will always be orthogonal to $B_1$ and $M$. Considered to be inside the rotating frame, the $B_1$ gradient is a static vector in the $xy$-plane and the magnetization, $M$, is a static vector aligned with the $z$-axis. So for example if the $B_1$ gradient is aligned with the $x$-axis, then the magnetization will move towards the $y$-axis, and when aligned it will continue to move towards being aligned with the negative $z$-axis, and then continue to rotate as long as the gradient is turned on. As soon as the $B_1$ field is switched off the magnetization will once again align with the $B_0$ field. The total movement of the magnetization vector is called the flip angle and depends on the strength of the $B_1$ field and the duration it is turned on, it can be calculated according to

$$\alpha = \tau \int_0^\tau \gamma B_1(t) \delta t$$  \hspace{1cm} (1.8)

The resonance properties of the RF-pulse has another important task, it will make the protons precess in phase. This is very important since just turning the magnetization to the transverse plane such that the coils have a signal to pick up, would still leave the protons precessing randomly in that plane. If the protons precess with different phase the resulting signal is weak, while it is strong if they precess in phase. As soon as the RF pulse is ended the protons will begin to dephase.
and the picked up signal will decay. The dephasing of the protons will decrease the signal and is a property of different tissue. The variable describing how fast the signal decays due to phase incoherence is called \( T_2 \). The protons will again go back to being aligned with the magnetic field, the time for realigning is different for different tissues and the variable describing the time is called \( T_1 \). The state when the protons are aligned with the magnetic field is called thermal equilibrium. The pulse sequences producing the images can consist of either gradient echoes, GE, or spin echoes, SE. Gradient echoes use a single RF pulse followed by a gradient pulse to create an echo. The spin echoes use two RF pulses to create the echo. The first RF pulse is usually a \( 90^\circ \) pulse and the second is a \( 180^\circ \) pulse. The second pulse will flip the dephasing and the protons will eventually return to a state in phase and the signal is acquired. Both type of sequences can produce \( T_1 \), \( T_2 \) and proton density, PD, weighted images. When using these pulse sequences the operator selects the flip angle, repetition time, TR, and the echo time, TE. For example if the \( T_1 \) property is to be studied a sequence that gives the largest signal difference between the tissues must be choosen. By using a short TE the signal will be sampled before the dephasing begins, and by using a short TR the tissues will realign with the magnetic field differently before the next RF pulse arrives and resulting in the best signals recieved from the tissue that is able to realign before every TR. For example fluids which have long \( T_1 \) times will be very dark in the images. Reasoning in the same fashion, the \( T_2 \) weighted images are created by using a long TE and a long TR. To achieve great differences between the tissues the signals have to dephase before collecting the echo. A long TR is needed since the tissue have to realign with the magnetic field before repeating the procedure. If a long TR and a short TE is used we will get a proton density weighted image.

**Slice selection**

The only way to make the protons emit a signal is to use the Larmour frequency, the frequency making equation 1.4 equal. By knowing this resonance frequency it is possible to select regions of interest in the body. By applying a gradient field that alters the strength of the \( B_0 \) field from top to toe, there will be only a small region along the body that will give resonance when using a certain frequency and only the protons that belong to that volume will be excited. The slice thickness depends on the bandwidth of the RF-pulse and the strength of the gradient field. Therefore when visualizing a 2D image, every pixel contains information from a small volume. A small sketch can be seen in figure 1.5.

**The math of k-space**

The following section is a summary and can be found in a greater context in [4]. After selecting a region of interest and exciting those protons, information that is spatially coded is gathered to be able to produce an image. For doing that gradients are applied to change the magnetic field \( B \) locally, according to

\[
B(\bar{x}) = B_0 + G(\bar{x}) = B_0 + g\bar{x}^T n
\]  

(1.9)
1.4 Quantitative MRI

The total magnetic field gives us a local magnetization, \( m(x,t) \)

\[
m(x,t) = m_0(x)e^{-i\omega t}
\]  

(1.10)

where

\[
\omega = \omega_0 + \gamma G(x) = \omega_0 + \gamma (g^T \pi)
\]  

(1.11)

Now look at the phase, which is the integral of the frequency, \( \omega \),

\[
\varphi_{\text{absolute}} = \int_0^t (\omega_0 + \gamma (g^T \pi)) d\tau = \omega_0 t + \gamma (g^T \pi)t
\]  

(1.12)

\( \omega_0 t \) is constant in the entire region of interest and the term can be removed by the coils. The other term on the other hand changes with location, the signal is the integral of the magnetization over the whole region

\[
S(t) = \int m_0 e^{i\varphi} d\vec{x} = \int m_0 e^{i\gamma g^T \pi t} d\vec{x} = \int m_0 e^{i\pi^T \pi t} d\vec{x}
\]  

(1.13)

where \( \pi \) is the 3D frequency vector. The equation shows that what the signal actually consist of is the magnetization sampled in the Fourier domain, or k-space as it is called in MRI studies. An image can thus be created by taking the inverse Fourier transform of the signal. With the help of the gradients it is possible to navigate through k-space and therefore gather the frequency information of the images. When comparing a general way of expressing a multidimensional Fourier transform

\[
F = \{m(\vec{x})\} = \int m(\vec{x})e^{-i2\pi^T \vec{\pi}} d\vec{x}
\]  

(1.14)

with the derivated expression in equations 1.12 and 1.13 it is possible to show that there is a connection between the gradients and the positions in k-space.

1.4 Quantitative MRI

Ever since the increased relaxation times in tumours was found in the seventies a great deal of interest have been put to the relaxation times in biological tissue.
The ideal situation searched for was distinct ranges of relaxation times for different tissues for exact identification. In classical MR images the discrepancy between tissues are carried out with the help of the scanner timing parameters TR and TE. Depending on these settings a variety of images with alternating contrasts between tissues can be obtained. Instead of characterizing the tissue by its appearance in different sequences, it could be characterized by the parameters $T_1$, $T_2$ and PD, assuming that every voxel consists of a single tissue.

### 1.4.1 Measuring the parameters

The principles of measuring the relaxation times are covered in [5] and can be further understood by reading [6].

**Measuring $T_1$ relaxation**

The definition of the $T_1$ relaxation time is derived from the Bloch equation for longitudinal relaxations:

$$\frac{dM_z(t)}{dt} = \frac{M_0 - M_z(t)}{T_1}$$  \hspace{1cm} (1.15)

The solution will set off at some starting point, $M_z(0^+)$, and then move towards equilibrium, $M_0$,

$$M_z(t) = M_0 + (M_z(0^+) - M_0)e^{-t/T_1}$$  \hspace{1cm} (1.16)

where the starting point is defined as the equilibrium flipped, $M_z(0^+) = M_z(0^-) \cos \theta$. $M_z(0^+)$ and $M_z(0^-)$ are the values before and after a pulse and if the pulse is repeated with TR, $M_z(TR) = M_z(0^-)$ and the steady-state solution is given by

$$M_z(0^-) = M_0 \frac{1 - e^{-TR/T_1}}{1 - \cos \theta e^{-TR/T_1}}$$  \hspace{1cm} (1.17)

which is proportional to the transverse magnetization, $M_{xy}$, given by

$$M_{xy}(t) = M_0 \frac{1 - e^{-TR/T_1}}{1 - \cos \theta e^{-TR/T_1}} \sin \theta$$  \hspace{1cm} (1.18)

There are four different ways of determining T1. Here follows a short description. For a detailed explanation, see [5].

1. **Partial saturation recovery**

   This approach uses repeated 90° pulses, usually with spin echo. Equation 1.18 then boil downs to

   $$M_{xy}(t) = M_0(1 - e^{-TR/T_1})$$  \hspace{1cm} (1.19)

2. **Spoilt gradient echo**

   In this approach spin echos are substituted with spoilt gradient echoes. This is reducing the repetition time, whilst keeping a reasonable SNR. The image sequence is thereby faster.
3. Inversion recovery

This method is slower than the methods above. Although it is not sensitive to $B_1$ errors. The inversion recovery sequence is using two repeated pulses separated by an inversion time.

4. Specialist methods

The specialist methods differ from the main approach described above. Among the specialist methods is Look-Locker, DESPOT, DESPOT2 and TAPIR. The methods are often very fast, but usually they require access to the MR imager to implement the sequences.

Measuring $T_2$ relaxation

The definition of the $T_2$ decay originates from the Bloch equation, by looking at the transverse magnetisation.

$$\frac{dM_{xy}(t)}{dt} = -\frac{M_{xy}(t)}{T_2}$$ (1.20)

The decay of the signal depends both on the dephasing of the protons and also the relaxation back to equilibrium. The dephasing is caused by time-invariant sources, for example local static field inhomogenities caused by $B_0$ inhomogenities. The dephasing can be counteracted by applying another RF pulse which reverses these effects and brings the protons to phase again. Therefore both the repetition time, TR, and the echo time, TE, influences the signal strength according to

$$M_{xy}(TR, TE) = M_0(1 - e^{-TR/T_1})e^{-TE/T_2}$$ (1.21)

1.4.2 QRAPMASTER

QRAPMASTER (Quantification of Relaxation Times and Proton Density by Multi-echo acquisition of a saturation-recovery using Turbo spin-Echo Readout) is a method developed at CMIV (Center for Medical Image Science and Visualization) in Linköping for fast simultaneous quantification of the relaxation times, $R_1$ and $R_2$, and the proton density. This section is a summary and can be found in a more circumstantial description in [1]. The method is a substantially improved version of the method QRAPTEST developed in 2007 [7]. The mathematical description of the curve fitting does not originate from these sources. The search for faster and more accurate methods in MRI has steered the interest towards quantitative MRI. However one major setback of the quantification have been the time required. One of the major advantages of the QRAPMASTER method is that the quantification can be done in a time that is clinically acceptable. The robustness of the quantification is also increased since all parameters are quantified within a single scan. The amplitude of the local $B_1$ field is also quantified in the method.
Pulse sequence

A pulse sequence is a protocol that determines how the k-space is collected by the MR scanner. In QRAPMASTER an average of several acquisitions are used to increase the signal to noise ratio (SNR). Every acquisition starts with a saturation pulse. The saturation pulse is a pulse combination that is supposed to remove longitudinal and transversial magnetization. After the saturation pulse a FLASH (Fast Low Angle SHots) pulse is applied. The relaxation back to thermal equilibrium is shorter than the normal $T_1$ relaxation, and is called $T_1^\ast$. During the relaxation four points on the $T_1^\ast$ relaxation curve are sampled. The points are not sampled during the same flash relaxation, several flash pulses are used and the sampling is divided into four phases, one for each datapoint. For each flash two points on the $T_2^\ast$ relaxation curve is also sampled by doing a twin echo.

Measuring $T_1$

Since the validation and evaluation of the work of this master thesis is limited to the fitting of $T_1$ and not the $T_2$ and PD, only the $T_1$ estimation will be described. After setting up the model for the parameters, a curve fitting method needs to be implemented. One approach, weighted linear least square fitting, is presented in the following paragraph. To solve a least square error problem that includes an exponential function will generate a great deal of problems. An easy way around the problem is to use the logarithm of the derivate instead

$$\frac{dM_z(t)}{dt} = \frac{1}{T_1}(M_0 - M_0^\ast)e^{-t/T_1}$$  (1.22)

$$\log \frac{dM_z(t)}{dt} = -\log T_1 + \log M_0 - M_0^\ast - t/T_1$$  (1.23)

which can be expressed as a function of $t$

$$g(t) = \beta_1 + \beta_2 t$$  (1.24)

With this linear description the least square error approach gets a much more appealing appearance. The sampled points from the datasets must be processed in the same way as the original model. That means that the derivate between the data points must be calculated and logarithmed. There are some considerations regarding the weights that must be considered. Datapoints close to the $M_z(0^+) \equiv M_0$ have a steeper derivate and are of great importance for the derivate fitting, although the points that are closer to the equilibrium have a higher SNR. The weights in the implementation in this thesis were chosen with respect to the first consideration. They were chosen to be the derivates in the corresponding data point. The error minimized is defined as:

$$\arg \min_{\beta} \epsilon^2 = \arg \min_{\beta} \sum_i w_i |y_i - g(\beta, t_i)|^2 = \arg \min_{\beta} \|W^{1/2}(y - X\beta)\|^2$$  (1.25)

where
same expressions can bring the other two unknown parameters \( A \) and \( W = (y, X) \) and \( \beta = [\beta_1, \beta_2] \) setting the derivative, with respect to \( \beta \), equal to zero will give the solution, that is best in the weighted least squares sense.

\[
\frac{de^2}{d\beta} = -2(W^{1/2}X)^T||W^{1/2}(y - X\beta)|| = 0 \tag{1.26}
\]

and by using the facts that \((ab)^T = b^Ta^T\) and \(W^{1/2}W^{1/2} = W\), this can be expressed as

\[
X^TWX\beta = X^TWy \tag{1.27}
\]

\( \beta \) is thus estimated by

\[
\hat{\beta} = (X^TWX)^{-1}X^TWy \tag{1.28}
\]

Since the datasets considered in this master thesis only contain four volumes every voxel only has three valid derivative points. Since the term \(X^TWX\) will boil down to a 2 x 2 matrix, this saves a lot of computational power since if: \( A = \begin{bmatrix} a & b \\ c & d \end{bmatrix} \) then

\[
A^{-1} = \frac{1}{ad-bc} \begin{bmatrix} d & -b \\ -c & a \end{bmatrix}. \]

An explicit expression for the solution and the searched parameters is given by

\[
\begin{bmatrix} \hat{\beta}_1 \\ \hat{\beta}_2 \end{bmatrix} = \frac{1}{\sum_i w_i \sum_i t_i^2 w_i - (\sum_i t_i w_i)^2} \left[ \sum_i t_i^2 w_i \sum_i w_i y_i - \sum_i w_i t_i \sum_i w_i t_i y_i \right] \tag{1.29}
\]

where \( T_1 = \frac{1}{\beta_2} \). If the found \( T_1 \) value is assumed to be true, another curve fitting can bring the other two unknown parameters \( M_0 \) and \( M_0^* \). Starting over with the same expressions

\[
f(t) = M_0 - (M_0 - M_0^*)e^{-t/T_1} = \beta_1 + \beta_2 e^{-t/T_1} = \beta_1 + \beta_2 a(t) \tag{1.30}
\]

and a new least square error problem

\[
\arg \min_{\beta} \epsilon^2 = \arg \min_{\beta} \sum_i w_i|y_i - f(\beta, a(t_i))|^2 = \arg \min_{\beta} ||W^{1/2}(y - X\beta)||^2 \tag{1.31}
\]

where

\[
W = \begin{bmatrix} w_1 & 0 & 0 & 0 \\ 0 & w_2 & 0 & 0 \\ 0 & 0 & \ddots & 0 \\ 0 & 0 & 0 & w_n \end{bmatrix}, y = \begin{bmatrix} y_1 \\ \vdots \\ y_n \end{bmatrix}, X = \begin{bmatrix} 1 & a(t_1) \\ 1 & a(t_2) \\ \vdots & \vdots \\ 1 & a(t_n) \end{bmatrix} \text{ and } \beta = \begin{bmatrix} \beta_1 \\ \beta_2 \end{bmatrix} = \begin{bmatrix} M_0 \\ M_0^* - M_0 \end{bmatrix}
\]

\( \hat{\beta} \) can then be calculated as

\[
\hat{\beta} = \frac{1}{\sum_i w_i \sum_i a(t_i)w_i - (\sum_i a(t_i)w_i)^2} \left[ \sum_i a(t_i)^2 w_i \sum_i w_i y_i - \sum_i w_i a(t_i) \sum_i w_i a(t_i) y_i \right. \\
\left. - \sum_i w_i a(t_i) y_i - \sum_i a(t_i) \sum_i w_i a(t_i) y_i \right] \tag{1.32}
\]
1.4.3 Registration in qMRI

Since the QRAPMASTER method is significantly decreases the scan time of an MRI quantification, the importance of non moving patients increases. When motion occurs it is continuous and will effect the volumes of the scan. If the motion is strictly increasing the datasets will have growing alterations. The registration of the qMRI volumes are performed between the volumes of the dataset. Ideally the motion would only occur between the sampling of the different volumes. The motion is however continuous and is happening throughout the scan and not just during the changes between phases. Motion during scans is an old problem and several ghosting artifacts are common, as can be seen in [8]. Despite the effects of motion during the scan, four volumes are still produced and the question to be answered in this master thesis is what effect post-processing in the form of registration will have on these volumes. Earlier it has been shown that phase based registration can be applied to the datasets of qMRI [2] with successful results.

1.5 Abbreviations

In the master thesis some abbreviations are used. These concern the algorithms and the parameter settings of the algorithms. In the SPM package one method is found under Realign and the other under Coregister. Since the inventors of the first algorithm described their algorithm as a solution for the most general problem formulation it is abbreviated GR in this master thesis, which stands for General Registration. The SPM coregistration algorithm is based on mutual information and is therefore abbreviated MI.

The registration methods are abbreviated as

PB = Phase based registration
GR = General Registration
MI = Mutual information registration

To clarify what scales are used som information is provided here:
For the phase based registration:
10 = 10 x 10 x 10 mm voxels
5 = 5 x 5 x 5 mm voxels
3 = 3 x 3 x 5 mm voxels
1 = 1 x 1 x 5 mm voxels

The algorithms of the statistical parametric mapping, SPM, package[9] have some parameters that are possible to adjust. When dealing with the scale of the algorithms the separation parameter is used in mutual information and in the general registration. The separation parameter is an average distance between sampled points in mm. Example:
PB(10-5-3) means that the phase based algorithm was used with scales 10,5 and 3.
GR(8-4) means that the general registration was used with separation set to 8
followed by 4.

The tolerances in mutual information are doubled from their default values for faster convergence. The algorithm stops when the differences between the estimates in each iteration are less than the tolerance. The default values are 0.02 mm for the translations and 0.001 radians for the rotations. There are also six additional tolerances.

In the thesis a specific coordinate system is used to explain some concepts. When the text is concerning the images then the xy-plane is the same as the transverse plane. A person lying in a MR scanner will have an increasing z value from toe to head.

The default interpolation method used in the algorithms was trilinear interpolation.
Chapter 2

Theory of image registration

Image registration in medical imaging can be classified into a number of different techniques. Emerging from stereotactic surgery, there are the frame-based and the landmark-based approaches. The frame-based technique is very robust, but is of obvious reasons not a postprocessing technique. The technique, based on landmark, is for the same reason not applicable if the landmarks are outside the head. If some inside anatomy is used, it must be visible in all volumes from the different modalities or settings. The remaining techniques are then the surface-based and the voxel-based techniques. For finding usable surfaces, segmentation algorithms first have to be applied. The voxel-based algorithms only takes into account the values in each voxel and does not depend on a segmentation algorithm and are therefore not limited by the performance of a prior algorithm.

The voxel based approach

The greatest problem with voxel based approaches, when registering images from different modalities or settings within the modalities, is the fact that each voxel only contains a grayscale value representing the intensity. When collecting information from different modalities, these intensities will not match. A straightforward intensity based algorithm will therefore not be able to solve the problem. For that reason one must find another measure that is based on the information within the image, rather than using the intensity directly.

2.1 Phase based registration

The phase based algorithm is, as the name suggests, using the phase of the images. As long as mutual features, such as lines and edges, occur, it has a good chance of succeeding. The locale phase and magnitude can be calculated from a filter response. The magnitude is heavily dependant on the intensity, while the local phase is not. The description of the phase based algorithm will start off by describing the filter class used.
2.1.1 Usage of filters

As will be discovered in the section of the mathematical theory of the phase based algorithm, some filters will be needed. As presented earlier, some features of the volumes that is independent to intensity and can be used as information in the registration is searched for. Lines and edges therefore becomes of certain interest and one way to handle them is to use the local phase of the analytical signal. A popular filter class used in computer vision and especially motion detection is quadrature filters [10]. The math below is further explained along with some examples of usage, in the review note by Derpanis [11].

Quadrature filters

The theory of quadrature filters is strongly related to the Hilbert transform. The Hilbert transform, $F_h(\omega)$ of a signal, $f(x)$, is defined as:

$$F_h(\omega) = isign(\omega) F(\omega)$$  

(2.1)

where $F(\omega)$ is the Fourier transform of $f(x)$ and

$$sign(\omega) = \begin{cases} 1, & \omega > 0 \\ 0, & \omega = 0 \\ -1, & \omega < 0 \end{cases}$$  

(2.2)

The amplitude is conserved while positive and negative frequencies are shifted by $\pm \pi/2$. By adding the Hilbert transform to the original signal, an analytical signal is created,

$$f_a(x) = f(x) - if_h(x)$$  

(2.3)

In the Fourier domain this can be written as

$$F_a(\omega) = (1 - i(isign(\omega)))F(\omega) = (1 + sign(\omega))F(\omega) = \begin{cases} 2F(\omega), & \omega > 0 \\ 1, & \omega = 0 \\ 0, & \omega < 0 \end{cases}$$  

(2.4)

The analytical signal does not have any negative frequency components. Quadrature filters are often used to estimate the analytical signal and at the same time applies a bandpass filtering. The quadrature filters $Q$ used in the phase based algorithm can mathematically be written as

$$Q = R(||u||)D(u)$$

where $R(||u||)$ is a radial function:

$$R(||u||) = e^{\frac{-4}{B^2} \ln^2 \left( \frac{||u||}{u_0} \right)}$$  

(2.5)

where $B$ is the bandwidth and $u_0$ is the center frequency of the filter. $D(u)$ determines the direction of the filter, which is a necessity for using the filters to acquire phase information, since phase has a direction. $D(u)$ is defined as

$$D_k(u) = \begin{cases} (u^T \hat{n}_k)^2, & u^T \hat{n}_k > 0 \\ 0, & \text{otherwise} \end{cases}$$  

(2.6)
where \( \hat{n} \) is the direction of the \( k \):th filter. The filter is complex valued in the spatial domain, see figure 2.1. The imaginary part of the filter is odd and therefore detects edges. The real part is even and is good for finding lines. When optimizing the filters we have two ideas of how an ideal filter is supposed to look, one in the spatial and one in the frequency domain. To change the image, or volume, as little as possible, the filter should be a dirac impulse of height one in the origin of the filter. In this case the actual value of the voxel will be selected. In the Fourier domain there is also an ideal appearance of the filter. In [12] Knutsson et al. show that an error estimation technique embracing the design in both domains can be used to create optimal filters. The filter parameters used in the thesis were \( B = 3 \) and \( u_0 = \pi/3 \).

2.1.2 The math of the phase based registration

The registration algorithm used in the phase based registration is based on two assumptions given below

I. The difference between the volumes can be said to have been accomplished by a motion \( \Delta x \) that locally can be expressed as

\[
I(\vec{x},t) = I(\vec{x} + \Delta \vec{x}, t + 1) \tag{2.7}
\]

II. The intensity of the image can locally be seen as a leaning plane

\[
I(\vec{x} + \vec{v}(\vec{x}), t + 1) = I(\vec{x}, t + 1) + \nabla I^T \vec{v} \tag{2.8}
\]

where \( \vec{v}(\vec{x}) = [v_x v_y v_z]^T \). The variable \( t \), often the abbreviation for time, is in this case rather an index of which of the volumes refered to. In figure 2.2 the first assumption is shown in 1D. Using equations 2.7 and 2.8 together gives

\[
I(\vec{x},t) = I(\vec{x} + \Delta \vec{x}, t + 1) = I(\vec{x}, t + 1) + \nabla I^T \vec{v}
\]
we can derive us the optical flow equation
\[ \nabla I^T \mathbf{v} - \Delta I = 0 \tag{2.9} \]
where \( \Delta I = I(x, t + 1) - I(x, t) \). The problem with these assumptions is that assumption I demands that the intensity has not changed between the images. In the case of qMRI the intensity between the volumes differ significantly, as described earlier. By applying quadrature filters to the images filter responses are received that can be divided into magnitude and phase. The magnitude is strongly correlated with the intensity, the phase, however, is not. It is therefore a good idea to substitute the intensity in the optical flow equation with the complex valued local phase \( \varphi \)
\[ \nabla \varphi^T \mathbf{v} - \Delta \varphi = 0 \tag{2.10} \]
where the differences between the phase of the volumes is calculated as
\[ \Delta \varphi = \varphi_1 - \varphi_2 = arg(\varphi_1, \varphi_2^*) \tag{2.11} \]
The indices 1 and 2 corresponds to the phase of the filter responses from volume 1 and 2 (reference volume and target volume).

The movement \( \mathbf{v}(x) \) of the second volume is modelled with the help of 12 parameters
\[ p = [p1, p2, p3, p4, p5, p6, p7, p8, p9, p10, p11, p12]^T \]
The first three represent the translations of the volume and the last nine represent the transformation matrix:
\[ \mathbf{v}(x) = \begin{bmatrix} p1 \\ p2 \\ p3 \end{bmatrix} + \begin{bmatrix} p4 & p5 & p6 \\ p7 & p8 & p9 \\ p10 & p11 & p12 \end{bmatrix} \begin{bmatrix} x \\ y \\ z \end{bmatrix} \tag{2.12} \]
Equation 2.12 can then be modified into

$$
\bar{v}(x) = \begin{bmatrix}
1 & 0 & 0 & x & y & z & 0 & 0 & 0 & 0 & 0 & 0 \\
0 & 1 & 0 & 0 & 0 & 0 & x & y & z & 0 & 0 & 0 \\
0 & 0 & 1 & 0 & 0 & 0 & 0 & 0 & 0 & x & y & z
\end{bmatrix} \overline{p} \tag{2.13}
$$

The transformation matrix, p4-p12, can handle all affine transformations; skewing, mirroring, rotation and scaling. Although it is intuitive to believe that the motion of the head is a rigid transformation, that is a pure translation and a rotation, one can therefore think that only six parameters will be needed. This subject will be covered in greater detail later in section 3.1.1. We also define a certainty measure based on the magnitude of the filter responses:

$$
c = \sqrt{|q_1q_2| \cos \left( \frac{\Delta \phi^2}{2} \right)} \tag{2.14}
$$

The certainty measure make sure that in the event of similar phases from the two filter responses the magnitude has to be high as well. The local phase is not meaningful to interpret if the magnitude is low. The certainty measure is calculated for each filter response. Now taking the optical flow equation with the phase, 2.10, and the parametrization, 2.13, we can formulate an error that we want to minimize

$$
\epsilon^2 = \sum_k \sum_i (c_{ik} (\nabla \varphi)^T B(\mathbf{x}_i) \overline{p} - \Delta \varphi_k (\mathbf{x}_i))^2 \tag{2.15}
$$

The summation over k is the directions specified by the filters and the summation over i stands for all the voxels. The best solution for 2.15 can be found by derivat- ing the equation with respect to the parameter vector and setting it to zero, i.e. \( \frac{\delta \epsilon^2}{\delta \overline{p}} = 0 \).

$$
\sum_k \sum_i c_{ik} B^T_i \nabla \varphi_{ik} \nabla \varphi^T_{ik} B_i \overline{p} = \sum_k \sum_i c_{ik} B^T_i \nabla \varphi_{ik} \Delta \varphi_{ik} \quad \Rightarrow \quad \boxed{\overline{p} = A^{-1} \mathbf{h}} \tag{2.16}
$$

One advantage of this method compared to other methods is that the best solution can be found by solving a 12 variable linear equation system instead of searching for a optimal similarity between the volumes. The optimal movement of each voxel is calculated and put into this parameter vector. The best global solution can therefore not be found in one iteration. So why do not all local equations of each voxel give the same result? It depends on what the filters can see in those voxels. All neighbourhoods do not contain lines or edges; the sum of the proposed movements from all voxels is therefore thought to be a more correct estimate. Due to several reasons the algorithm has to be iterated to find the optimal parameter
vector. It is important to build up the parameter vector, and not iteratively move
the volume since each movement requires interpolation and interpolations have
smoothing effects. The altered volume should only have been moved once.

2.2 The techniques of SPM package

The SPM program created for Matlab there are two different techniques for image
registration. The first, called the realignment algorithm, is thought of as some
kind of preprocessing tool for fMRI volumes and the other, called co-registration,
is presented as more of an algorithm for different modalities, although it is also
found under the fMRI section of the program. Even though they have their place
in the program, both are applicable for registering volumes.

2.2.1 A general technique

Maybe the most general approach to this problem is the one made by Friston
et al [13]. When assuming perfect alignment of the two volumes that are to be
registered, an intensity operator transforms intensity values between a specified
position in the images. The second component of the algorithm is then proposed
to eliminate the misalignment between the images. These components can be
summarized into:

$$f\{I_1(x)\} = I_2(q(x)) \quad (2.18)$$

where $f\{\cdot\}$ is the operator changing the intensity and $q(x)$ is a movement function.
Here we also assume no difference between the images. Some constraints are then
put on the intensity transformator $f\{\cdot\}$, for example it is assumed to be locally
stationary meaning that the operator can change within the volume but is the same
in a small neighbourhood. When dealing with rigid body movements the spatial
transformation function can be constrained to six parameters, three representing
the translation and three the rotation. $f\{\cdot\}$ is equal to a nonlinear function $\gamma(.)$
convolved with a kernel $c(x)$

$$f\{\cdot\} = c(x) \ast \gamma(.) \quad (2.19)$$

The nonlinear function can then be expanded into $\gamma(.) = \sum u_i(x)f^iI_1(x)$ where
$f^i$ consists of some mathematical expansion, e.g. a polynomial or a Taylor series.
$u_i$ on the other hand can be chosen as some smooth spatial basis functions

$$u_i(x) = \sum u_{ij}\beta_{f_i}(x) \quad (2.20)$$

The movement function can be expanded in a similar way:

$$q(x) = x + \sum q_k\beta_{q_k}(x) \quad (2.21)$$

With these expansions equation 2.18 is modified into the following equation

$$c(x) \ast \sum f^iI_1(x) \sum u_{ij}\beta_{f_j}(x) = I_2(x + \sum q_k\beta_{q_k}(x)) \quad (2.22)$$
If we use a Taylor expansion of the right hand side of equation 2.22 then we get

\[ I_2(x + \sum q_k \beta_{q_k}(x)) = I_2(x) + \sum q_k \beta_{q_k}(x)dI_2/dx. \]

The validity of this particular expansion is described extensively in [13]. After bringing the simplifications from the Taylor expansion to equation 2.22 we get that

\[ c(x) \ast \sum f^i I_1(x) \sum u_{ij} \beta_{f_j}(x) - \sum q_k \beta_{q_k}(x) dI_2/dx = I_2(x) \quad (2.23) \]

This equation can then be put into a matrix form

\[ A[u_0 u_1 \ldots q]^T = I_2(x) \quad (2.24) \]

the parameter vector \([u_0 \ldots q]^T\) can then be solved analytically

\[ [u_0 u_1 \ldots q]^T = (A^TA)^{-1}A^TI_2(x) \quad (2.25) \]


### 2.2.2 The mutual information approach

Mutual information is a concept used in probability theory and information theory. Loosely it can be explained to be a measurement that tries to answer the question of how much two variables have in common. The mathematical description is given by

\[ I(X,Y) = \sum_{x \in X} \sum_{y \in Y} p(x,y) \log \left( \frac{p(x,y)}{p(x)p(y)} \right) \quad (2.26) \]

where \(p(x,y)\) is the joint probability distribution and \(p(x)\) and \(p(y)\) are the marginal distributions. Wells et al. [14] introduced the concept to image registration of medical images. They proposed a measure \(T\) to maximize that is based on mutual information

\[ \hat{T} = I(r(x), T(v(x))) \quad (2.27) \]

where \(r(x)\) is a voxel from the reference volume and \(v(x)\) is a voxel from the volume to be registered, \(T(\cdot)\) is the transformation function. Mutual information can be expressed in terms of entropy according to

\[ I(x,y) = h(x) + h(y) - h(x,y) \quad (2.28) \]

where \(h(\cdot)\) is the entropy of a random variable and is defined as

\[ h(x) \equiv -\int p(x) \log p(x) dx. \]

The joint entropy is defined as

\[ h(x,y) \equiv \int p(x,y) \log p(x,y) dxdy \]

and by rewriting equation 2.27 with entropy instead we get

\[ \hat{T} = h(r(x)) + h(T(r(x))) - h(r(x), T(v(x))) \quad (2.29) \]

where \(x\) is thought of as a random variable. We can already see that the first term in equation 2.29, \(h(r(x))\), does not depend on the transformation \(T\). The algorithm is constructed to search for the mutual information between 2-D histograms over the intensities from the volumes[15]. This measure is assumed to be maximal if
the volumes are perfectly aligned. It can be seen as a mapping between intensity values in the images. This approach makes it insensitive to inversion of intensities. The joint and marginal distributions used when calculating the entropies can be obtained by a normalization of the joint and marginal histograms of the overlapping parts. The criterion is then formulated as a function of the movement parameters. For brain volumes it is only sufficient to allow rigid transformations. When searching for the optimal solution the Powell’s multidimensional direction set with Brent’s one-dimensional optimization algorithm for the line minimizations is used in the SPM implementation. For increasing the robustness of the algorithm the order of parameters to optimize can be chosen. The algorithm is designed to find movements in the z-plane first, since such motion are not as constrained by the shape of the head, as motion in the the other planes.

2.3 Rotational center

When finding the correct movement between two images or volumes, an origin has to be chosen for the algorithm. In the case of SPM the choice is on of the upper corners, and in the implemented phase based algorithm the choice is the center of the data. The placement of the origin does not matter, other than that a pure rotation between the volumes can be described without any translation with this approach.

If the chosen origin is denoted \( \mathbf{r} \), a point is denoted \( \mathbf{p} \) and the true center of rotation is denoted \( \mathbf{s} \)

\[
\mathbf{r} = \begin{bmatrix} r_x \\ r_y \\ r_z \end{bmatrix}, \mathbf{p} = \begin{bmatrix} p_x \\ p_y \\ p_z \end{bmatrix}, \mathbf{s} = \begin{bmatrix} s_x \\ s_y \\ s_z \end{bmatrix}
\]  

(2.30)

and the true rotation is described by the rotation matrix \( \mathbf{R} \). The new position is calculated by

\[
\mathbf{v} = \begin{bmatrix} p_x - s_x \\ p_y - s_y \\ p_z - s_z \end{bmatrix}
\]  

(2.31)

\[
\mathbf{Rv} = \mathbf{v}^* 
\]  

(2.32)

\[
\mathbf{v}_2 = \begin{bmatrix} p_x - r_x \\ p_y - r_y \\ p_z - r_z \end{bmatrix}
\]  

(2.33)

\[
\mathbf{Rv}_2 = \mathbf{v}_2^* 
\]  

(2.34)

\[
t = v^* - v_2^* = R(v - v_2) = R(p - s - (p - r)) = R(r - s)
\]  

(2.35)

Where the difference between rotating around the true rotation center and the chosen is a translation independent of position.
Chapter 3

Implementation

The implementation chapter is merely describing new implementations of the phase based algorithm. There are some references to the SPM program package in the end of the chapter.

3.1 Phase based registration

The phase-based algorithm was mostly implemented in Matlab in order to make a comparison to SPM. Therefore a greater deal of work was done to optimize the phase based method and just use the SPM package as a reference of speed and robustness, rather than trying to optimize both. There are three rather big changes made from the original phase-based algorithm described earlier. The first is adapting the algorithm to assuming that the motion is rigid. The other is a speed-up adjustment based on assumptions about the algorithm. The last adaptation is the introduction of certainty thresholds.

3.1.1 Rigid transformations

If the algorithm finds the proper solution to a rigid registration problem, the transformation matrix should turn out to consist of pure rotations, however this is not always the case. If we consider a 3D-rotational matrix it can be divided into three separate rotations, one around each axis

\[
\begin{bmatrix}
\cos \alpha & -\sin \alpha & 0 \\
\sin \alpha & \cos \alpha & 0 \\
0 & 0 & 1
\end{bmatrix}
\begin{bmatrix}
\cos \beta & 0 & \sin \beta \\
0 & 1 & 0 \\
-\sin \beta & 0 & \cos \beta
\end{bmatrix}
\begin{bmatrix}
1 & 0 & 0 \\
0 & \cos \gamma & -\sin \gamma \\
0 & \sin \gamma & \cos \gamma
\end{bmatrix}
\]
We cannot express the connection between the angles $\alpha$, $\beta$ and $\gamma$ and the parameters with the help of linear base vectors and the linear parametrization in 2.13 is crucial for solving the final equation system in the phase based algorithm. Looking at matrix B once again,

\[
B = \begin{bmatrix}
1 & 0 & 0 & x & y & z & 0 & 0 & 0 & 0 & 0 \\
0 & 1 & 0 & 0 & 0 & x & y & z & 0 & 0 \\
0 & 0 & 1 & 0 & 0 & 0 & 0 & 0 & x & y & z
\end{bmatrix}
\]

(3.1)

it shows the base vectors that makes the movement in each voxel possible, and the base vectors are all independent, leading to allowing affine movements. To be able to restrict the movement to a rigid body movement, some changes have to be made. Basically two strategies have been tested and will be described in the following paragraphs, where the rotational base vectors have proven to be the best choice.

**SVD - Single Value Decomposition**

The intuitive solution to this problem might be to try to find the rotation matrix closest to the proposed affine transformation matrix. If we apply a transformation matrix on a vector the new vector is

\[
\bar{x}_{\text{new}} = \begin{bmatrix}
a_1 & a_2 & a_3 \\
a_4 & a_5 & a_6 \\
a_7 & a_8 & a_9
\end{bmatrix} \bar{x}
\]

(3.2)

and the matrix describing the motion

\[
V = A - I
\]

(3.3)

If the found movement is true then A should be a rotation matrix. A single value decomposition can be made of every matrix [16], when dealing with full ranked square matrices this will be the same as finding the eigenvalues, a rotation matrix is however not square. A feature of rotation matrices is that all their singular values are equal to one. Every matrix can be decomposed by

\[
A = USV^T
\]

(3.4)

where $U$ and $V$ are orthogonal matrices and $S$ is a diagonal matrix. In the diagonal of $S$ we have the singular values. A way of transforming the transformation matrix of the affine phase based registration into a rotation matrix could therefore be done by doing the decomposition and then forcing the singular values to be one. This approach was, however, not succesful and the algorithm did not converge in a stable fashion. This is probably due to the fact that this method is not a method of finding the closest rotation matrix. For finding a solution for such a problem, manifolds can perhaps be helpful.
Rotational base vectors

The base vectors of the transformation matrix is exchanged with three "rotational" base vectors. Proper rotational vectors are not linear and cannot be used here, but vectors that imitate them can be used.

\[
B = \begin{bmatrix}
1 & 0 & 0 & -y & z & 0 \\
0 & 1 & 0 & x & 0 & -z \\
0 & 0 & 1 & 0 & -x & y
\end{bmatrix}
\] (3.5)

So why do these vectors imitate rotations and how can they be used? First of all when studying an arbitrary point, \((x, y, z)\), assumed to be part of a sphere, the rotational base vectors are all orthogonal to the vector pointing from the origin through the point, for example \((x, y, z)(-y, x, 0) = 0\). The rotational base vectors are therefore spanning up a tangent plane to the sphere containing the point, see figure 3.1. The rotational base vectors can for that reason not point directly to the true new point although the direction can be used to guide us to the true rotation.

In the general 3D case it can be argued that the vector to rotate around is

figure 3.1: The blue dot represents the ideal movement. The grid is the tangent-plane of the point to be rotated and the red line is the vector connected to the ideal movement

the parameter vector and the angle of choice is connected to the parameter vector according to \(||\vec{p}|| = \sin \gamma\). This can be proven to be true if one assumes that the parameter vector is the axis to rotate around and that the angle is either very small or dominated by one of the euclidian angles. For a proof of this, see appendix A. The found vector should not be used to make the correct movement as were the case in the original phase based algorithm. It should rather guide to find the true rotation. By using the parameter vector as rotation vector, and \(||\vec{p}|| = \sin \gamma\) as the angle the true movement can be estimated. See figure 3.2 for a intuitively understanding.
28 Implementation

(a) proposed vector in 2D
(b) proposed vector in 3D

Figure 3.2: In the 2D case (a) it is easy to see that the length of the vector relates to the angle according to \( \sin \alpha = |v| \). A similar relationship can be intuitively seen in 3D (b).

3.1.2 Speed up

There are some speedups of the algorithm that can be done when calculating the \( A \) matrix and \( h \) vector. The first is based on an assumption about the phase gradients and the other is an implementation for switching between the scales.

3.1.3 The gradients

First we recall the expressions given earlier in section 2.1.2

\[
A = \sum_k \sum_i c_{ik} B_i^T \nabla \varphi_{ik} \nabla \varphi_{ik}^T B_i
\]

\[
h = \sum_k \sum_i c_{ik} B_i^T \nabla \varphi_{ik} \Delta \varphi_{ik}
\]

For each of the three filter responses there are three directions with one gradient calculation in each. However the local phase is only defined for the direction of the filter. Therefore it is not necessary to use the phase gradients in the other directions. This leaves us with the following appearance of the gradients in each voxel

\[
\nabla \varphi_x = \begin{bmatrix} g_x \\ 0 \\ 0 \end{bmatrix}, \nabla \varphi_y = \begin{bmatrix} 0 \\ g_y \\ 0 \end{bmatrix}, \nabla \varphi_z = \begin{bmatrix} 0 \\ 0 \\ g_z \end{bmatrix}
\] (3.6)
This introduces a lot of zeros in the calculations and looking only at one voxel in every direction

\[ c_x B^T \nabla \varphi_x \nabla \varphi_x^T B = \]

\[ c_x \begin{bmatrix}
1 & 0 & 0 \\
0 & 1 & 0 \\
0 & 0 & 1 \\
-y & x & 0 \\
z & 0 & -x \\
0 & -z & y
\end{bmatrix}
\begin{bmatrix}
g_x \\
g_x \\
0 \\
0 \\
0 \\
0
\end{bmatrix}
\begin{bmatrix}
1 & 0 & 0 & -y & z & 0 \\
0 & 1 & 0 & x & 0 & -z \\
0 & 0 & 1 & 0 & -x & z
\end{bmatrix} =
\]

and the other directions will have similar appearances, this will decrease the amount of necessary computations since we can take advantage of knowing the zeros and the symmetry of the matrices and calculate the elements explicitly instead.

### 3.1.4 Next scale

If any of the bases in the algorithm is decided not to describe any movement, the calculation of \( A \) and \( h \) can be adjusted not to look for movement along that base. If one studies the complete \( A \) matrix and the \( h \) vector after the assumption regarding the gradients, one can see that every base is responsible for the values in one row and one column in \( A \) and one row, which is one value, in \( h \). This means that depending on which bases still are active, calculations can be removed and the \( A \) matrix and \( h \) vector can be shrunked. The main goal of the implementation is to quickly decide whether no motion is present in the dataset. If such decision can be made before the last scale, a lot of time is saved. Every iteration of the last scale takes approximately four seconds. If all three volumes iterated twice on the last scale, the elapsed time would increase with 24 seconds. If not all base vectors are removed, some time will still be saved since fewer calculations have to be made when calculating the \( A \) matrix and the \( h \) vector. This time is however not in the magnitude of seconds. However, it is important to understand the relations between the different base vectors. It seems that especially the rotational base vectors around \( x \) and \( y \) are closely related, and should only be removed if both are considered to not have found motion. The rotational base vectors are also adjusted together with the translations in the plane they are rotating in. The translational base vectors should not be removed either if the rotational base vector is still used to search for motion. If this behaviour is connected to the anisotropy or the construction of the rotation matrix is not investigated since all datasets are anisotropic.
3.1.5 Truncation

When using the filters in the phase based registration their are some edge effects one must consider. For speed considerations, the convolution with the edge and line finding filters are done in the Fourier domain. Because of the periodic behaviour of the discrete Fourier transform the volume is repeated in all three dimensions. This means that we will have non valid filter responses from the borders of the volume. A simple and convenient way to handle this problem is to throw away those voxels in the algorithm. The lower the resolution the more information is stored in each voxel and a large piece of the total volume will in those cases get thrown away. To handle this problem, voxels must be added allowing the voxels on the edges to be considered as valid information. Since the information searched for is phase, it is important not to add information that could influence the algorithm. One easy way to add phase-free information is to fill out the volume with half the filter size out the edges with the last row and column, also known as edge extraction. After calculated on this new volume, half the filter size can be thrown away, and the valid information all the way to the edges is regarded. Depending on the look of the volume this truncation step is not always necessary. If the object is within the volume by some voxels the truncation will not affect the registration. Also when the size of the volume increases the percentage of information thrown away will decrease, which can make the truncation redundant. In figure 3.3 it is obvious

![Image](image.png)

Figure 3.3: The volumes with a region of voxels that won’t be thrown away (inside the square). (a) the reference volume (b) volume to be registered

that the registration will not work without truncation since all mutual edges are outside the kept region. With truncation the entire object will contribute to the registration, see figure 3.4.
3.1 Phase based registration

3.1.6 Anisotropic voxels

In general it is important to implement the algorithm such that the grid used corresponds to real world measures. In the 10 x 10 x 10 mm scale the algorithm have to be constructed so that every data point is considered to have 10 mm distance to the next data point in all directions. This is of importance when switching between the scales since no alterations on found movements have to be done if the algorithm is consistent. The anisotropcity must also be considered when the filters are constructed. When the implementation was done, three strategies were tested.

I. Since the algorithm looks for three translations and three rotations one could weight the findings depending on what direction they influence. If the voxel are sampled 1 x 1 x 5 mm then rotations in the xy-plane must have been found in the xy-planes which were denser sampled. Therefore the rotation found around the z-axis is more certain than those around x and y.

II. The second way of thinking about the problem is the field of view of the filter. We sample down the volumes such that bigger movements can be seen within the filter sizes. But if the filter is isotropic the size of the filter corresponding the real world will differ. A cubic filter of voxel size 9 will correspond a 9x9x45 mm box if the voxel is sampled 1x1x5 mm. The solution should be to have an isotropic size in the real world. If the voxel size is 1x1x5 mm the filter should be 9x9x9/5 (9x9x2, since it should be integers).

III. Since the voxels are anisotropic we can think of the dataset as isotropically sampled and averaged or lowpass filtered in one or two directions. This means that we have removed high frequencies in those directions, which should be considered

Figure 3.4: Same volumes as in figure 3.3, but here the edge extraction has been used. (a) the reference volume (b) volume to be registered.
Implementation

when creating the filters. The filters used in the phase based algorithm are based on radial functions. One way to alter the filters is to sample denser in the lowpass filtered directions, which will have the effect of adjusting the filter to pick up lower frequencies. The handling can be compared with the Nyquist theorem, since it is of no use to search for certain frequencies if the sample frequency is too low. This approach was later chosen since it seemed most stable.

The first approach is the worst since it is obvious that in contrast to the third approach, it will operate on frequencies that does not exist in the z-direction. This approach is focusing on the symptoms, rather than the disease. The second approach is not trying to fight the symptoms, but the short range that is forced in the z-direction makes it extremely hard to pick up information.

3.1.7 NaN values

A problem that arises in the phase based algorithm is how to handle values moved into the volume from a signal space outside the original volume. Those voxels will be marked as a Not a Number, NaN, by Matlab. It is important to handle these voxels in some way and since the registration is not intensity based these voxels cannot simply be put to zero since edges will be introduced by doing so. One solution to the problem is to broaden the concept of certainty in the algorithm. If a NaN voxel is marked as uncertain, one could use that information to lower the importance of the filter responses influenced by that voxel. This however means that a certainty map have to simultaneously be handled and updated with every movement in the registration. Furthermore it is probably not wise to used binary valued certainty but a contionuous certainty between 0 and 1. A fix for the problem is to rather try to fill out the NaN's with values that does not introduce new phase information. When iterating the algorithm, one can use the latest values of the latest volume for those position. If the found corrections are quite large, this is not a good way of starting a new scale since the information we are filling spaces with can be full of phase information. It is better to use an upsampled version of an earlier scale that has filled the holes iteratively with neighbouring voxel values. The problems with just exchanging NaN values with zeros was not noticed during the registration, it was rather a problem when introducing motion to datasets since distinct edges were introduced. These edges sometimes affected the results.

3.2 SPM packages

Since SPM offers a developed software for analysis of brain imaging, the algorithms were already implemented and free to use. The code however were open-source but embedded in their package. Therefore the decision to just use the interface given were made and the adjustments made for suiting the qMRI data sets were limited to the change of parameters offered in the GUI. Though for the GR scales were used even though the GUI does not provide the possibility. The algorithm could however be used by function calls in Matlab where the result of movements found in previous scales could be used as starting points in the up-coming scales. What parameter settings used are explained in the section Abbreviations.
Figure 3.5: The GUI of the SPM package [9]. It can be downloaded from: http://www.fil.ion.ucl.ac.uk/spm/


3.3 Using several scales

The phase based algorithm is based on using several scales. In the SPM package the possibility exists as well, although the process is not automated.

3.3.1 Phase based registration

The second assumption made in the phase based algorithm, that the image locally can be seen as a leaning plane, is a quite weak assumption leading to the usage of iterations. Therefore the time consumption increases and it is a good idea to use downsampled volumes to increase the rate of each iteration. The filtersize also inhibits the algorithm in the way that the movement must be seen in the filter area otherway it cannot be found. By downsampling the volumes, the region of the filter contains more information and greater movements can be found. By that reason four different scales are used, where the downsampled volumes are supposed to find the great movements on a coarse scale and the following scales should make fine adjustments. The result should hopefully be that the number of iterations decreases from scale to scale, and at the most time consuming scale, the original resolution, we only need a couple of iterations.

![Figure 3.6: Slices of the different scales of the registration](image)

(a) 1x1 mm  (b) 3x3 mm  (c) 5x5 mm  (d) 10x10 mm

3.3.2 SPM packages

In the SPM packages several scales can be used. In the mutual information approach, there is a built in possibility to use several scales. The alignment approach however only offers the option to make the alignment with a lower resolution. The results from the lower resolutions can on the other hand be saved and put into a higher resolution as a starting point which adjusts this method to imitate the other two. Through the GUI this is however inconvenient for the user.

3.4 Stop criterium

Since the algorithms are based on finding the solution iteratively, and by using several scales, there are four thresholds that need to be considered. As for now
the stop criteriums were designed and implemented in the phase based algorithm, but the concept is applicable to the other algorithms as well. The thresholds are

1. Judge the final suggested solution
2. Too small solution from a scale
3. Uncertain solution from a scale
4. Stop criterium for the iterations in each scale

**Judge the final suggested solution**

A good rule of thumb is that if the movement is less than a voxel, the interpolated information is probably not more correct than the original. The translations in each direction follow quite easily from this although some calculus is needed for the rotations. Consider a movement introduced by a rotation around one of the euclidian axis

\[
\begin{align*}
v &= \begin{bmatrix} \cos \alpha & \sin \alpha & 0 \\ -\sin \alpha & \cos \alpha & 0 \\ 0 & 0 & 1 \end{bmatrix} \begin{bmatrix} x \\ y \\ z \end{bmatrix} - \begin{bmatrix} x \\ y \\ z \end{bmatrix} = \begin{bmatrix} x(\cos \alpha - 1) + y \sin \alpha \\ -x \sin \alpha + y(\cos \alpha - 1) \\ 0 \end{bmatrix}
\end{align*}
\] (3.8)

The total length of that movement is given by

\[
|v| = \sqrt{v_x^2 + v_y^2 + v_z^2} = \sqrt{2(x^2 + y^2)(1 - \cos \alpha)}
\] (3.9)

For simplicity the distance to move is calculated as the total distance even though the movement is divided in two directions, the threshold is an average between the directions influenced.

\[
|v| > \sqrt{2(x^2 + y^2)(1 - \cos \alpha)}
\] (3.10)

The condition should hold true for every voxel of the object and therefore the function of \( x \) and \( y \) should be optimized, e.g. find the voxel in the object with the greatest coordinate square sum.

\[
\frac{|v|^2}{2} > max(x^2+y^2)(1-\cos \alpha) \iff \cos \alpha > 1 - \frac{|v|^2}{2(x^2 + y^2)} \iff \alpha < \cos^{-1}(1 - \frac{|v|^2}{2(x^2 + y^2)})
\] (3.11)

The last expression is only valid if the angle is within 0 to 45 degrees. With these rules of thumb we can put up conditions on the smallest corrections performed.

**Too small solution from a scale**

If a suggested solution is not using one or several of the bases for the suggested movement, the algorithm should not search for movements along this base or bases. It is hard to motivate how these thresholds should be set. It is possible to calculate new rules as in 3.11 with a smaller allowed distance, or just adjust that result with a division.
Uncertain solution from a scale

The expression in equation 3.11 and the reasoning behind it can be used as an uncertainty measure in every scale. The scales with lower resolution will contain less data points, but since the coordinate grid is rescaled to fit the reality where the points are sampled the distance $x^2 + y^2$ will be the same. The one parameter that is changing between the scales is the distance between every sample, calculated as the mean between two samples in each direction. Equation 3.11 can therefore be modified with a parameter telling how the direction have been downsampled according to

$$\alpha < \cos^{-1}(1 - \frac{|(d_x v_x + d_y v_y)/2|^2}{2(x^2 + y^2)})$$

(3.12)

Assume that the voxel in the object most effected with a rotation around $z$ is $p = (230, 27, \ast)$ which is of distance $(100, 13, \ast)$ from the origin. This voxel can be found by defining the object as all voxel with values above the mean value of the volume and finding the voxel maximizing the expression above. Assume also that the size of the voxels is $1 \times 1 \times 5$ mm. If the scale with the lowest resolution uses a voxel size of $10 \times 10 \times 10$ mm the difference between the allowed angles, in radians, can be calculated as

$$\alpha < \cos^{-1}(1 - \frac{|(10 \ast 1 + 10 \ast 1)/2|^2}{2((10 \ast 100/10)^2 + (10 \ast 100/10)^2)}) = 0.071$$

(3.13)

$$\alpha < \cos^{-1}(1 - \frac{|(1 \ast 1 + 1 \ast 1)/2|^2}{2((1 \ast 100)^2 + (1 \ast 100)^2)}) = 0.0071$$

(3.14)

between scale $(1, 1, 5)$ and scale $(10, 10, 10)$. It is easy to vary the criterias if for instance we want half the voxel distance to be the limit, or if the limit should be set half way to the border of the object.

Stop criterium for iterations in each scale

This parameter cannot be as elegantly suggested as the parameters above. The parameters have to be decided by studying the progress of registration in several test data sets. Since the most important evaluation is the effect on the $T_1$ mapping one could study the curves of the found motion and study the effect on the $T_1$ map if the algorithm has stopped at a different number of iterations. This approach is however only valid on the last scale since the other scales are of no interest to fit. Since the data is lowpass filtered to receive the different scales there will be more information available when moving to the next scale. This is the main idea of the scales that the registration should be finer and finer but it is not certain that the steps in the iterations will be finer in the beginning of a new scale, since the data is altered. Considering this effect it might be unnecessary to register the previous scale too accurate since there might be a big change in the beginning of the next scale. Appropriate cutoff criterias must probably be motivated from empiri. One could reinforce the decisions by using the calculations of uncertainty and decide at each scale how many iterations that seems fair to allow, for finding the movement of for example one voxel.
Chapter 4

Evaluation

The evaluation chapter starts of with a section about movements in qMRI and the effect on the $T_1$ quantification. The other part of the chapter describes the methods used for comparing between the performance of different algorithms. The measurements used for studying the effect of registration in quantification is also presented.

4.1 Effects of motion on the $T_1$ map

Motion artefacts in MRI is a known problem area. Although most of those are addressing artifacts that occure during the k-space scans and can be seen within the images or volumes. The motion correction in qMRI is instead focusing on the motion seen between the volumes collected along the $T_1$ relaxation curve. When the curvefitting, previously described, is disturbed by motion the results are degraded. As can be seen in table 4.1 the error minimized in the fitting error grows when motion is introduced. The original dataset used is dataset 1. Dataset rotation 1 has a one degree rotation around the z-axis in all three volumes, rotation 3 has a three degree rotation around the z-axis and dataset translation 1 have a
Table 4.1: The evaluation measurements on volumes with applied motion. The square error is the error minimized in the curve fitting. Here it is presented as the mean error of each point in each curve fitting in each voxel, thus a intensity value. The error is growing when motion is applied.

<table>
<thead>
<tr>
<th>Dataset</th>
<th>Square error</th>
</tr>
</thead>
<tbody>
<tr>
<td>original</td>
<td>25.2</td>
</tr>
<tr>
<td>rotation 1</td>
<td>31.5</td>
</tr>
<tr>
<td>rotation 3</td>
<td>43.7</td>
</tr>
<tr>
<td>Translation 1</td>
<td>39.7</td>
</tr>
</tbody>
</table>

one voxel of translation in the x and y direction in all volumes. The effects are also seen in figure 4.1 where especially the edges are harder and harder to quantify (the white is a threshold for unsuccesfully quantified voxels) and also the details within the brain is getting fuzzier.

4.2 Evaluation strategy

The evaluation is divided into two separate parts. There is the evaluation strategy for comparison between the different registration algorithms and there is the evaluation of the effect of registration in the quantification of the magnetic properties. Since the quantification is based on a minimization of a least square fit the measurements are closely related to this problem. There are specific tests for the registration evaluation that are independent of the $T_1$ fitting. On the other hand the quantification evaluation can also be used for separating the algorithms as well as just being used to study effects. The quantification effects will also be used for deciding parameters of the algorithms. The registration evaluation consist of two strategies

I. Visual inspection of the registered volumes.
II. Calculating intensity differences

The quantification evaluation consists of four tests:

I. Visual inspection of the $T_1$ map.
II. Studying the error of the $T_1$ curve fitting.
III. Count the number of valid points from the $T_1$ fitting.
IV. Look at the structure content of the $T_1$ error map.

These tests should be done after registration with the different algorithms and also after doing the $T_1$ fitting without registration of the volumes.
4.2 Evaluation strategy

4.2.1 Visual inspection of the registered volumes

The most intuitive approach for evaluation is to just look at the volumes after registration. If there is a distinct movement between the volumes, the improvement should be easily spotted with the eye. By comparing the reference volume, the un-registered and the registered volume, the correction should be noticed. This is however only a good test for spotting distinct movement and to validate the registration algorithms on a coarse scale. This test is not applicable for fine differences between the solutions of the different algorithms.

4.2.2 Intensity differences

Since the volume have differences in intensity it is not obvious how one could distinguish the solutions of the algorithms. A visual inspection might be sufficient if one only wants to decide if the registration succeeded or not. This is however not sufficient in order to compare the result from different algorithms. If a rigid transformation was the only difference between the volumes, then one could simply calculate the total square error between the reference volume and the registered one. This simple test is spoiled by the intensity differences. There are however two other ways of imitating this test which are applicable for this situation:

1. A circle scheme
2. Artificial movement

A circle scheme

Since the QRAPMASTER method contain four volumes, one could create a chain of registration. First register volume B to A, resulting in B*, and then C to B*, and finally A to C*. After that, A and A* could be compared based on intensity. Then the registration algorithms have to pass three times and the evaluation can still be done between images of the same intensity. The measurement of the intensity difference could either be done by a square error or by mutual information. The phase based algorithm however have a built in uncertainty principle that would cancel a suggested movement if it is not bigger than a voxel. Assuming that the first two registrations succeeds within these limits then the last registration will be considered as unnecessary and volume A* will be set to A. Between the two algorithms of the SPM package this test is applicable. If the uncertainty principles of the phase based algorithm were removed the test could be carried out, but since the algorithm is not constructed in that fashion the results would be quite uninteresting.

<table>
<thead>
<tr>
<th>reference volume</th>
<th>registered volume</th>
<th>result</th>
</tr>
</thead>
<tbody>
<tr>
<td>A</td>
<td>B</td>
<td>B*</td>
</tr>
<tr>
<td>B*</td>
<td>C</td>
<td>C*</td>
</tr>
<tr>
<td>C*</td>
<td>A</td>
<td>A*</td>
</tr>
</tbody>
</table>

Table 4.2: The scheme for testing registration algorithms
Artificial movement

If there is no movement between two volumes of different intensities, then movement can be applied to one of the volumes and then perform the registration. When this is done one can compare the original volume with the moved and registered. The measurement can once again be either a square error or mutual information. The setback of this evaluation is that it cannot be done with true motion, since the volumes have to be aligned at the beginning.

4.2.3 Visual inspection of the $T_1$ map

The problems that occur in the $T_1$ mapping are situated at the borders between different tissues. A large volume of tissue should still give valid $T_1$ values even if the voxels inside the region are moved. On the borders on the other hand a curve fitting will be made with data from different tissues resulting in non-valid results. The movement will either give smoothing effects on the borders or give values that are completely wrong. These effects should be spotted when looking at the $T_1$ map.

4.2.4 $T_1$ fitting error

The $T_1$ fitting is based on a weighted linear least square solution, as described in the implementation chapter. The curve fitting minimizes an error in every voxel to get the best match. If the registration is successful this minimized error should decrease as the points on the curve will have a higher probability to originate from the same tissue. The $T_1$ fitting error should be tested on the registered and the original dataset.

4.2.5 Valid points

In the $T_1$ fitting there are some condition that have to be met, in order to get a valid $T_1$ value. Depending on the result of the faulty points, their values will be windowed. If there is a perfect fit between the volumes, every voxel should be given a valid number. If the volumes are misaligned there will be voxels that fail the fitting. The number of windowed values should therefore increase in the misaligned case. The perfectly aligned volumes might still have values adjusted to the allowed window, but these voxels should be the same in both cases and should not influence the outcome of the test.

4.2.6 Structure in the $T_1$ error map

Since a mean value of the error map is correlated with noise, another measure that focuses on the features of the error map is proposed. As described above, the largest errors should exist at the borders between different tissues. The result of the errors at the borders should propagate to the calculated error map. In theory, the error map should because of that reason have more structure at the borders if there is movement in the volumes. A way of evaluating the movement is therefore
4.2 Evaluation strategy

To use structure tensors\cite{17} on the error map to find the structure. One could call attention to the fact that the error map will always visualize the noise in the volumes and since different tissues are influenced differently, the error map will have structure even though the movement defaults. The structure is assumed to increase and not to appear because of movement, and the method should still be valid. This test in comparison to the $T_1$ fitting error should be more robust on finding true registration since the $T_1$ fitting error probably should decrease by just doing smoothing and increase the SNR. The error on the borders should however become worse by smoothing.

**Structure tensors**

Structure tensors are calculated in each voxel and are represented as a 3x3 matrix. The eigen values of the structure tensor are calculated in a fashion that they indicate the amount of found structure in the direction of their corresponding eigen vector. In a neighbourhood with random numbers (pure noise), the eigen values will be of the same size. In a neighbourhood with one clear structure, one eigen value will be 100% of the total eigen value sum. When the structure tensor has been calculated, the error map can be recalculated with a weight function, according to

$$\text{error} = \sum \epsilon^2 f(\lambda_1, \lambda_2, \lambda_3) \quad (4.1)$$

The eigenvalue function $f$ should give a large weight if there is structure present and a small weight otherwise, it is thus constructed as follows

$$f(\lambda_1, \lambda_2, \lambda_3) = \frac{\lambda_1 - \lambda_3}{\lambda_1} \quad (4.2)$$

If the voxel contains a distinct structure $\lambda_1 >> \lambda_3$ gives $f = 1$ meanwhile a voxel only containing noise $\lambda_1 = \lambda_3$ gives $f = 0$.

4.2.7 Environment

The evaluation was done on a Sony Vaio laptop with a dual core processor, 2.13 GHz. The computer had 4 GB RAM memory. The calculation was done with double precision. The interpolation of the phase based algorithm was designed to use the dual cores. The tolerance parameter of the mutual information algorithm was set to twice the default value for faster convergence, if nothing else is stated.

All registration methods were implemented through Matlab with aid of mex-files (c programmed Matlab functions) and the tests were done on the same computer. None of the algorithms had therefore any advantages thanks to advanced programming technique.
Chapter 5

Results

The result chapter is divided in three section. In the first section the outcome of the registration, depending on what scales that are used, is presented. In the second section the results of different registration scenarios are presented. This section shoud be seen as the basis for separating between the algorithms. The last section presents the effect of registration in the quantification. This section is also used as a basis for the comparison between the algorithms. Before the results are presented, a small description of the datasets used in the master thesis will be given.

Datasets

This master thesis have included ten different datasets in the evaluation. Here follows a description of each dataset so that the viewer can broaden the understanding of the result part. The suggested movements in the descriptions were given by the phase based algorithm and the verification of the suggestion were done visually slice by slice.

Dataset 1-6
Dataset 1-6 are scans of the same patient. The volumes have the dimension 224 x 224 x 28 voxels. The only difference between the datasets is the resolution which differs between the scans. All scans are considered to be free of motion.

Dataset 7
This is the dataset with most motion. The volumes of the dataset have big rotations around the z-axis, from 10 to 40 degrees. There are also some other rotations around the other axis. Dataset 7-9 are of the same patient but with different movements. The datasets have the dimensions 256 x 256 x 27 voxels.

Dataset 8
This dataset have a big motion around the y-axis in every volume. It also have some other smaller rotations around the other axis. This dataset have the dimensions 256 x 256 x 27 voxels.
Dataset 9
This dataset is considered to be free of motion. This dataset have the dimensions 256 x 256 x 27 voxels.

Dataset 10
This dataset contains a probable patient case. There is a continuous motion through the datasets. The motion is a rotation around the z-axis, which makes the volumes differ with 1-2 degrees from the reference. Some translational moves are included since the rotation center is neither the dataset center nor the upper corner. This dataset is more noisy than the others, since the data originate from another MR scanner. This dataset have the dimensions 256 x 184 x 20 voxels.

5.1 Scales

The first part of the results concerns the scales of the algorithms. The usage of time in each scale is presented and also the outcome of the registrations when different scales were used.

5.1.1 Phase based algorithm

Execution times

The values in table 5.1 is the time required for downsampling and truncation for all of the four volumes. The filter response column is the time required for the calculation of the reference volume filter response which is done once. All values are given in seconds. According to theory the truncation is only needed where there is data within a half filter size from the edges. The truncation is needed in all directions in scale 10 but only in one direction in the other scales. The dataset used for this is dataset 7 (256x256x27 voxels). In figure 5.1 the estimated rotations

<table>
<thead>
<tr>
<th>scale (mm)</th>
<th>downsampling</th>
<th>truncation</th>
<th>filter response</th>
<th>iteration</th>
</tr>
</thead>
<tbody>
<tr>
<td>10x10x10</td>
<td>0.04</td>
<td>0.01</td>
<td>0.05</td>
<td>0.029</td>
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<tr>
<td>5x5x5</td>
<td>1.41</td>
<td>0.01</td>
<td>0.09</td>
<td>0.13</td>
</tr>
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<td>3x3x5</td>
<td>0.81</td>
<td>0.02</td>
<td>0.24</td>
<td>0.54</td>
</tr>
<tr>
<td>1x1x5</td>
<td>-</td>
<td>0.25</td>
<td>1.91</td>
<td>4.25</td>
</tr>
</tbody>
</table>

Table 5.1: Times in seconds of the different parts of the phase based algorithm

as a function of time is plotted. Note the change of course that takes place when changing the scale. In figure 5.2 the uncertainty principle of PB is resetting the found motions which in the end turns out to be a correct move since no motion is found.
Figure 5.1: Typical development on how the rotations are found iteratively, dataset 7 and volume 4. The rings are marking the change of scales. Observe the small adjustments made in the middle when the algorithm changes between scales of resolution. The first graph is the rotation around x, then y and last z.

Figure 5.2: If the found motion is judged uncertain the motion is reset, dataset 9 volume 4. The rings are marking the change of scales. The upper and middle plot is considered to have uncertain motion at the first change of scale. The lowest rotation angle on the other hand is considered to be without motion and is cancelled. Eventually all rotations are considered to not find any motion.
The judgement on whether the registration succeeds or not is based on a visual inspection. This evaluation is more conceptual and the registration status is either \textit{ok} or \textit{failed}. If a certain scale is used then the number of iterations will be given otherwise the field is left with a -. When studying table 5.2 notice that in the datasets with motion, 7, 8 and 10, there is a small gain in time when using the most low resoluted scale and a more distinct gain when using scale 5. It is also worth noting that dataset 7 is only succesfully registered when scale 10 is used. In the datasets without motion, 1-6 and 9, scale 10 is delaying the registration. If scale 5 is removed two additional volumes are failing the registration.
Table 5.2: The number of iterations on each scale used in the phase based algorithm and the time elapsed. The times in seconds. The registration ok/failed is based on a visual inspection and is a coarse validation.
5.1.2 SPM

In the SPM general registration there is built in for pre-processing, but no extraction of phase. The only numbers are therefore the number of iterations when the scales are used and the time taken for each iteration in every scale. In table 5.4, the scale with the highest resolution is omitted since it takes several minutes to finish. The mutual information approach is based on the same downsampling, the separation parameter, and shows similar results regarding time saving. Therefore the results of the mutual information is omitted.

Times

The times were collected when the algorithm worked on dataset 7. The general registration algorithm

<table>
<thead>
<tr>
<th>scale</th>
<th>time per iteration (seconds)</th>
</tr>
</thead>
<tbody>
<tr>
<td>8</td>
<td>0.17</td>
</tr>
<tr>
<td>4</td>
<td>1.44</td>
</tr>
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<td>2</td>
<td>2.37</td>
</tr>
<tr>
<td>1</td>
<td>60</td>
</tr>
</tbody>
</table>

Table 5.3: The times for the different scales in GR
### 5.1 Scales

<table>
<thead>
<tr>
<th>Dataset</th>
<th>Volume</th>
<th>8</th>
<th>4</th>
<th>2</th>
<th>time (sec)</th>
<th>registration</th>
</tr>
</thead>
<tbody>
<tr>
<td>1-6</td>
<td>2</td>
<td>2</td>
<td>2</td>
<td>1</td>
<td>5.59</td>
<td>ok</td>
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<td>1-6</td>
<td>2</td>
<td>-</td>
<td>2</td>
<td>1</td>
<td>5.25</td>
<td>ok</td>
</tr>
<tr>
<td>1-6</td>
<td>2</td>
<td>-</td>
<td>-</td>
<td>2</td>
<td>4.74</td>
<td>ok</td>
</tr>
<tr>
<td>1-6</td>
<td>3</td>
<td>5</td>
<td>3</td>
<td>1</td>
<td></td>
<td>failed</td>
</tr>
<tr>
<td>1-6</td>
<td>3</td>
<td>-</td>
<td>5</td>
<td>2</td>
<td></td>
<td>failed</td>
</tr>
<tr>
<td>1-6</td>
<td>3</td>
<td>-</td>
<td>-</td>
<td>4</td>
<td></td>
<td>failed</td>
</tr>
<tr>
<td>1-6</td>
<td>4</td>
<td>5</td>
<td>2</td>
<td>2</td>
<td>8.47</td>
<td>ok</td>
</tr>
<tr>
<td>1-6</td>
<td>4</td>
<td>-</td>
<td>5</td>
<td>2</td>
<td>11.94</td>
<td>ok</td>
</tr>
<tr>
<td>1-6</td>
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<td>-</td>
<td>5</td>
<td>11.85</td>
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</tr>
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<tr>
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<td>-</td>
<td>9</td>
<td>21.33</td>
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<td>-</td>
<td>17</td>
<td>2</td>
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</tr>
<tr>
<td>7</td>
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<td>-</td>
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<td>-</td>
<td>9</td>
<td></td>
<td>failed</td>
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<td>2</td>
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<td>1</td>
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<td>2</td>
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<td>-</td>
<td>4</td>
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<td>7.54</td>
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<td>1</td>
<td>8.13</td>
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<td>-</td>
<td>4</td>
<td>9.48</td>
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<td>1</td>
<td>5.76</td>
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<td>-</td>
<td>3</td>
<td>1</td>
<td>6.69</td>
<td>ok</td>
</tr>
<tr>
<td>10</td>
<td>3</td>
<td>-</td>
<td>-</td>
<td>3</td>
<td>7.11</td>
<td>ok</td>
</tr>
<tr>
<td>10</td>
<td>4</td>
<td>4</td>
<td>2</td>
<td>1</td>
<td>5.93</td>
<td>ok</td>
</tr>
<tr>
<td>10</td>
<td>4</td>
<td>-</td>
<td>3</td>
<td>1</td>
<td>6.69</td>
<td>ok</td>
</tr>
<tr>
<td>10</td>
<td>4</td>
<td>-</td>
<td>-</td>
<td>3</td>
<td>7.11</td>
<td>ok</td>
</tr>
</tbody>
</table>

Table 5.4: The iterations of each scale used in GR and the time in seconds elapsed. The judgement on the registration is based on a visual inspection where it is possible to judge the success down to a degree on a computer screen.
5.2 Registration results

This part of the result section only mentions the result of the registration between the volumes of the datasets. The results are the basis for the comparison between the tested algorithms. The effect of the quantification can be seen in the next section. The visual inspection starts with some special cases to illustrate some of the differences between the algorithms.

5.2.1 Visual inspection of the volumes

The visual inspection is divided into two parts, first there are some registration results on some special cases with artificial volumes. The second part consists of images of the registration results of the three algorithms and all datasets.

Special cases

Fading cross:
Since all of the algorithms are said to solve the registration even with intensity differences one can create a simple test with an image with fading intensity, see figure 5.3. The solution of the mutual information approach has diverged and the cross has moved outside the image.

![Figure 5.3: The registration case. (a) the original image (b) altered and faded. Registration is made by (a) PB, (b) GR and (c) MI](image)
Inverted intensities:
A simple test on how robust the algorithms are to a change of intensity, is to register a volume that has had its intensity values inverted. This is done by setting all the voxel values to the maximum intensity of the volume minus the voxel value. The registration of the inverted volume could only be performed successfully by

![Registration with an inverted volume](image1)

Figure 5.4: Registration with an inverted volume. (a) reference volume (b) original volume to register (c) the volume in (b) inverted

the mutual information algorithm. If the energy instead was fetched with the help of one isotropic lowpass filter and three directed bandpass filters, the other two algorithms handled the problem. As a pre-processing for PB this maneuver can

![Energy images](image2)

Figure 5.5: The energy (tensor magnitude) images of the volumes in figure 5.4

be seen as removing the sign of the phase. This is however time consuming and takes about two seconds per volume.

The datasets
Here follows the registration results of the ten datasets. The datasets are all three dimensional. The visual result will however be done with carefully chosen slices. The default slice will be a transverse plane from the middle of the dataset, other
configurations will be declared.

**Dataset 1 – 6**

Since dataset 1-6 is of the same patient, only one result will be shown from the registrations. The result of the different registrations had only slight differences. Observe the difference in the CSF regions (in the middle) in volume 3 registered by GR, seen in figure 5.7. This alteration is the basis for failing this registration. The error can be seen throughout the volume.

<table>
<thead>
<tr>
<th>Method</th>
<th>Time</th>
<th>Registration</th>
</tr>
</thead>
<tbody>
<tr>
<td>PB(10-5-3-1)</td>
<td>7 sec</td>
<td>ok</td>
</tr>
<tr>
<td>GR(8-4-2)</td>
<td>1 min 17 sec</td>
<td>small failure</td>
</tr>
<tr>
<td>GR(8-4)</td>
<td>19 sec</td>
<td>small failure</td>
</tr>
<tr>
<td>MI(8-4)</td>
<td>30 sec</td>
<td>ok</td>
</tr>
<tr>
<td>MI(8)</td>
<td>20 sec</td>
<td>ok</td>
</tr>
</tbody>
</table>

Table 5.5: The average times of the registration for dataset 1-6 for all three volumes to register. See figure 5.7(d) to verify the failures.

![Figure 5.6: Dataset 1. (a) The reference volume (b) The original volume 2 (c) registered by PB(10-5-3-1) (d) registered by GR(8-4-2) (e) registered by MI(8-4). No differences between the methods are visible.](image)
Figure 5.7: Dataset 1. (a) The reference volume (b) The original volume 3 (c) registered by PB(10-5-3-1) (d) registered by GR(8-4-2) (e) registered by MI(8-4). Observe the difference in the registration done by GR, it is considered to be a failure.

Figure 5.8: Dataset 1. (a) The reference volume (b) The original volume 4 (c) registered by PB(10-5-3-1) (d) registered by GR(8-4-2) (e) registered by MI(8-4). No differences between the methods noticeable.
## Dataset 7

<table>
<thead>
<tr>
<th>Method</th>
<th>Time</th>
<th>Judgement</th>
</tr>
</thead>
<tbody>
<tr>
<td>PB(10-5-3-1)</td>
<td>47 sec</td>
<td>ok</td>
</tr>
<tr>
<td>PB(10-5-3)</td>
<td>24 sec</td>
<td>ok</td>
</tr>
<tr>
<td>GR(8-4-2)</td>
<td>1 min 49 sec</td>
<td>ok</td>
</tr>
<tr>
<td>GR(8-4)</td>
<td>19 sec</td>
<td>failed</td>
</tr>
<tr>
<td>MI(8-4)</td>
<td>2 min 3 sec</td>
<td>failed</td>
</tr>
<tr>
<td>MI(8)</td>
<td>46 sec</td>
<td>failed</td>
</tr>
</tbody>
</table>

Table 5.6: The times of the registration for dataset 7. See figure 5.11 to verify the failures

Figure 5.9: Dataset 7. (a) The reference volume (b) The original volume 2 (c) registered by PB(10-5-3-1) (d) registered by GR(8-4) (f) registered by MI(8-4). All methods handle the movement. They are all aligned with the reference volume after the registration.
5.2 Registration results

Figure 5.10: Dataset 7. (a) The reference volume (b) The original volume (c) registered by PB(10-5-3-1) (d) registered by GR(8-4) (f) registered by MI(8-4). All methods successfully registers the volume to match the reference volume.

Figure 5.11: Dataset 7. (a) The reference volume (b) The original volume (c) registered by PB(10-5-3-1) (d) registered by GR(8-4) (e) registered by GR(8-4-2) (f) registered by MI(8-4). Only PB and the slow version GR registers the volume correct.
Dataset 8

<table>
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<th>Time</th>
<th>Judgement</th>
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</thead>
<tbody>
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<td>ok</td>
</tr>
<tr>
<td>PB(10-5-3)</td>
<td>20 sec</td>
<td>ok</td>
</tr>
<tr>
<td>GR(8-4-2)</td>
<td>1 min 31 sec</td>
<td>ok</td>
</tr>
<tr>
<td>GR(8-4)</td>
<td>22 sec</td>
<td>ok</td>
</tr>
<tr>
<td>MI(8-4)</td>
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</tr>
<tr>
<td>MI(8)</td>
<td>1 min 6 sec</td>
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</tr>
</tbody>
</table>

Table 5.7: The times of the registration for dataset 8

Figure 5.12: Dataset 8. (a) The reference volume (b) The original volume 2 (c) registered by PB(10-5-3-1) (d) registered by GR(8-4-2) (e) registered by GR(8-4) (f) registered by MI(8-4). All methods register correctly.

Figure 5.13: Dataset 8. (a) The reference volume (b) The original volume 3 (c) registered by PB(10-5-3-1) (d) registered by GR(8-4-2) (e) registered by GR(8-4) (f) registered by MI(8-4). All methods register correctly.
5.2 Registration results

Figure 5.14: Dataset 8. (a) The reference volume (b) The original volume (c) registered by PB(10-5-3-1) (d) registered by GR(8-4-2) (e) registered by GR(8-4) (f) registered by MI(8-4). All methods register correctly.

Dataset 9

<table>
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<th>Time</th>
<th>Judgement</th>
</tr>
</thead>
<tbody>
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<td>8 sec</td>
<td>ok</td>
</tr>
<tr>
<td>PB(10-5-3)</td>
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<td>ok</td>
</tr>
<tr>
<td>GR(8-4-2)</td>
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</tr>
<tr>
<td>GR(8-4)</td>
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<td>ok</td>
</tr>
<tr>
<td>MI(8-4)</td>
<td>55 sec</td>
<td>ok</td>
</tr>
<tr>
<td>MI(8)</td>
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<td>ok</td>
</tr>
</tbody>
</table>

Table 5.8: The times of the registration for dataset 9

Figure 5.15: Dataset 9. (a) The reference volume (b) The original volume (c) registered by PB(10-5-3-1) (d) registered by GR(8-4-2) (e) registered by GR(8-4) (f) registered by MI(8-4)
Figure 5.16: Dataset 9. (a) The reference volume (b) The original volume 3 (c) registered by PB(10-5-3-1) (d) registered by GR(8-4-2) (e) registered by GR(8-4) (f) registered by MI(8-4)

Figure 5.17: Dataset 9. (a) The reference volume (b) The original volume 4 (c) registered by PB(10-5-3-1) (d) registered by GR(8-4-2) (e) registered by GR(8-4) (f) registered by MI(8-4)
5.2 Registration results

Dataset 10

<table>
<thead>
<tr>
<th>Method</th>
<th>Time</th>
<th>Judgement</th>
</tr>
</thead>
<tbody>
<tr>
<td>PB(10-5-3-1)</td>
<td>19 sec</td>
<td>ok</td>
</tr>
<tr>
<td>PB(10-5-3)</td>
<td>10 sec</td>
<td>ok</td>
</tr>
<tr>
<td>GR(8-4-2)</td>
<td>49 sec</td>
<td>ok</td>
</tr>
<tr>
<td>GR(8-4)</td>
<td>12 sec</td>
<td>ok</td>
</tr>
<tr>
<td>MI(8-4)</td>
<td>40 sec</td>
<td>ok</td>
</tr>
<tr>
<td>MI(8)</td>
<td>35 sec</td>
<td>ok</td>
</tr>
</tbody>
</table>

Table 5.9: The times of the registration for dataset 10

Figure 5.18: Dataset 10. (a) The reference volume (b) The original volume 2 (c) registered by PB(10-5-3-1) (d) registered by GR(8-4-2) (e) registered by GR(8-4) (f) registered by MI(8-4). All methods successfully altered the one degree motion.

Figure 5.19: Dataset 10. (a) The reference volume (b) The original volume 3 (c) registered by PB(10-5-3-1) (d) registered by GR(8-4-2) (e) registered by GR(8-4) (f) registered by MI(8-4). All methods successfully altered the one degree motion.
Figure 5.20: Dataset 10. (a) The reference volume (b) The original volume 4 (c) registered by PB(10-5-3-1) (d) registered by GR(8-4-2) (e) registered by GR(8-4) (f) registered by MI(8-4). All methods successfully altered the two degree motion.

### Dataset 7 – 9

Datasets 7-9 are scans of the same patient but with different motion. Since it is the same patient the volumes of the different datasets could be registered to each other. Since every dataset consists of four volumes and there are three datasets, 132 test cases was performed. The exact result on which volume that was unsuccessful to register to which is presented in the appendix B. With a visual inspection as the validation the succeeded registrations are given in table 5.10

<table>
<thead>
<tr>
<th>Method</th>
<th>Result</th>
</tr>
</thead>
<tbody>
<tr>
<td>PB</td>
<td>132 / 132</td>
</tr>
<tr>
<td>GR</td>
<td>126 / 132</td>
</tr>
<tr>
<td>MI</td>
<td>127 / 132</td>
</tr>
</tbody>
</table>

Table 5.10: The number of successfully registered volumes in all pair combinations of dataset 7-9

#### 5.2.2 The circle scheme

The circle scheme was performed with three volumes included. The volume of the qMRI with the highest signal intensity was used as a reference volume, A. Volume B was the second volume of the qMRI sequence, and volume C was volume number three. The data set had obvious movement in it. The registration scheme is given in table 5.11. The square error and the mutual information were calculated

<table>
<thead>
<tr>
<th>reference volume</th>
<th>registered volume</th>
<th>result</th>
</tr>
</thead>
<tbody>
<tr>
<td>A</td>
<td>B</td>
<td>B*</td>
</tr>
<tr>
<td>B*</td>
<td>C</td>
<td>C*</td>
</tr>
<tr>
<td>C*</td>
<td>A</td>
<td>A*</td>
</tr>
</tbody>
</table>

Table 5.11: The scheme for testing registration algorithms

between A and A*. The measurements were only calculated in the voxels that had
valid intensities throughout the registration. The phase based algorithm concluded that there were no differences between $C^*$ and $A$ and therefore let $A^*$ be $A$ and the square error was for that reason zero. For comparison the phase based algorithm was altered and was not allowed to decide that movement in the xy-plane was too small to be valid. The phase based algorithm used all scales, the general registration algorithm used scales 8-4-2 and the mutual information algorithm used scales 8-4-2. The circle scheme was performed with dataset 8, where volume 1-3 corresponds to A-C. The phase based algorithm was altered to keep the found motion from the finest scale.

<table>
<thead>
<tr>
<th>method</th>
<th>square error (%)</th>
<th>mutual information</th>
</tr>
</thead>
<tbody>
<tr>
<td>GR(8-4-2)</td>
<td>32.1</td>
<td>2.62</td>
</tr>
<tr>
<td>MI(8-4-2)</td>
<td>10.4</td>
<td>3.41</td>
</tr>
<tr>
<td>PB(10-5-3-1)</td>
<td>0</td>
<td>7.06</td>
</tr>
<tr>
<td>PB*(10-5-3-1)</td>
<td>1.1</td>
<td>5.23</td>
</tr>
<tr>
<td>PB**(10-5-3-1)</td>
<td>10.5</td>
<td>4.40</td>
</tr>
</tbody>
</table>

Table 5.12: The results of the circle scheme test. PB is implemented with the uncertainty principle, PB* does not remove small movements in the xy-plane. PB** does not remove small movements at all. The scheme was done with dataset 8, volume 1-3.

### 5.2.3 The intensity test

The test was carried out with dataset 9 rotated around every axis. The volumes were truncated before rotated and then cut to avoid edge errors. The measurements made between the original unaltered volume and the registered volume were a square error and the mutual information measure. The test was done on all three volumes of the dataset and then averaged. The times are also averages of the three registrations. BR is an abbreviation for back rotated and is the volume with the inverse rotation matrix applied, which should be the ideal movement. Tables 5.13 and 5.14 contains values from registration with one dataset altered five degrees around every axis in all volumes and one dataset altered two degrees around every axis in one volume, three degrees in the second volume and four degrees in the third.
<table>
<thead>
<tr>
<th>method</th>
<th>square error (%)</th>
<th>mutual information</th>
<th>time (sec)</th>
</tr>
</thead>
<tbody>
<tr>
<td>GR (8-4-2)</td>
<td>31.3</td>
<td>2.48</td>
<td>1 min 26 sec</td>
</tr>
<tr>
<td>GR (8-4)</td>
<td>32.1</td>
<td>2.46</td>
<td>15 sec</td>
</tr>
<tr>
<td>MI (8-4)</td>
<td>27.4</td>
<td>2.60</td>
<td>31 sec</td>
</tr>
<tr>
<td>MI (8)</td>
<td>29.1</td>
<td>2.56</td>
<td>29 sec</td>
</tr>
<tr>
<td>PB* (10-5-3-1)</td>
<td>24.6</td>
<td>2.67</td>
<td>30 sec</td>
</tr>
<tr>
<td>PB (10-5-3-1)</td>
<td>28.8</td>
<td>2.59</td>
<td>21 sec</td>
</tr>
<tr>
<td>PB (10-5-3)</td>
<td>33.0</td>
<td>2.44</td>
<td>8 sec</td>
</tr>
<tr>
<td>BR</td>
<td>20.1</td>
<td>2.78</td>
<td>-</td>
</tr>
</tbody>
</table>

Table 5.13: The intensity difference between the original and registered volume, after a five degree alteration around every axis. PB* used tricubic interpolation. The time is an average of the three registrations made.

<table>
<thead>
<tr>
<th>method</th>
<th>square error (%)</th>
<th>mutual information</th>
<th>time (sec)</th>
</tr>
</thead>
<tbody>
<tr>
<td>GR (8-4-2)</td>
<td>33.4</td>
<td>2.49</td>
<td>1 min 25 sec</td>
</tr>
<tr>
<td>GR (8-4)</td>
<td>34.0</td>
<td>2.48</td>
<td>15 sec</td>
</tr>
<tr>
<td>MI (8-4)</td>
<td>28.0</td>
<td>2.65</td>
<td>30 sec</td>
</tr>
<tr>
<td>MI (8)</td>
<td>37.9</td>
<td>2.39</td>
<td>12 sec</td>
</tr>
<tr>
<td>PB* (10-5-3-1)</td>
<td>27.0</td>
<td>2.67</td>
<td>25 sec</td>
</tr>
<tr>
<td>PB (10-5-3-1)</td>
<td>28.6</td>
<td>2.59</td>
<td>14 sec</td>
</tr>
<tr>
<td>PB (10-5-3)</td>
<td>31.8</td>
<td>2.52</td>
<td>9 sec</td>
</tr>
<tr>
<td>BR</td>
<td>19.3</td>
<td>2.96</td>
<td>-</td>
</tr>
</tbody>
</table>

Table 5.14: The intensity difference between the original and registered volume, the alteration is increasing around every axis. Two degrees in the first volume, three in the second and four degrees in the third volume. PB* used tricubic interpolation. The time is an average of the three registrations made.
5.3 Quantification results

Here follows the quantification results. It begins with a visual inspection of the calculated $T_1$ maps of the datasets with found motion. In the second paragraph the results of the quantification measurements are listed.

5.3.1 Visual inspection of the $T_1$ map

Only the datasets with motion will be presented in this section. The white areas in the $T_1$ maps are voxels that have failed the curve fitting, those values have been windowed to physically valid values. As have been presented earlier, edges will be covered with more failed voxels and areas within the brain will get fuzzier because of motion. The images should be studied with this in mind. Since the reference volume have the largest error and structure error, the intensity levels on those categories are set from the reference volume. This leads to very black images of the registered volumes. This is a proof of the advances of registration rather than badly chosen images. When studying the T1 error maps one can see that the regions of CSF is very white. The voxel intensities of CSF is not following the physical model. The first point of the curve is situated above the second which does not coincide with the suggested exponential behaviour. The seen effect can be explained by the long $T_1$ times of CSF. The regions are effected by the magnetization that remains in the transverse plane between the repetitions. This magnetzation is called spurious echoes. This is probably effecting the CSF regions even though the QRAPMASTER sequence is constructed with saturation pulses, that are supposed to remove the effect.
dataset 7:

Figure 5.21: The $T_1$ map (a-d), the error map (e-h) and the structure error map (i-l) for the reference volume (a, e, i), PB (b, f, j), GR (c, g, k) and MI (d, h, l)
dataset 8:

Figure 5.22: The $T_1$ map (a-d), the error map (e-h) and the structure error map (i-l) for the reference volume (a, e, i), PB (b, f, j), GR (c, g, k) and MI (d, h, l)
dataset 10:

Figure 5.23: The $T_1$ map (a-d), the error map (e-h) and the structure error map (i-l) for the reference volume (a, e, i), PB (b, f, j), GR (c, g, k) and MI (d, h, l).
5.3 Quantification results

5.3.2 $T_1$ fitting

The error map consists of the sum of square errors in each voxel. In table 5.15 the error is divided into each point and the value is recalculated to the absolute error instead of the square error. The value presented can be thought of as the absolute error in every point of the fitting curve. The structure error originate from the error map, but is calculated in the same way. Some of the fitting algorithms are not supplied with a smart NaN-filling function. The voxels with a zero value in the registered volumes will therefore not be counted in any method. In the cases where the PB algorithm did not find motion the rows are filled with ref, standing for reference. The default settings of the GR algorithm were used. The default tolerances of the MI algorithm were doubled for faster convergence. In addition to the results in numbers a curve fitting of a voxel showing the concept of registration together with the curve fitting is presented.

Observe, in table 5.15, the decrease in error and structure error and the increase in valid points after registration in the datasets with motion (dataset 7, 8 and 10). Also worth noting is the increase in error for the GR algorithm in the datasets without motion (dataset 1-6 and 9).

![Figure 5.24: A voxel to be fitted before registration, red pixel](image)
Figure 5.25: The voxel fitting curve before registration

Figure 5.26: A voxel to be fitted after registration, red pixel
Figure 5.27: The voxel fitting curve after registration
<table>
<thead>
<tr>
<th>method</th>
<th>dataset</th>
<th>error</th>
<th>structure error</th>
<th>valid points (%)</th>
<th>time</th>
</tr>
</thead>
<tbody>
<tr>
<td>Reference 1-6</td>
<td>25.2</td>
<td>6.8</td>
<td>94.4</td>
<td>-</td>
<td></td>
</tr>
<tr>
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<td>ref</td>
<td>ref</td>
<td>ref</td>
<td>7 sec</td>
<td></td>
</tr>
<tr>
<td>PB (10-5-3)</td>
<td>ref</td>
<td>ref</td>
<td>ref</td>
<td>7 sec</td>
<td></td>
</tr>
<tr>
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<td>36.5</td>
<td>9.5</td>
<td>91.1</td>
<td>1 min 17 sec</td>
<td></td>
</tr>
<tr>
<td>GR (8-4)</td>
<td>35.8</td>
<td>9.3</td>
<td>91.2</td>
<td>19 sec</td>
<td></td>
</tr>
<tr>
<td>MI (8-4)</td>
<td>24.6</td>
<td>6.8</td>
<td>94.4</td>
<td>31 sec</td>
<td></td>
</tr>
<tr>
<td>MI (8)</td>
<td>26.0</td>
<td>7.3</td>
<td>94.4</td>
<td>20 sec</td>
<td></td>
</tr>
<tr>
<td>Reference 7</td>
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<td>76.7</td>
<td>-</td>
<td></td>
</tr>
<tr>
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<td>8.4</td>
<td>89.3</td>
<td>46 sec</td>
<td></td>
</tr>
<tr>
<td>PB (10-5-3)</td>
<td>36.6</td>
<td>8.9</td>
<td>88.9</td>
<td>22 sec</td>
<td></td>
</tr>
<tr>
<td>GR (8-4-2)</td>
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<td>9.0</td>
<td>89.0</td>
<td>1 min 49 sec</td>
<td></td>
</tr>
<tr>
<td>GR (8-4)</td>
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<td>8.9</td>
<td>88.7</td>
<td>24 sec</td>
<td></td>
</tr>
<tr>
<td>MI (8-4)</td>
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<td>8.2</td>
<td>89.4</td>
<td>2 min 3 sec</td>
<td></td>
</tr>
<tr>
<td>MI (8)</td>
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<td>8.5</td>
<td>89.1</td>
<td>46 sec</td>
<td></td>
</tr>
<tr>
<td>Reference 8</td>
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<td>-</td>
<td></td>
</tr>
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<td>6.5</td>
<td>90.1</td>
<td>41 sec</td>
<td></td>
</tr>
<tr>
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<td>6.5</td>
<td>89.9</td>
<td>20 sec</td>
<td></td>
</tr>
<tr>
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<td></td>
</tr>
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<td>22 sec</td>
<td></td>
</tr>
<tr>
<td>MI (8-4)</td>
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<td>6.8</td>
<td>90.2</td>
<td>3 min 2 sec</td>
<td></td>
</tr>
<tr>
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<td>6.8</td>
<td>90.0</td>
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<td></td>
</tr>
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<td>95.2</td>
<td>-</td>
<td></td>
</tr>
<tr>
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<td>ref</td>
<td>ref</td>
<td>ref</td>
<td>8 sec</td>
<td></td>
</tr>
<tr>
<td>PB (10-5-3)</td>
<td>ref</td>
<td>ref</td>
<td>ref</td>
<td>8 sec</td>
<td></td>
</tr>
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<td>24 sec</td>
<td></td>
</tr>
<tr>
<td>MI (8-4)</td>
<td>18.1</td>
<td>5.4</td>
<td>94.6</td>
<td>55 sec</td>
<td></td>
</tr>
<tr>
<td>MI (8)</td>
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<td>5.6</td>
<td>94.6</td>
<td>18 sec</td>
<td></td>
</tr>
<tr>
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<td>27.6</td>
<td>87.5</td>
<td>-</td>
<td></td>
</tr>
<tr>
<td>PB (10-5-3-1)</td>
<td>86.4</td>
<td>15.7</td>
<td>89.1</td>
<td>18 sec</td>
<td></td>
</tr>
<tr>
<td>PB (10-5-3)</td>
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<td>16.8</td>
<td>89.0</td>
<td>10 sec</td>
<td></td>
</tr>
<tr>
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<td>17.6</td>
<td>87.9</td>
<td>5 min 13 sec</td>
<td></td>
</tr>
<tr>
<td>GR (8-4-2)</td>
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<td>17.3</td>
<td>87.9</td>
<td>49 sec</td>
<td></td>
</tr>
<tr>
<td>GR (8-4)</td>
<td>90.5</td>
<td>17.2</td>
<td>88.0</td>
<td>12 sec</td>
<td></td>
</tr>
<tr>
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<td></td>
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<tr>
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<td>16.1</td>
<td>88.1</td>
<td>40 sec</td>
<td></td>
</tr>
<tr>
<td>MI (8)</td>
<td>95.8</td>
<td>18.8</td>
<td>87.4</td>
<td>35 sec</td>
<td></td>
</tr>
</tbody>
</table>

Table 5.15: The quantification evaluation. Observe the test run of finer scales in dataset 10.
Chapter 6
Discuss

When constructing artificial test cases or working with extreme motion it is quite clear that the phase based algorithm is the best. It can be seen in dataset 7, with a 40 degree rotation, and in the fading intensity test. When it comes to normal motion it can be hard to separate the registration algorithms when it comes to performance. Although it is quite clear that none of the SPM algorithms neither is faster nor more robust in those cases. With the uncertainty principle the phase based algorithm is superior since the other algorithms rather impair the volumes rather than improves them. This principle is however probably applicable to the other constructions as well.

When studying the quantification it is clearly stated that the results are improved by the registration. It is stated by every of the three measurements and seen in all datasets with motion. The phase based algorithm has the fastest registration done in all datasets. Of the three datasets with motion the phase based algorithm is both the fastest and gives the best result in two of them. In the third the results are decreasing when the time spent is decreasing. This is shown by all algorithms and none is superior to the others.

6.1 General discussion of the structure of the algorithms

Since both GR and PB solves a least square problem exactly, the algorithm should be more robust. An optimization strategy is always sensitive to converging into a local maxima or minima.

GR and PB have a quite similar structure when it comes to breaking down the problem. They seem to be possible to trim to about the same speeds. Both are solving a least square problem crystallized from one or several Taylor expansions. The approach of the intensity difference are different though. While GR tries to approximate a basis of spatial functions, PB is trying to extract information from the volume. Considering a lot of different configurations of intensity differences the GR algorithm should fail eventually while PB should succeed as long as mutual
information exists. The information extracted for PB is quite sensitive. The sign of the local phase have to be the same in the images otherwise the certainty will be zero and the information not regarded.

As for now the PB algorithm is implemented with some advantages regarding the voxel size and MI have embedded some ideas regarding the constraint of some motions of the head. These implementations can of course be adapted by the other algorithms making them more robust. A similar implementation to PB to put into GR might get a bit tricky though since GR is estimating additional parameters in the least square problem. In PB a relationship between the rotations around the x- and y-axis have been noted, which should be handled carefully. There might be relationships that resembles this, including the parameters of the spatial basis parameters.

6.2 Scales

6.2.1 Phase Based Algorithm

Regarding the concept of scales it is quite obvious that scales will improve both robustness and speed. The choice of specific scales can though be questioned.

Scale 10

The most low resolution scale, scale 10, is improving the time in all cases of found motion. In dataset 7 it is essential for finding a valid solution for every volume. The conclusion drawn from these datasets is that scale 10 is improving both robustness and speed of the algorithms. In the datasets without known motion, the effect of the scale is negative. In those datasets the coarse scale rather leaves traces that following scales have to clean up. Scale 10 is then to be used when there is motion, but the algorithm itself is the one in charge of finding them. Since only one volume in all 10 datasets failed without scale 10, and that is a volume with found motion of 40 degrees, which would be extremely unlikely to occur in normal cases, the question is whether or not the scale is necessary. The scale can be adjusted into being even more coarse which could remove the negative effects of datasets without motion. Although some time are saved in the cases of motion, even in the small movement dataset. This question could be solved by a quantitative study where the question to answer would be if the time savings in motion cases would make up for delaying a decision of no motion.

6.2.2 SPM

The scales of the general registration approach improve speed and robustness. The effects of the coarse scale in the phase based algorithm cannot be seen here since finer and finer scales cannot handle the volumes without motion either. The other two algorithms have, as will be discussed later, constraints against small movements.
6.3 Registration

6.3.1 Visual inspection of the volumes

Special cases

The fading cross gives a hint that the phase based algorithm handles the extreme cases of alternating intensities the best. In this case the intensity is steadily decreasing and this is a hard test for GR since it only handles local stationary intensity differences. Even though MI is said to handle images from different modalities, the technique strongly depend on the intensity values. This is established by this simple test. Mutual information can be thought of mapping between intensity values and will of that reason have a problem when the intensities are fading. The inverted intensities on the other hand is getting PB in trouble as well. The phase based algorithm get’s a lot of information from the fat signal of the edge of the brain. The lower the resolution (the first scale for instance) the more important is the edge. If the intensities are inverted then the phase information will change it’s sign, since going into the object will be going from low to high intensity values and the opposite if inverted. Since the bridge between tissue and CSF is making this inversion between volume 1 and volume 3, and the same bridge contains a lot of phase information, it could be wise to implement a pre-processing. If one extract the energy information from the image then all edge passages will have the same sign. Mutual information on the other hand handles this kind of inversion. As long as the fat will give a higher signal than the neigbouring tissue the phase based algorithm will have a strong phase to rely on.

The datasets

The special case tests is used to point to some important problems of the algorithms. The fading cross demonstrates that the procedure of PB is probably best suited for registration with quite unusual intensity differences. The visual inspection is a very coarse test. It can basically only be used to observe the registration of bigger movements. One can question the relevance of finding motion as big as rotations of 40 degrees (dataset 7). These conditions are extreme and are very unlikely to occure. However, to measure robustness one must create such test case since the result hints what intervals of motion the algorithm can handle. If GR uses scale 2 it can handle the problem. This however might be a catch of luck since the bigger movements should be found in earlier scales and not the finest. In dataset 1-6 it can be seen that GR is finding motion that does not exist since the original volume seems to be better aligned than the registered one. This is a good indication that their should be a threshold on small motions.

6.3.2 The circle scheme

There is a remarkable difference between the SPM package test. The mutual information approach seems much better. Although the reason for this is probably quite simple. The mutual information algorithm has a built in priority for movements in
the xy-plane since it is most likely to occur. The phase based algorithm also has constraints, although those are calculated from the anisotropism. Since the data have a lower resolution in the z-direction, a greater error will be introduced if the final solution is influenced by neighbouring slices. Since the last registration pair is always supposed to have a small error as possible, the constraints of the phase based algorithm and the mutual information algorithm will give huge advantages against the other SPM approach. The last pair of volumes to register will always have this relationship unless the registration have failed, which can be seen with the eyes. This relationship between the pair in the last registration will be closely aligned, regardless the motion to begin with. This test can therefore not provide any valid new information regarding what algorithm is the best. Since the results are so heavily dependent on the interpolation it is hard to construct a test that separates the algorithms on a fine scale. Since the interpolation have smoothing effects, i.e. lowpass filtering effects, one could lowpass filter the datasets so that the influence of the interpolation was smaller.

6.3.3 The intensity differences

This test is more fair if the movements introduced are applied around all axis. If the movement is only applied in the xy-plane this test will suffer from the same conditions as the circle scheme test. The error calculated is quite big even though the algorithms solve the problem, according to a visual judgement. This depends on the interpolation when the volumes are altered. Once again data from different slices are mixed which will effect the result. We see that the errors from the back rotated volumes are of the same magnitude. There is a tradeoff in accuracy when the algorithms are optimized. Since the motion is artificially created there will arise regions of voxels with NaN values, these regions are filled with the quick fix solution for not introducing phase information. This procedure will probably have negative effects on the phase based algorithm that would not be seen in true datasets. We can also see the effect of the interpolation. The phase based algorithm had its result improved by using the tricubic interpolation instead of trilinear interpolation. Since the interpolation is so important for the results it is very hard to distinguish between the registration methods.

6.4 Quantification

6.4.1 Visual inspection of the $T_1$ map

In this test it is quite obvious that the quantification is getting better after registration. The number of failed fittings decreases, which can be seen as the number of white voxels decreases. The tissue regions within the brain also became more distinct. Both of these visual indication have been shown to move in the opposite direction when motion is introduced and are therefore good markers. The test cannot however separate between algorithms and settings, and can only be used as a coarse scale measure. The test could be further developed if the inspector has medical training and experience of MRI.
6.4.2 $T_1$ fitting

There are two things that the results is quite clear about. The first thing is that registration have a positive effect on quantification. It can be seen in the images and all the separate tests verify that the results are better after the registration. The effect is seen in every dataset with motion and in every evaluation. The other conclusion established is that some assumption regarding motion in the xy-plane is necessary to include. MI is prioritizing it’s search in the plane and can therefore handle the volumes with no motion and even improve the result with a decimal. The effect can however also be created with just adding some random small translation in the xy-plane, the effect seen is rather the smoothing of the interpolation than a correct registration. These small improvements should not be implemented with registration since the edges will be smoothed. Fine adjustments can probably be achieved with adaptive filtering which would preserve the edges. GR is the only algorithm without arrangements on the whereabouts of the motion. It is also quite clear that the results of the fitting is made worse.

Regarding specific algorithms one can observe that GR seems to handle the motion problems equally good with and without scale two. The time is then decreased without effecting the measures. This is of course is a big time saver since scale two is quite slow. With PB the scale is working as supposed. For gaining in speed the finer adjustment have to be omitted.

The structure error seems to be working in the datasets of no motion. The MI algorithm is lowering the square error in every point. This is probably due to smoothing effects of the registration. Of that reason the structure error is growing since the smoothing is troublesome for the $T_1$ fitting of the edges.

In dataset 10 the finer scales of the SPM algorithms were tested. There are just slight improvements in some of the results, and even a degradation of the results in some measurements. The time elapsed however is increasing hugely. If time is an important factor these scales cannot be used.

6.5 Final conclusions

The result have clearly stated that datasets with motion can be greatly improved by registration. The motions however were quite exaggerated and should be further investigated with more "normal" datasets.

The phase based algorithm is the most robust. It was the only registration method that could handle all datasets. The general registration algorithm had problems with both artificial test cases while the phase based algorithm and the mutual information algorithm had problems with one each. A promising way of handle the problem of the phase based algorithm was suggested.

Some considerations about anisotropy and the probability of motion in certain directions must be done. The assumption on motion made in the mutual information approach and the handling of the voxels in the phase based registration impacted the result positively.

The phase based algorithm was the fastest method. The general registration method could in some solitary case match the rate of the phase based registration.
Chapter 7

Future

7.1 Quantitative verification of the algorithm

The future goal of a study of this kind is to see the registration algorithm in a clinical use. Since this master thesis is aimed at presenting a method for fast and robust registration in the version of qMRI presented in the study, the amount of test data is not enough. This thesis used ten original 3D sets, and some digitally constructed.

7.2 Other bodyparts

As have been discussed in the thesis, one of the main features for successfully registering the volumes is the high intensity of fat around the head. Since the fat signal is high throughout all the volumes the sign of the phase will be the same and the registration will work. If the region of interest would move towards other part of the body this important feature might not be present. If the features of the new images will have inverted regions of intensity, like the CSF region in one of the qMRI volumes, then only mutual information registration can handle the problem. If the phase based algorithm is still to be used, more effort have to be put into extracting the energy of the images, it has shown that it can solve such problems. Since the phase based algorithm have shown to be a quicker algorithm and more robust to big movements, it can probably still be chosen if the new region of interest contains a lot of fat or if there are no region with inverted intensities.

7.3 Improving the algorithm

If the demands of spent time increases or if it is necessary to add for example the energy extraction, the speed of the algorithm have to increase. Graphic card programming is an area that has gained more interest the last years. By locating calculations that can be done in parallel, the rate of the registration can increase. In a study Eklund et al. [18] increased the rate of calculations 50 times for the
phase based algorithm. It might be possible to increase the speed by changing from double to single float precision.

If one decides that the phase is the best information to base the registration on, but the optical flow approach is not. One can apply mutual information on the phase. This approach would remove the problem of different signs in the local phases from the images. This have been done succesfully by Mellor and Brady[19].
Bibliography


Appendix A

Proof of rotational base vectors

Take an arbitrary coordinate, or vector, in the volume \( \vec{x} = (x, y, z) \) it points in the \((x,y,z)\) direction. The proposed rotational base vectors are all orthogonal to this vector:
\[(x, y, z) \cdot (-y, x, 0) = 0, \quad (x, y, z) \cdot (z, 0, -x) = 0\] and \((x, y, z) \cdot (0, -z, y) = 0\). Assume that the arbitrary point is a coordinate on a sphere with radius \( r = \|\vec{x}\|\), which is convenient because it is about to be rotated. In this case the rotational base vectors will span up the tangent plane on the sphere containing our arbitrary point. Now assume that the correct rotation is caused by rotational matrix \( M \), then the correct place for the new coordinate is \( \vec{x}_n = M \vec{x} \). The movement vector from the algorithm will then be a vector in the tangent plane of the original coordinate. The vector will point to the coordinate in the plane closest to the new coordinate of the sphere. To find an explicit expression of the connection between the best point in the plane and the true point one assumption have to be maid. The proof is also narrowed down to two special cases. The assumption:

1. The vector to rotate around is \( \vec{p} = (p_4, p_5, p_6)^T \)

and the special cases:

1. The rotation angle is really small

2. The rotation around one euclidian angle is great while the others are small

Before finding the expression note that a total rotation with one rotation around each euclidian axis can be exchanged for one rotation around one axis. Take a rotation matrix, calculated as previous from the three euclidian rotations, there have to be one axis that satisfies: \( R\vec{x} = \vec{x} \), this have to be the rotational axis. The angle is then found by taking a vector perpendicular to the axis, \( \vec{v} \cdot \vec{x} = 0 \). This vector is situated in the plane with the rotational axis as its normal. Now apply the rotational matrix to \( \vec{v} \) and the angular difference between the resulting vector,
still situated in the plane, and $\theta$ will be the angle of rotation. So a rotation matrix can be exchanged for a rotation axis and an angle.

The assumption about which rotational axis to choose, can be intuitively understood by studying the case of rotations in the 2D-case. Assume that the rotation is around the z-axis. Take a point, $x = (x, y)$, in that plane. Choose the base vectors in the plane according to:

$\hat{e}_1 = \frac{1}{||x||}(x, y)$ and $\hat{e}_2 = \frac{1}{||x||}(-y, x)$.

The position after the rotation can be expressed as $x_n = ||x||((\cos\alpha - 1)\hat{e}_1 + \sin\alpha\hat{e}_2)$. The ideal movement is therefore $v_{\text{ideal}} = x_n - x = ||x||((\cos\alpha - 1)\hat{e}_1 + \sin\alpha\hat{e}_2)$. The rotational base vector in the plane is $\vec{v} = p(-y, x)^T = p||x||\hat{e}_2$. Now minimize the distance between these vectors with respect to $p$:

$$
\epsilon^2 = |v_{\text{ideal}} - v|^2 = ||x||^2(\cos\alpha - 1)^2 + ||x||^2(\sin\alpha - p)^2
$$

(A.1)

This is obviously minimized if $\sin\alpha = p$. The greater the angle the greater $p$ gets. Each parameter is therefore some kind of measurement of the rotation around that euclidian axis. It is therefore reasonable to believe that the parameters of the rotational base vectors point in the direction of the rotational axis. Assuming this is correct it is time to study the two special cases. Try to imagine a patient trying to lie still in an MR-scanner the assumption that the rotational angle is small seems fairly correct. And if the patient is rotating its head it is probably around the axis directed as the body leading to special case two. The connections in the special cases can now be derivated.

Assume that there is a coordinate on a sphere $\vec{x} = (x, y, z)$ and that a true movement is described by angle $\gamma$ and an axis, $\vec{p} = (p_1, p_2, p_3)$, to rotate around. Then the new position $\vec{x}_n$ can be calculated according to:

$$
\vec{x}_n = M\vec{x}
$$

(A.2)

where $M$ is a rotation matrix that rotates $\gamma$ around $\vec{p}$. $M$ can be derivated according to this: If vector (or coordinate) $\vec{x}$ is about to be rotated around $\vec{p}$ then the vector have to be projected $\vec{x}$ into the plane where $\hat{p}$ is a normal vector, because it is no use to rotate the part of the vector directed in the way of the rotation axis. The base vectors of the rotational plane can be found by taking the cross product between $\hat{p}$ and $\vec{x}$, and then taking that vector and take the cross product with $\hat{p}$ leading to three orthogonal vectors, $\hat{p}, e_1$ and $e_2$.

$$
e_2 = \hat{p} \times \vec{x}
$$

(A.3)

$$
e_1 = e_2 \times \hat{p} = \hat{p} \times \vec{x} \times \hat{p}
$$

(A.4)

When $\vec{x}$ is projected onto the plane the result will be $e_1$. Because of that a rotation in the plane is now easy to calculate:

$$
\vec{x}_n\vec{p} = \cos\gamma e_1 + \sin\gamma e_2 = \cos\gamma(\hat{p} \times \vec{x} \times \hat{p}) + \sin\gamma(\hat{p} \times \vec{x})
$$

(A.5)

This is the new position in the plane and have to be moved to the correct new position this is done by adding the offset that was removed when the vector was projected onto the plane: $\vec{x}_p = \vec{x} - e_1$. The new position is therefore:

$$
\vec{x}_n = \vec{x} - e_1 + \cos\gamma e_1 + \sin\gamma e_2
$$

(A.6)
and giving us our ideal movementfield:

\[ v_{\text{ideal}} = \overline{x_n} - \overline{x} = (\cos \gamma - 1)e_1 + \sin \gamma e_2 \]  

(A.7)

The cross products can be exchanged with skew matrices:

\[ \begin{bmatrix} a_2b_3 - b_2a_3 \\ a_3b_1 - b_3a_1 \\ a_1b_2 - b_1a_2 \end{bmatrix} = \begin{bmatrix} 0 & -a_3 & a_2 \\ a_3 & 0 & -a_1 \\ -a_2 & a_1 & 0 \end{bmatrix} \begin{bmatrix} b1 \\ b2 \\ b3 \end{bmatrix} \]  

(A.8)

\[ \hat{p} \times \overline{x} = \frac{1}{||p||} \begin{bmatrix} 0 & -p_3 & p_2 \\ p_3 & 0 & -p_1 \\ -p_2 & p_1 & 0 \end{bmatrix} \overline{x} = P\overline{x} \]  

(A.9)

and because of the anti commutative property of the cross product:

\[ \overline{x} \times \hat{p} = -\hat{p} \times \overline{x} \]  

(A.10)

This leads to the following expression of \( e_1 \):

\[ e_1 = \hat{p} \times \overline{x} \times \hat{p} = -\hat{p} \times \hat{p} \times \overline{x} = -P^2\overline{x} \]  

(A.11)

Therefore our movement field can be expressed:

\[ v_{\text{ideal}} = ((1 - \cos \gamma)P^2 + \sin \gamma P)\overline{x} \]  

(A.12)

The rotational base vectors,

\[ v = R\overline{p} = \begin{bmatrix} 0 & z - y & x \\ -z & 0 & x \\ y & -x & 0 \end{bmatrix} = P^*\overline{x} = \begin{bmatrix} 0 & -p_3 & p_2 \\ p_3 & 0 & -p_1 \\ -p_2 & p_1 & 0 \end{bmatrix}\overline{x} \]  

(A.13)

gives a vector in the tangent plane orthogonal to the normal out from the sphere in the arbitrary point, the best vector in that plane minimizes the distance between the ideal movement with the one created by the rotational bases:

\[ \epsilon^2 = |v_{\text{ideal}} - V|^2 = |((1 - \cos \gamma)P^2 + \sin \gamma P - P^*)\overline{x}|^2 = \]

\[ (x(v_{11}^*) + y(v_{12}^* + p_3) + z(v_{13}^* - p_2))^2 + (x(v_{21}^* - p_3) + y(v_{22}^* + z(v_{23}^* + p_1))^2 + (x(v_{31}^* + p_2) + y(v_{32}^* - p_1) + z(v_{33}^*))^2 \]

Now looking at the two special cases:

1. The rotational angle is really small:

If this is the case then the ideal movement can be approximated to something easier:

\[ v_{\text{ideal}} = ((1 - \cos \gamma)P^2 + \sin \gamma P)\overline{x} = \sin \gamma P\overline{x} \]  

(A.15)

Which gives the square error:

\[ \epsilon^2 = \]  

(A.16)
(y(-\sin \gamma p_3^2 + p_3) + z(\sin \gamma p_1^2 - p_3))^2 + (x(\sin \gamma p_3^2 - p_3) + z(-\sin \gamma p_1^2 + p_1))^2 +
(x(-\sin \gamma p_2^2 + p_2) + y(\sin \gamma p_2^2 - p_1))^2
= (yp_3(-\sin \gamma + ||p||) + zp_2(\sin \gamma - ||p||))^2 + (xp_3(\sin \gamma - ||p||) + zp_1(-\sin \gamma + ||p||))^2 +
(xp_2(-\sin \gamma + ||p||) + yp_1(\sin \gamma - ||p||))^2

As we can see this error is minimized if the angle is \sin \gamma = ||p||
The second special case:

2. The rotation is great around one of the euclidian axis.

Assume that the rotation is great around the z-axis, the other two rotations can
be regarded as zero, \hat{p} = (0, 0, 1) and \overrightarrow{p} = (0, 0, p_3) then:

\[
v_{ideal} = (1 - \cos \gamma)
\begin{bmatrix}
-1 & 0 & 0 \\
0 & -1 & 0 \\
0 & 0 & 0
\end{bmatrix}
+ \sin \gamma
\begin{bmatrix}
0 & -1 & 0 \\
1 & 0 & 0 \\
0 & 0 & 0
\end{bmatrix}
= \begin{bmatrix}
(cos \gamma - 1) & -\sin \gamma & 0 \\
\sin \gamma & (cos \gamma - 1) & 0 \\
0 & 0 & 0
\end{bmatrix}
\]

which could be recognized as the standard rotation matrix if the identity matrix
is added. The error is now:

\[
e^2 =
(x(\cos \gamma - 1) + y(-\sin \gamma + p_3))^2 + (x(\sin \gamma - p_3) + y(\cos \gamma - 1))^2
= x^2(\cos^2 \gamma + 1 - 2 \cos \gamma) + y^2(\sin^2 \gamma + p_3^2 - 2 p_3 \sin \gamma) - 2 xy(\cos \gamma - 1)(-\sin \gamma + p_3) +
x^2(\sin^2 \gamma + p_3^2 - 2 p_3 \sin \gamma) + y^2(\cos^2 \gamma + 1 - 2 \cos \gamma) - 2 xy(\sin \gamma - p_3)(\cos \gamma - 1)
= x^2(2 + p_3^2 - 2 \cos \gamma - 2 p_3 \sin \gamma) + y^2(2 + p_3^2 - 2 \cos \gamma - 2 p_3 \sin \gamma)

If we take the derivative with respect to \(p_3\):

\[
\frac{\delta e^2}{\delta p_3} = 2 p_3 (x^2 + y^2) - 2 \sin \gamma (x^2 + y^2) = 0
\]

which gives the solution:

\[
p_3 = \sin \gamma
\]

Which can be expressed as the solution in special case 1:

\[
||p|| = \sin \gamma
\]
Appendix B

Result of registration of dataset 7-9

Registering dataset 7-9. Since dataset 7-9 are scans of the same patient pairwise registration could be done with any volume from any dataset. This enabled 132 test cases. In the table each combination of registration is presented with a 1 for successful registration and 0 for unsuccessful. The judgement is based on a coarse visual inspection.
### Result of registration of dataset 7-9

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#### Table B.1: Registering dataset 7-9 to each other with PB(10-5-3-1)

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#### Table B.2: Registering dataset 7-9 to each other with GR(8-4)

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#### Table B.3: Registering dataset 7-9 to each other with MI(8-4)