ABSTRACT

ELASTIC BRAIN IMAGE REGISTRATION USING MUTUAL INFORMATION

by
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Image Registration is the determination of a geometrical transformation that aligns points in one image of an object with corresponding points in another image. The source image is geometrically transformed to match the target image. The geometric transformation can be rigid or non-rigid. Rigid transformations preserve straight lines and angles between straight lines. The basic rigid transformations are rotation, scaling and translation.

In this thesis non-rigid registration using B-splines is the method being used to take into account the elastic change in the brain structure. The B-spline equation is a type of curved transformation that does not preserve the straightness of lines, as is the case with rigid transformation.

A similarity measure is based on similar pixel values in the image pairs. It is used as a cost function to measure the similarity between the source and target image. Mutual information is a similarity measure based on the probability density function. Optimization of both rigid and non-rigid registration techniques is performed to obtain the registration parameters that define the best geometrical transformation. The parameters are optimized based on the mutual information.

Neurosurgery is an application of image registration and requires accurate surgical planning and guidance because of complex and delicate structures in the brain. Over the course of the surgery, the brain changes its shape in reaction to mechanical and physiological changes associated with the surgery such as loss of cerebrospinal fluid and gravity forces.

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by
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APPROVAL PAGE

ELASTIC BRAIN IMAGE REGISTRATION USING MUTUAL INFORMATION

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To my beloved God and Savior Jesus Christ

~

He that dwelleth in the secret place of the Most High

Shall abide under the shadow of the Almighty. I will say of the LORD,

He is my refuge and my fortress: my God; In Him will I trust – Psalms 91:1-2

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CHAPTER 1

INTRODUCTION

1.1 Introduction

Medical scans such as magnetic resonance (MR) and computed tomography (CT) are currently common diagnostic tools in surgical applications. Typically, information contained in these medical scans is neither in the coordinate system of the patient as positioned in the world, nor does it reflect the viewpoint of the surgeon during an operation. Any correspondences between the medical images and the actual patient environment have to be drawn mentally by the surgeon during the procedure.

The approach of medical image registration computes these correspondences automatically and then augments the real environment with information contained in medical scans.

1.2 Image Registration

Image registration is finding the geometrical match between any two images. It is broadly divided into rigid and non-rigid or elastic methods. Rigid registration methods are used when the image position is modified by rotation, translation or change of scale. Non-rigid registration is divided into many different methods, and is used when the shape of the object is modified elastically.

A typical image-processing algorithm dealing with elastic registration usually always includes rigid registration. The rigid registration component takes care of change in shape caused by the change in the position of the patient. The non-rigid component takes care of the elastic change, caused by more complicated reasons like loss of tissue, loss of cerebrospinal fluid etc.

After the geometrical transformation is determined, the similarity between the two images is evaluated using a similarity measure. Optimizing the similarity measure gives the best parameter of registration, and hence defines the best match between the pre-operative and intraoperative image pair.

1.3 Applications of Image Registration

Imagine looking inside the body and seeing everything in precise. Three-dimensional view – shows the lobe of a brain, the twisting passageways of nasal cavities, the structure of vertebrae in the spine. That is the intricate view more and more surgeons are seeing with the next generation of image-guided surgery technology. Image registration is a necessary component in such medical applications. Image guided neurosurgery is also an important application which uses image registration.

Image-guided surgery technology has revolutionized traditional surgical techniques by providing surgeons with a way to navigate through the body using three-dimensional images as their guide. Furthermore, those images can be changed, manipulated and merged to provide a level of detail not seen before in the operating room. The technology is similar to that used by today's global positioning satellite systems, which can track the exact location and direction of vehicles at any point on the globe [2].

Because of the precision that the image guided surgery technology provides, surgeons are able to create an exact, detailed plan for the surgery – where the best spot is to make the incision, the optimal path to the targeted area, and what critical structures must be avoided. The technology allows surgeons to see or visualize the human body – a dynamic, three-dimensional structure itself in 3D.

The technology creates images that allow surgeons to see the abnormality, such a brain tumor, and distinguish it from surrounding healthy tissue. It also enables them to manipulate the view in real-time surgery. The constant flow of information helps surgeons make minute adjustments to ensure they are treating the exact areas they need to treat.

The technology also aids in shortening operating times, decreasing the size of the patient's incision, reducing the procedure's invasiveness – all of which can lead to better patient outcomes and faster recoveries. Image guided surgery also provides new alternatives for patients with multiple medical problems, patients who may not be able to tolerate large, invasive surgeries, and patients whose conditions in the past would have been considered inoperable.

Prior to image-guided surgery, the patient undergoes diagnostic testing such as a CT (computed Tomography) scan or MRI (magnetic resonance imaging). These images are then converted into three-dimensional images showing the patients organs, muscles, tissue and nerves. This is the information surgeons use to plan the operation.

By matching the pre-surgery information to the patient's real anatomy, surgeons can manipulate the view to see precisely what they need to see. It also allows them to track instruments during the surgery, including the position of the instrument and the angle at which it is entered into the body, with tremendous precision.

Image-guided surgery has revolutionized traditional surgical techniques by providing a precise treatment guidance system that can help ensure the safety of vital structures, while providing the best outcome for patients. The brain is probably the most complicated structure in the universe, making it necessary to approach surgery carefully with extreme planning to minimize the risk to the patient [2].

Image-guided surgery systems strive to enhance the surgeon's capability to utilize medical imagery to decrease the invasiveness of surgical procedures and increase their accuracy and safety. These systems can be categorized into performing one or more of the following functions: data analysis, surgical planning, surgical guidance, and surgical guidance with intra-operative updates. The systems focused on surgical guidance tend to present the surgeon with data that was gathered prior to the surgery, track surgical instruments within the operating field and render the tracked devices along with the data.

The major shortcoming of image-guided systems is that the use of pre-surgically acquired data does not account for intra-operative changes in brain morphology. The systems with intraoperative updates have been introduced to fill that void, but they are not able to provide full information disclosure to the surgeon.

The need for better image quality and relation between the pre-operative and intraoperative images arises because some anatomical structures are difficult to distinguish on interventional MR images, but are clearer on conventional, diagnostic MRI that benefits from a higher magnetic field and longer imaging times [3].

Image registration is an useful in image guided neurosurgery as the brain changes its shape due to anatomical changes in the brain structure caused by loss of cerebrospinal fluid, tissue resection etc. An image guided neurosurgery system with such updates showing critical brain structures is very useful in the real time environment.

CHAPTER 2

2.1 Image Registration Method

Any image registration method takes two images as inputs, which have to be registered. A geometrical transformation is applied to one of the images. A similarity measure is used to calculate the similarity between the two images. The value of the similarity measure explains how much of one image is similar to the other based on the parameters of the geometric transformation.

This similarity measure is a measure based on only one particular set of geometric parameters. It does not define the highest value of similarity measure. A higher or the highest similarity measure defining the best geometrical transformation may be available. So the parameters of the geometric transformation giving the maximum possible similarity measure transform one image to look like the other.

It is an iterative process and the geometric transformation is applied to the image in a loop structure. The process keeps changing the parameters of the geometric transformation till an optimum value of the similarity measure is obtained. Optimizing the similarity measure causes the loop to be executed till the maximum possible value is reached.

The flow-chart in Figure 2.1 explains the registration process. One of the images in the two inputs is known as the source image and the other is the target image. The source image undergoes the transformation till it becomes similar to the target image. After the similarity measure is optimized, the best parameters obtained are applied to the source image to give the registered image as the output.

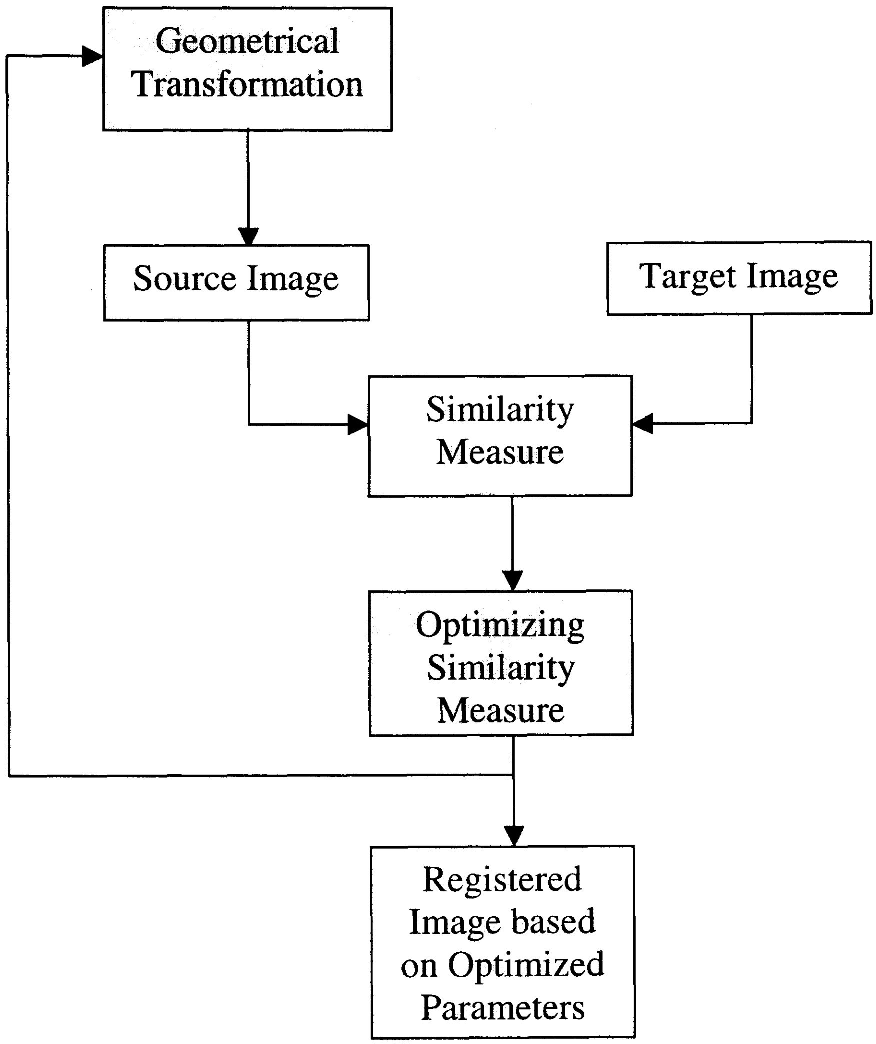

Figure 2.1 Image Registration System

2.2 Image Registration

Registration is the determination of a geometrical transformation that aligns points in one view of an object with corresponding points in another view of that object or another object. We use the term "view" generically to include a three-dimensional image, a two-dimensional image, or the physical arrangement of an object in space. Three-dimensional images are acquired by tomographic modalities, such as CT, MR, SPECT, and PET, in which a contiguous set of two-dimensional slices provides a three-dimensional array of image intensity values.

Typical two-dimensional images may be X-ray projections captured on film or as a digital radiograph or projections of visible light captured as a photograph or a video frame. In all cases we are concerned primarily with digital images stored as discrete arrays of intensity values. In medical applications, which are our focus, the object in each view will be some anatomical region of the body. The two views are typically acquired from the same patient, in which case the problem is that of *intrapatient registration*, but *interpatient registration* has application as well.

From an operational view the inputs of registration are the two views to be registered; the output is a geometrical transformation, which is merely a mathematical mapping from points in one view to points in the second. To the extent that corresponding points are mapped together, the registration is successful. The determination of the correspondence is a problem specific to the domain of objects being imaged, which is in our case the human anatomy.

To make the registration beneficial in medical diagnosis or treatment the mapping that it produces must be applied in some clinically meaningful way by a system which will typically include registration as a subsystem. The larger system may combine the two registered images by producing a reoriented version of one view that can be "fused" with the other.

This fusing of two views into one may be accomplished by simply summing intensity values in two images, by imposing outlines from one view over the gray levels of the other, or by encoding one image in hue and the other in brightness in a color image. Regardless of the method employed, image fusion should be distinguished from image *registration*, which is a necessary first step before fusion can be successful.

The larger system may alternatively use the registration simply to provide a pair of movable cursors on two electronically displayed views linked via the registering transformation so that the cursors are constrained to visit corresponding points. This latter method generalizes easily to the case in which one view is the physical patient and one of the movable "cursors" is a physical pointer held by the surgeon.

The registration system may be part of a robotically controlled treatment system whose guidance is based on registration between an image and the physical anatomy. Drills, for example, may be driven robotically through bone by following a path determined in CT and registered to the physical bone. Gamma rays produced by a linear accelerator or by radioactive isotopes may be aimed at tissue that is visible in MR but hidden from view during treatment with the aiming being accomplished via automatic calculations based on a registering transformation.

Registration also serves as a first step in multimodal segmentation algorithms that incorporate information from two or more images in determining tissue types. Fusion, linked cursors, robotic controls, and multimodal segmentation algorithms exploit knowledge of a geometrical relationship between two registered views in order to assist in diagnosis or treatment.

Registration is merely the determination of that relationship. The goal of registration is thus simply to produce as output a geometrical transformation that aligns corresponding points and can serve as input to a system further along in the chain from image acquisition to patient benefit.

Each view that is involved in a registration will be referred to a coordinate system, which defines a space for that view. Our definition of registration is based on geometrical transformations, which are mappings of points from the space X of one view to the space Y of a second view. The transformation $\mathcal{T}$ applied to a point in X represented by the column vector x produces a transformed point x'.

$$x' = \mathcal{T}(x)$$

If the point y in Y corresponds to x, then a successful registration will make x' equal, or approximately equal, to y. Any nonzero displacement $\mathcal{T}(x) - y$ is a registration error. The set of all possible $\mathcal{T}$ maybe partitioned into rigid and non-rigid transformations with the latter transformations further divided into many subsets [4].

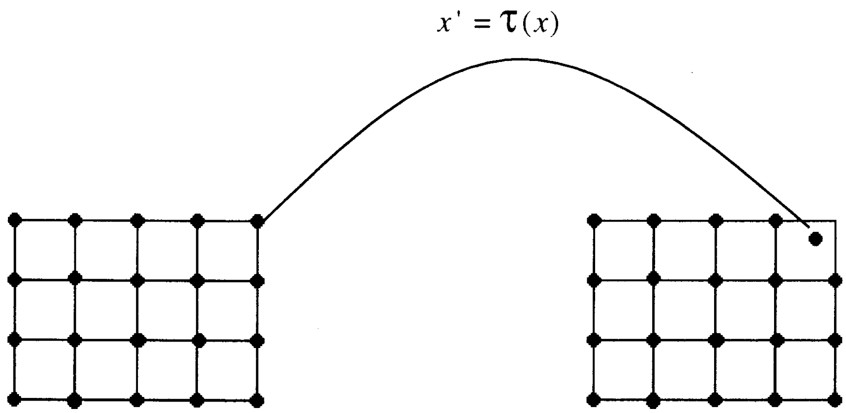

Figure 2 Geometric Transformation between two images

The illustration above shows the relation of a point or pixel location in the source image related to the transformed point or pixel location in the target image. The point pair are related by a geometrical transformation, which is either rigid or non-rigid. It can also be seen that the transformed location may not fall on the matrix grid. It is required that all the pixel locations need to be on the matrix grid. So interpolation of the intensity value or location needs to be done to replace the transformed point on the grid.

2.3 Rigid Geometric Transformations

Rigid transformations, or rigid mappings, are defined as geometrical transformations that preserve all distances. These transformations also preserve the straightness of lines (and the planarity of surfaces) and all nonzero angles between straight lines.

The rigid registration transformation on the reference image is a 2D rotation, 2D translation along the x, y-axes. The Image is taken as 2D matrix and the transformation is applied.

Translation:

Suppose the geometric transformation is translation of the x and y coordinates to a new location by using displacements (X_O, Y_O), the translation is easily accomplished by using the equations shown below:

$$X^* = X + X_O,$$
$$Y^* = Y + Y_{O,}$$

Where (X^*, Y^*) are the coordinates of the new point. It can be expressed in a matrix form hence the transformation T is as shown below:

$$T = \begin{bmatrix} 1 & 0 & X \\ 0 & 1 & Y \\ 0 & 0 & 1 \end{bmatrix}$$

Scaling:

When the geometric transformation is scaling of the x and y coordinates are scaled to a new location by using the parameters (S_X, S_y), the scaling is easily accomplished by using the equation shown below:

$$S = \begin{bmatrix} S_x & 0 & 0 \\ 0 & S_y & 0 \\ 0 & 0 & 1 \end{bmatrix}$$

Rotation:

The transformations used for three-dimensional rotation are inherently more complex than the transformations discussed so far. The simplest form of these transformations is for rotation of one point about the coordinate axes. With reference to the figure shown below the rotation about all the three axes are shown.

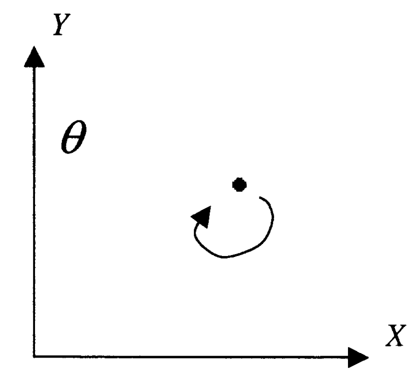

Figure 2.2 Rotation of a point about the coordinate axes

With reference to the Figure 2.2 rotation of a point about the x and y- coordinate axis by an angle θ is achieved by using the transformations shown below

$$R_\theta = \begin{bmatrix} \cos\theta & \sin\theta & 0 \\ -\sin\theta & \cos\theta & 0 \\ 0 & 0 & 1 \end{bmatrix}$$

The rigid transformation thus is the multiplication of the rotation, translation and scaling parameters with the respective parameters specified. V* is thus the transformed point after the transformation matrices have been applied to the point V in the same order specified below, because matrix multiplication is not reversible [5].

$$V^* = R_\theta(S(T.V))$$

2.4 Non-rigid Geometric Transformations

A geometric transformation of an image or a matrix relates to each point in the transformed image i.e. each point in the source image has a geometrical transformation to relate it to its respective location in the target image. Rigid transformation methods are limited to only a few changes like rotation, translation, scaling shearing etc. i.e. they are limited by the ability to register parallel structures or structures which deform in any random manner like a piece of elastic or rubber.

Rotation, translation and scaling transformations cannot account for change in human anatomy, which require non-rigid curve like transformations. Hence non-rigid transformations are inevitable when registering the brain structure, which undergoes change of shape resulting from the surgery.

In curved transformations, the simplest functional form for the transformation τ is a polynomial as shown below.

$$x' = \sum_{i,j}^{I,J} C_{i,j} x^i y^j$$

Where $C_{i,j}$ is the three-element vector of coefficients for the i, j term in the polynomial expression for the three components $x^i y^j$ of X'. These transformations are rarely used with values of I, J greater than two to avoid spurious oscillations.

These oscillations can be reduced or eliminated by employing piecewise polynomials. Transformations called splines are used to model the deformable object as a mesh of control points. The object takes a change in shape depending upon the movement of the control points in a two or three-dimensional axis.

mesh of control points. The object takes a change in shape depending upon the movement of the control points in a two or three-dimensional axis.

For example, a polynomial of degree 2 is represented as shown below

$$x' = a_0 x + a_1 x + a_2 y + a_3 xy + a_4 x^2 + a_5 y^2$$
$$y' = b_0 y + b_1 x + b_2 y + b_3 xy + b_4 x^2 + b_5 y^2$$

The coefficients of the polynomial are calculated as shown below:

$$\begin{bmatrix} n & \sum_i x_i & \sum_i y_i & \sum_i x_i y_i & \sum_i x_i^2 & \sum_i y_i^2 \\ \sum_i x_i & \sum_i x_i^2 & \sum_i x_i y_i & \sum_i x_i^2 y_i & \sum_i x_i^3 & \sum_i x_i y_i^2 \\ \sum_i y_i & \sum_i x_i y_i & \sum_i y_i^2 & \sum_i x_i y_i^2 & \sum_i x_i^2 y_i & \sum_i y_i^3 \\ \sum_i x_i y_i & \sum_i x_i^2 y_i & \sum_i x_i y_i^2 & \sum_i x_i^2 y_i^2 & \sum_i x_i^3 y_i & \sum_i x_i y_i^3 \\ \sum_i x_i^2 & \sum_i x_i^3 & \sum_i x_i^2 y_i & \sum_i x_i^3 y_i & \sum_i x_i^4 & \sum_i x_i^2 y_i^2 \\ \sum_i y_i^2 & \sum_i x_i y_i^2 & \sum_i y_i^3 & \sum_i x_i y_i^3 & \sum_i x_i^2 y_i^2 & \sum_i y_i^4 \end{bmatrix} \begin{bmatrix} a0 \\ a1 \\ a2 \\ a3 \\ a4 \\ a5 \end{bmatrix} = \begin{bmatrix} \sum_i u_i \\ \sum_i x_i u_i \\ \sum_i y_i u_i \\ \sum_i x_i y_i u_i \\ \sum_i x_i^2 u_i \\ \sum_i y_i^2 u_i \end{bmatrix}$$

Spatial transformations can be classified on the basis of their domain. The domain refers to the region of influence and can be either local or global. A spatial transformation is deemed global if its transformation is dependent on all the control points. If the spatial transformation is not dependent on all the control points, it is referred to as a local transformation affecting only parts of the image. For instance, rigid transformations are global transformations because it applies to the whole image.

In point-matching, set of n control points (p,q) are selected from the two images. A control point is a unique positional descriptor derived from an anatomical feature or location. A spatial transformation mathematically describes the spatial relationship between corresponding control-points.

Non-rigid geometric transformation relates each point in the source image to its transformed location in the target image based on some change that is accounted for by various elastic methods. We consider image data as a continuum, rather than a discrete array of pixels. Such a continuous modeling of the data is often required in medical imaging. When the image data is non-discrete, it can be modeled without the constraints of rigidity. This is the basis of interpolation.

Almost anyone involved with medical imaging has been using splines. The most commonly used interpolation algorithm – is bilinear interpolation. – Is equivalent to fitting the image with a spline of degree one. Splines however start revealing their true power as one moves to higher degrees. They provide the best cost-performance tradeoff. Since quality is a major concern with medical images, it makes good sense to use them in applications [6].

A Radial basis function is a scattered data interpolation method where the spatial transformation is a linear combination of radially symmetric functions, each centered on a particular control point. The choice of a radial function reflects the fact that the scattered data has no preferred orientation. It also provides smooth deformations with easily controllable behavior [5].

A radial basis function has the following general form

$$f(x) = P_{mk}(x) + \sum_{i=1}^{n} A_{ik}\, g(r_i)$$

The first component is a polynomial of degree 'm', or is not present. This global linear transformation assures a certain degree m of polynomial precision (accounting for global rigid changes that might have occurred).

The later component, is the sum of a weighted elastic or nonlinear basis function $g(r_i)$, where r_i denotes the Euclidean norm such that $r_i = [x - x_i]^{1/2}$, where $x = (x, y)$. Thus the mapping function $f(x)$ is a linear combination of a radially symmetric function $g(r_i)$ and a low degree polynomial [4].

The thin-plate splines are examples of the more general category of radial basis functions, which, for two-dimensional and three-dimensional spaces, have the same form of equation as above, but with the $g(r_i)$ replaced by $r_i^2 \ln r_i^2$.

Other examples of $f(x)$ that have been employed to interpolate among points in two or three dimensions include the 'multiquadric' $(r_i^2 + \delta)^{\pm\mu}$, the 'gaussian' $\exp(-r^2 / a)$, the 'shifted log', $\log\ (r_i^2 + \delta)^{3/2}$ [3]. Because none of these example functions has compact support, change in one control point has an effect on the transformation at all points.

Other curved transformations have been employed, including solutions to the equations of continuum mechanics describing elastic and fluid properties attributed to the anatomy being registered. These equations, which are derived from conservation of mass, momentum, and energy and from experimentally measured material properties, involve the displacement vector, $x' - x$, and the first and second spatial derivatives of its components. The non-rigid transformations that result from the numerical solution of these partial differential equations are appropriate for intrapatient registration when the anatomy is non-rigid, especially when surgical resection has changed its shape [4].

2.5 Free Form Deformations (FFDs)

The term spline originally referred to the use of long flexible strips of wood or metal to model the surface of ships and planes. These splines were bent by attaching different weights along their length. A similar concept can be used to model spatial transformations; for example, a 2D transformation can be represented by two separate surfaces' whole weight above the plane corresponds to the displacement in the horizontal or vertical direction.

Many registration techniques using splines are based on the assumption that a set of corresponding points or landmarks can be identified in the source and target images. This is analogous to the use of point landmarks for rigid or affine registration. These corresponding points are called control points.

At these control points, spline-based transformation either interpolate or approximate the displacements which are necessary to map the location of the control point in the target image into the corresponding counterpart in the source image. Between control points, they provide a smoothly varying displacement field. The interpolation condition can be written.

$$T(\phi_i) = \overline{\phi_i}$$

Where ϕ_i denotes the location of the control point $\overline{\phi_i}$ in the target image and denotes the location of the corresponding control point in the source image. There are a number of different ways to determine the control points. For example, anatomical or geometrical landmarks, which can be identified in both images can be used to define a spline-based mapping function, which maps the spatial position of landmarks in the source image into their corresponding position in the target image. In addition the location of the control points can be updated by optimization of a voxel similarity measure such as mutual information.

Alternatively, control points can be arranged with equidistant spacing across the image, forming a regular mesh. In this case the control points are only used as a parameterization of the transformation and do not correspond to anatomical or geometrical landmarks. Hence they can be referred to as quasi- or pseudo landmarks.

In general radial basis functions have infinite support. Therefore each basis function contributes to the transformation and each control point has a global influence on the transformation. In a number of cases the global influence of control points is undesirable since it becomes difficult to model local deformations. Furthermore, for a large number of control points the computational complexity of radial basis function splines becomes prohibitive.

An alternative is to use free form deformations (FFDs) which have been widely used for animations in computer graphics. FFDs based on locally controlled functions such as B-splines are a powerful tool for modeling 3D deformable objects and have been successfully used for image registration.

The basic idea of FFD is to deform an object by manipulating an underlying mesh of control points. In contrast to radial basis function splines, which allow arbitrary configurations of control points, spline based FFDs require a regular mesh of control points with uniform spacing [7,8].

A spline-based FFD is defined on the image domain $\Omega = \{(x, y) \mid 0 \leq x < X,\ 0 \leq y < Y\}$, where Φ denotes an $n_x \times n_y$ mesh of control points $\Phi_{i,j}$, with uniform spacing δ.

In this case the displacement field u is defined by the FFD can be expressed as the 2D tensor product of the familiar 1D cubic splines:

$$u(x, y) = \sum_{l=0}^{3} \sum_{m=0}^{3} \theta_l(u)\theta_m(v)\Phi_{i+l,j+m}$$

Where, $i = \left\lfloor \frac{x}{\delta} \right\rfloor - 1 . j = \left\lfloor \frac{y}{\delta} \right\rfloor - 1, u = \frac{x}{\delta} - \left\lfloor \frac{x}{\delta} \right\rfloor, v = \frac{y}{\delta} - \left\lfloor \frac{y}{\delta} \right\rfloor$

And θ_l represents the $l-th$ basis function of the B-splines:

$$\theta_0(s) = (1-s^3)/6$$

$$\theta_1(s) = (3s^3-6s^2+4)/6$$

$$\theta_2(s) = (-3s^3+3s^2+3s+1)/6$$

$$\theta_0(s) = s^3/6$$

FFDs are controlled locally, which makes them computationally efficient even for a large number of control points. In particular the basis functions of cubic splines have a limited support, i.e., changing the control point $\Phi_{i,j}$ affects the transformation only in the local neighborhood of that control point [7,8].

2.6 Similarity Measures

Registration methods are usually classified as being either feature-based or intensity-based. Methods from the former class proceed in two sequential steps. The first is to extract homologous geometrical landmarks in the images; these can be points, lines, surfaces or volumes. Then the problem consists of computing the transformation that 'best' matches these landmarks.

Intensity-based techniques do not deal with identifying geometrical landmarks. Their basic principle is to search, in a certain space of transformations, the one that maximizes a criterion measuring the intensity similarity of corresponding voxels or pixels. Over the last years, a number of monomodal, multimodal and rigid as well as non-rigid registration problems have been dealt with using similarity measure [9].

Choosing one measure adapted to a specific registration problem is not always straightforward for atleast two reasons. First, it is often difficult to model the physical relationship that exists between two images. Second, most of the similarity measures rely on imaging assumptions that are not fully explicit. Existing similarity measures may be classified into four main kinds of hypothesis:

Identity relationship: The basic assumption is that when matched the images are identical. This includes a number of popular measures: the sum of squared intensity differences (SSD), the sum of absolute intensity differences, cross-correlation, entropy of the difference image etc. Although these measures are not equivalent in terms of robustness and accuracy, none of them is able to cope with relative intensity changes from one image to the other [9].

Affine relationship: The step beyond is to assume that the intensities of the two images I and J to be registered are related by an affine mapping. The measures adapted to this situation are more or less variants from the correlation coefficient, defined as the ratio between the images' covariance and the product of individual standard derivations:

$$P(i,j) = \frac{COV(I,J)}{\sqrt{Var(I)}\sqrt{Var(J)}}$$

The correlation coefficient is generally used for matching images from the same modality.

Functional relationship: For multimodal images, more complex relationships are involved. The approach proposed assumes that, at the registration position, one image could be approximated in terms of the other by applying some intensity function, $I \approx \Phi(J)$. Making no assumptions regarding the nature of the function, a natural statistical measure is derived, the correlation value:

$$\eta^2(I/J) = 1 - \frac{Var(I - \Phi(J))}{Var(I)},$$

Where $\Phi(J)$ is the least square optimal non-linear approximation of I in terms of J

Statistical relationship: Finally, assuming a functional relationship is sometimes too restrictive. Then, it is more appropriate to use information theoretic measures, from which mutual information is today the most popular:

$$\mathrm{I}(I,J) = \sum_i \sum_j \log \frac{p(i,j)}{p(i)p(j)},$$

Where $p(i,j)$ is the intensity joint probability distribution of the images, and $p(i)$ and $p(j)$ the corresponding marginal distributions. The category is not fundamentally different from the previous one, as the ideal case is still perfect functional dependence. Mutual information is however theoretically more robust to variations with respect to this ideal situation. A number of comparison studies have shown that similarity measures yield performances depending on the considered modality combinations. There is probably no universal measure and, for a specific problem, the point is rather to choose the one that is best adapted to the nature of the images registered [9].

Non-rigid registration is a process for maximizing a spatial image correspondence of two images within constrains of an image transformation model, to bring the features of first image into alignment with those of the second image with possibly different content. Image correspondence is measured using similarity measures, which compares the data values at corresponding points in the images.

Similarity measures are a form of registration based on the intensity or feature properties of the images. It uses a cost-function to quantify the degree of similarity between the images. Registration models based on these cost-functions simply adjust the parameters of an appropriate spatial-transformation model until the cost function reaches a local optimum [6].

Cross-correlation was one of the first cost functions among a variety of similarity measures used for image registration. This cost-function multiplies the intensities of the two images at each pixel and sums the resulting product. The product is then normalized (CN) by dividing it by the product of the root-mean squared intensities of each of the two images. It is denoted in the following expression:

$$C(m,n) = \sum_{i}^{dx} \sum_{j}^{dy} C(i, j).R(i-m, j-n)$$

$$CN(m,n) = \frac{\sum_{i}^{dx}\sum_{j}^{dy} C(i,j).R(i-m,j-n)}{\left[\sum_{i}^{dx}\sum_{j}^{dy} C(i,j)^2\right]^{0.5}\left[\sum_{i}^{dx}\sum_{j}^{dy} R(i-m,j-n)^2\right]^{0.5}}$$

Correlation coefficient is an extension to correlation, which assumes that the intensities in the two images are linearly related. If the correlation coefficient is equal to one, then the images are perfectly matched. The correlation coefficient is given below in the following expression:

$$CC(m,n) = \frac{1}{N}\frac{\sum_{i}^{dx}\sum_{j}^{dy}\left[C(i,j)-\overline{C}\right]\left[R(i-m,j-n)-\overline{R}\right]}{\left\{\left[\sum_{i}^{dx}\sum_{j}^{dy}\left[C(i,j)^2-\overline{C}\right]\right]\left[\sum_{i}^{dx}\sum_{j}^{dy}\left[R(i-m,j-n)^2-\overline{R}\right]\right]\right\}^{0.5}}$$

The sum of squared differences is another similarity measure. When minimized it gives the result as zero, the images are correctly matched. It is denoted in the following expression.

$$SSD(m,n) = \sum_{i}^{dx}\sum_{j}^{dy}\left[C(i,j)-R(i-m,j-n)\right]^2$$

Mutual information is a basic concept from information theory, measuring the statistical dependence between two random variables or the amount of information that one variable contains about the other. The MI criterion presented here states that the MI of the image intensity values of corresponding pixel or voxel pairs is maximal if the images are geometrically aligned [4].

Because no assumptions are made regarding the nature of the relation between the image intensities in both modalities, this criterion is very general and powerful and be applied to a wide variety of applications.

The information or entropy of an image can be computed by estimating the probability distribution of the image intensities. We use the Shannon measure of entropy, $-\sum_{S} p(s)\log p(s)$ for a probability distribution P. The joint probability of two images is estimated by calculating a normalized joint histogram of the gray values. The marginal distributions are obtained by summing over the rows, respectively the columns of the joint histogram.

The definition of the mutual information of two images A and B combines the marginal and joint entropies of the two images in the following expression.

$$MI(A,B) = H(A) + H(B) - H(A,B)$$

Where H [A, B] is the joint entropy, H [A] and H [B] are marginal entropies given in the following expressions:

$$H[A,B] = -\sum_{j,k} PDF[j,k] \;\; \log PDF[j,k]$$

$$H[A] = \sum_{j}\left(\sum_{k} PDF[j,k] \log \sum_{l} PDF[j,k]\right)$$

$$H[B] = \sum_{k}\left(\sum_{i} PDF[j,k] \log \sum_{j} PDF[j,k]\right)$$

$$PDF[j,k] = \frac{HIST[j,k]}{\sum_{j,k} HIST[j,k]}$$

HIST is an n-dimensional joint histogram, where n is the number of images used to generate it. The axes of the histogram are the intensities in each image, and the value at each point denotes the number of voxels. If the joint histogram is normalized, it gives the PDF of intensities in the n- images [4].

For two images A and B related by a transformation $\mathcal{T}$, the following algorithm calculates two-dimensional PDF for intensity partitions $\{a\}$ and $\{b\}$

1. Allocate an $N_a \times N_b$ array of $HIST[j,k]$
2. Initialize the histogram $HIST[j,k]=0$ for all j,k
3. For each voxel $i \in A \cap B$, calculate intensity values $A(i)$ and $B(i)$, calculate the intensity partition numbers a and b corresponding to $A(i)$ and $B(i)$, and increment $HIST[a,b]$
4. Calculate $\sum_{j,k} HIST[j,k]$
5. Normalize the histogram to calculate the PDF:

$$PDF[j,k] = \frac{HIST[j,k]}{\sum_{j,k} HIST[j,k]}$$

The mutual information between the source and the target image can be calculated from the algorithm explained above. The PDF of the image gives the joint entropy. The marginal entropies are found out using PDF and when substituted in the relation give mutual information for a pair of images.

Many registration methods have been implemented using mutual information. Although the rigid or non-rigid geometric transformations vary, calculation of the similarity measure using mutual information has been very popular [8,10,13,14,15].

2.7 Minimization of Functions

Rigid registration and non-rigid registration have parameters that define the registration process, like angle of rotation, distance of translation and distance vectors etc. After finding the geometrical relation between the of two images, its necessary to find their optimum value of similarity measure over a parameter space with dimensionality defined by the degree of freedom of the transformation used [2]. Maximum mutual information tells us that the images are most similar at that particular parameter of the transformation (in the case of rigid registration, it is angle of rotation or amount of translation) [10].

The optimal registration parameter δ is given as below

$$\delta = \max_{\eta}\left(MI(\eta)\right),$$

Where, η is the mutual information.

The paragraph above introduces the idea of optimization as the vital part of the registration process. We will now look into different ways to optimize the registration algorithm giving the optimum registration parameters. The section below gives a brief outline of the different numerical methods used to optimize the similarity measure.

In a nutshell: A single function f depends on one or more independent variables. One wants to find the value of those variables where f takes on a maximum or minimum. The tasks of maximization or minimization are trivially related to each other, since one f could just as well be another's $-f$. The computational desiderata are the usual ones: Do be done quickly, cheaply, and in small memory [11].

Often the computational effort is dominated by the cost of evaluating f (and also perhaps its partial derivatives with respect to all variables, if the chosen algorithm requires them). In such cases simple surrogate sometimes replaces the desiderata: Evaluate f as few times as possible. The following paragraphs give a brief outline of the different methods for one and two-dimensional function minimization, explaining different methods commonly used.

There is unfortunately no perfect optimization algorithm and choice has to be made based on the type of function to be minimized, and its different constraints.

One must choose between methods that need only evaluations of the function to be minimized and methods that also require evaluations of the derivative of that function. In the multidimensional case, this derivative is the gradient of that function. In the multidimensional case, this derivative is the gradient, a vector quantity.

Algorithms using the derivative are somewhat more powerful than those using only the function, but not always enough as to compensate for the additional calculations of derivatives. One can easily construct examples favoring one approach or favoring the other. However if you can compute derivatives, one must be prepared to use them.

For one-dimensional minimization (minimize a function of one variable) without calculation of the derivative, Brent's method is commonly used. If the function has a discontinuous second or lower derivative, then the parabolic interpolation of the Brent's method is used. For one-dimensional minimization with calculation of the derivative, a variation of the Brent's method is available which makes limited use of the first derivative information

Now we turn to the case with more than one variable (two-dimensional). One must choose between methods that require storage of order N^2 and those that require only order of N where N is the number of dimensions. For moderate values of N and reasonable memory sizes this is not a serious constraint however, there might be a occasional application where storage can be critical.

The downhill simplex method due to Nelder and Mead is commonly used for its simplicity. This method just crawls downhill in a straightforward fashion that makes almost no special assumptions about the function. This can be both extremely slow but can also be extremely robust in some cases. It has a very concise code and completely self-contained. The storage requirement is of the order of N^2, and derivative calculations are not required.

There are other methods called direct-set methods, of which Powell's method is a prototype. These are methods of choice, which cannot easily calculate derivatives, and are not necessarily to be overlooked. Although derivatives are not needed, the method does require a minimization sub-algorithm, such as Brent's method. The storage is of order N^2.

There are two major families of algorithms for multidimensional minimization with calculation of first derivatives. Both families require a one-dimensional minimization sub-algorithm, which can itself either use, or not use, the derivative information, as you see fit (depending on the relative effort of computing the function and of its gradient vector). Neither family dominates the other, its just considered as an alternative.

The first family goes under the name of conjugate gradient methods, as typified by the Fletcher-Reeves algorithm and the closely related and probably superior Polak-Ribere algorithm. Conjugate gradient methods require only of order of a few times N storage, require derivative calculations and one-dimensional sub-minimization.

The second family goes under the names quasi-newton or variable metric methods, as typified by Davidon-Fletcher-Powell (DFP) algorithm (sometimes referred to as Fletcher-Powell) or closely related Broyden-Fletcher-Goldfarb-Shannon (BFGS) algorithm. These methods require of order N^2 storage, require derivative calculations and one-dimensional sub-minimization [11].

CHAPTER 3

IMAGE REGISTRATION USING THE B-SPLINE ALGORITHM

3.1 Image Registration method using B-Splines

The image registration algorithm combines the rigid and non-rigid transformations. Here again the input is two images to be registered. One is to be geometrically transformed to be as the other. The image undergoing the transformation is called the source image and the image to which the source has to be matched after registration is called the target image.

The geometric transformation that is to be performed on the source image deals with the rigid parameters like rotation angle, distance of translation and amount of scaling. A control grid with equally spaced control points is chosen on the source image. The rigid parameters are used to correct the change in the image, which might be caused by the patient moving while the pre-operative scan is taken or the instrument being placed a little distance away etc.

The non-rigid parameters account for the elastic change that occurs during the surgery. In this case both the source and the target images are rigidly transformed and there is no actual elastic change in the target. But the algorithm is being performed to prove the control grid parameters are optimized as just zeros even where there is no elastic change.

After the geometric transformation is performed the new intensity values are interpolated using bilinear interpolation. The mutual information between the interpolated image and target image is calculated. The process of changing the parameters and finding the right combination of parameters is done repetitively till the maximum mutual information is found.

Maximum mutual information helps obtain the optimized parameters, which are then used to transform the source image, making it look similar to the target image. Mean square error between the registered image and the target image is used to validate the registration method.

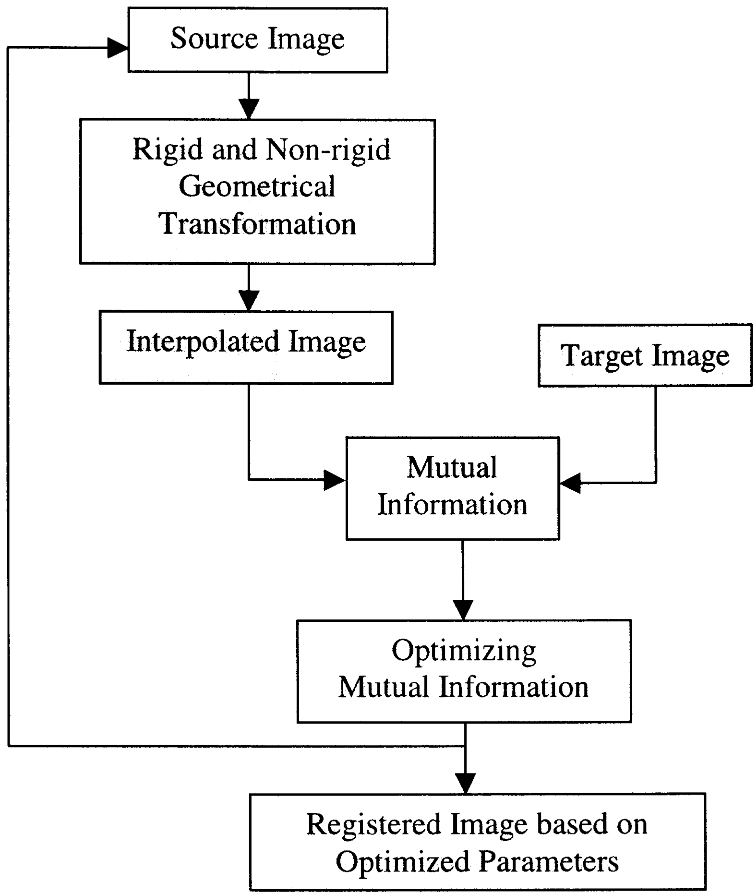

Figure 3.1 Image Registration using B-Spline

3.2 Registration Algorithm with B-Splines

Step 1. Let A and B be the source and target images.

Step 2. Choose a control grid with equally spaced control points.

Step 3. Apply the geometrical transformation with rigid and non-rigid parameters.

Step 4. Calculate Mutual Information between the source image A and target image B.

Step 5. Optimize mutual information using the simplex method.

Step 6. If the optimum parameters are found, then go to step 3 or else go to step 7.

Step 7. Apply the optimum parameters to the source image to get the registered image.

Step 8. Validate the registration method by finding the mean square error between the registered image and the target image.

The geometric transformation in this algorithm has two parts. One part is the rigid geometric transform, which has three parameters of rotation, translation, and scaling, in the two axes. So that gives us 6 degrees of freedom to optimize. The other part of the transformation is the free form deformation using B-splines, which has a number of parameters depending upon the number of control points chosen.

For instance if a 10 x 10 grid of control points is chosen, then we have 200 degrees of freedom. If the number control points increase, the degrees of freedom increase and the deformation on the volume is also more flexible. The disadvantage in increasing the number of control points on the grid is that the time taken to optimize it will also increase [6].

Rigid registration on a two-dimensional brain image is implemented by developing a function. The function takes the three parameters of rotation, translation and scaling in both x and y-axis. The mutual information between the source image and the target image is computed, and the mutual information is optimized to give the best parameters of rotation, translation and scaling, which denote the best match between the source and the target image.

After the transformation is applied, new location of the pixel may not be on the matrix grid. Hence another interpolation method is necessary to determine the value of the pixel in the new location. In this algorithm we use tri-linear interpolation to find the new pixel value and it is assigned back to its respective location.

The geometric transformation is one function. It will include the rigid parameters in x, y-axes, and the two vector matrices from the B-spline interpolation, in one function. The rigid changes like movement in the posture of the patient while the scan is taken, and non–rigid changes occurring during the surgical procedure are included in one transformation, thereby increasing the degrees of freedom.

3.3 Interpolation

When an image undergoes geometric transformation, the new position of the intensity locations change and is no longer on the grid or array location. Therefore interpolation is required to find new location for transformed pixels. The illustration below explains the need for interpolation:

$$x' = \tau(x)$$

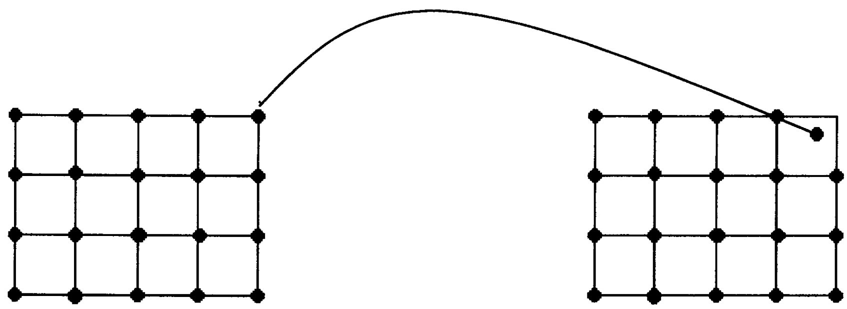

Figure 3.2 Illustration of the interpolation technique

The simplest method of interpolation is the nearest neighbor interpolation approach. It is also called zero-order interpolation. The distance of the new location of the pixel is calculated and the nearest pixel is assigned the transformed pixel. It is a very simple interpolation technique and often has the drawback of producing undesirable distortion of straight edges in images of high resolution. Smoother results can be obtained by using more sophisticated techniques like cubic interpolation. The price paid for smoother approximations generally are computationally burdensome.

For general-purpose image processing a bilinear interpolation approach that uses gray levels of the four nearest neighbors usually is adequate. This approach is also straightforward. Because the gray level of each of the four integral nearest neighbors of a nonintegral pair of coordinates is known, the gray-level value at these coordinates, denoted $v(x', y')$, can be interpolated from the values of its neighbors by using the relationship

$$v(x', y') = ax' + by' + cx'y' + d$$

Where the four coefficients are easily determined from the four equations in four unknowns that can be written using the four known neighbors of $v(x', y')$. When these four coefficients have been determined, $v(x', y')$ is computed and this replaces the original location from where it was transformed.

3.4 Optimization

The optimization of the mutual information in the registration algorithm is being performed using the Downhill Simplex Method in multidimensions (more than one optimizing parameter). The Downhill Simplex Method is due to Nelder and Mead, and is also called the Nelder and Mead Simplex Method. The function requires only function evaluations and it does not require the function derivatives.

A simplex is the geometrical figure consisting in N dimensions, of $N+1$ vertices and all their interconnecting line segments, polygonal faces etc. In two-dimensions, a simplex is a triangle. In three dimensions the simplex is a tetrahedron. In general we are only interested in simplexes that are nondegnerate, i.e., that enclose a finite inner N-dimensional volume. If any point of a degenerate simplex is taken as the origin, then the N other points define vector directions that span the N-dimensional vector space.

The Downhill Simplex method must be started not just with a single point, but with $N+1$ points, defining an initial simplex. If one thinks of one of these points (it does not matter which) as being your initial point P_0, then you can take the other N points to be

$$P_i = P_0 + \lambda e_i$$

Where e_i's are N unit vectors, and where λ is a constant, which is your guess of the problem's characteristic length scale. The downhill method now takes a series of steps, most steps just moving the point of the simplex where the function is largest ("highest point") through the opposite face of the simplex to a lower point. These steps are called reflections, and they are constructed to conserve the volume of the simplex (hence maintain its nondegeneracy). When it can do so, the method expands the simplex in one or another direction to take larger steps. When it reaches a "valley floor", the method contracts itself in the transverse direction and tries to ooze down the valley.

If there is situation where the simplex is trying to " pass through the eye of a needle", it contracts itself in all directions, pulling itself around its lowest (best) point. The routine is shown figuratively in the Figure 3.2

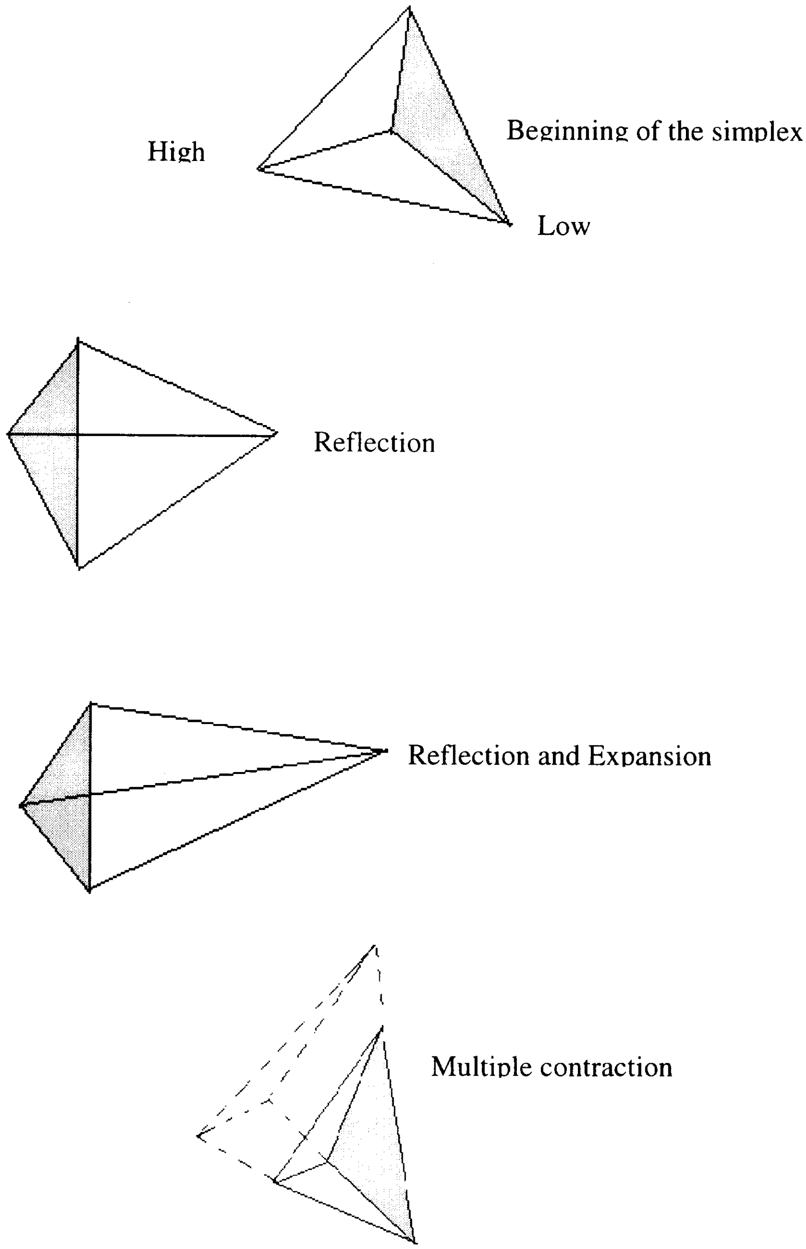

Figure 3.2 Illustrations of Possible Outcomes for a step in the Simplex Method

3.5 Validation of Registration

Validation of registration is to assess the success of the registration method. There are many aspects of validation and are usually precision, accuracy, robustness, stability etc. The measure of success in registration is usually an error measure between the source image A and the target image B. Mean square error is a commonly used error calculation because it is easy to compute and It is differentiable implying that a minimum can be sought. The *mean-square error* is defined by:

$$MSE = \frac{1}{MN} \sum_{m=0}^{M-1} \sum_{n=0}^{N-1} | a(m,n) - b(m,n) |^2$$

The difference between the intensity values of the registered image and the target image are computed. The difference is squared and divided by the total number of intensity values in both the images. This gives an error value of registration. If the error value is zero, then it denotes that the registration was successful. Optimum registration is performed when the registration error is zero.

CHAPTER 4

RESULTS AND DISCUSSION

4.1 Rigid Registration

Illustrative results and graphical information is presented in this section showing the various registration image results and the optimization graphs. The figures in this section are the source and target images. The registered image and the error of registration are also shown. The optimization graphs with the number of iterations against the mutual information are shown.

The mean square error of registration for the rigid registration is found to be 1.29e-12(almost zero), showing that the registration for rigid parameters of rotation, translation, and scaling are optimized successfully. The program was written in matlab code, using image processing toolbox and optimization toolbox.

In this experiment mutual information is optimized using the simplex method. It takes three hours and close to two hundred and thirty five iterations, depending upon the error difference between the source and the target images. The registration method was successful for about 10 sets of source and target image pairs.

The time taken was varying depending upon the difference between the source and the target images. The number of iterations also varies accordingly. It was observed that the difference in translation distance did not cause a significant change in the optimization time but change in rotation did show some change in terms of the time taken to optimize the registration.

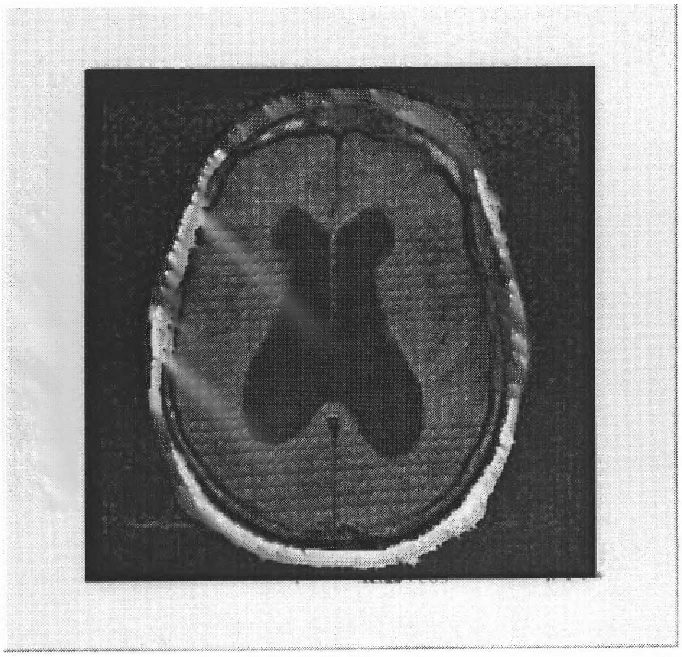

Figure 4.1.1 Source Image

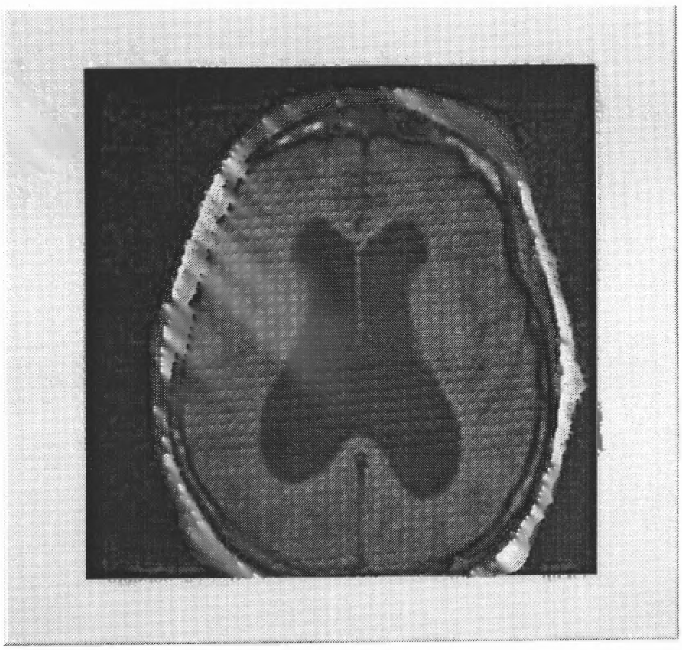

Figure 4.1.2 Target Image

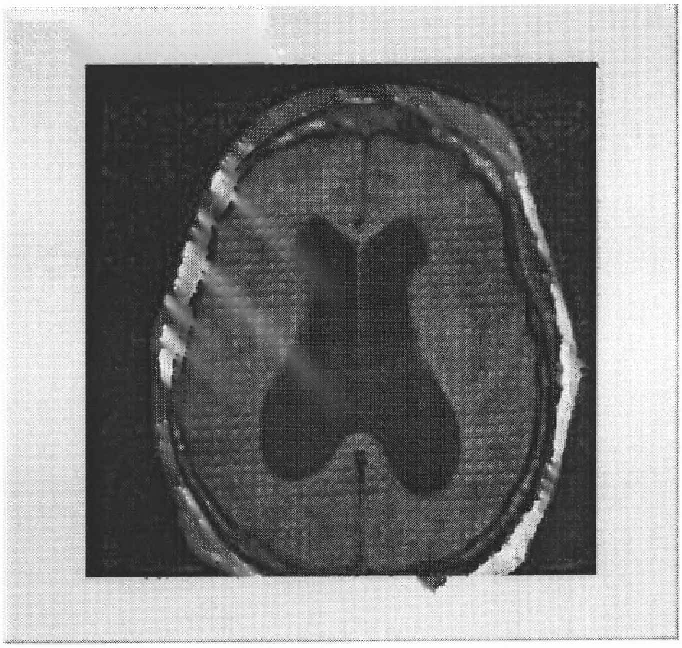

Figure 4.1.3 Registered Image

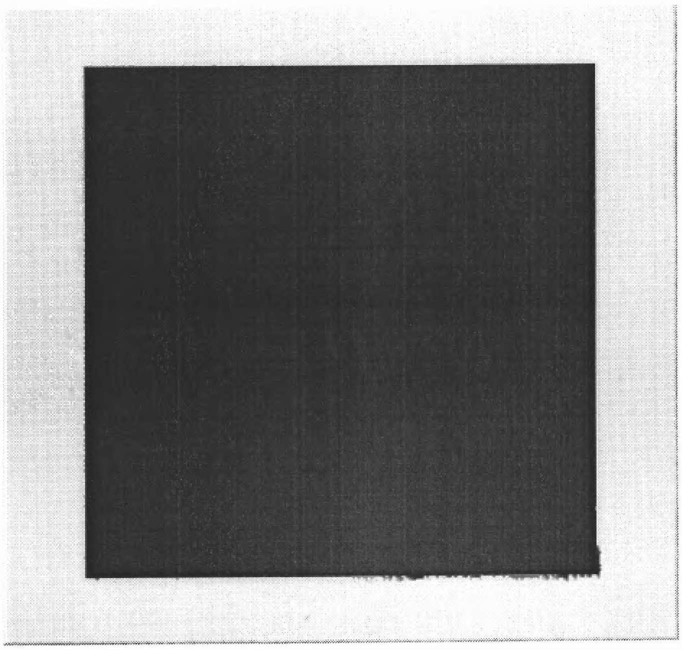

Figure 4.1.3 Registration Error Image

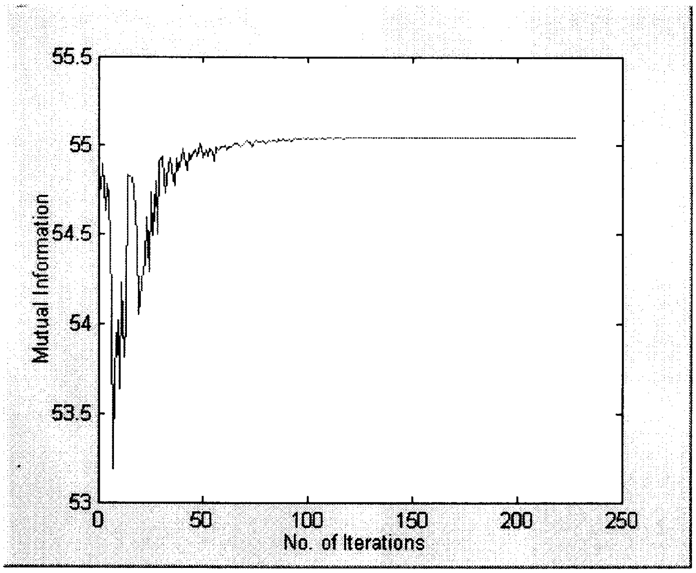

Figure 4.1.5 Optimization Graph

4.2 Non-rigid Registration

The illustrative images and optimization graphs here correspond to the non-rigid registration algorithm with the minimum number of control points (3 x 3) giving eighteen degrees of freedom in each axis. Hence it gives 18 degrees of freedom in x, y-axes. The rigid registration parameters of translation, rotation, and scaling are also included giving another 6 degrees of freedom. So combining the rigid and the non-rigid parts, we have twenty four parameters to optimize.

The mean square error of registration for the rigid registration is found to be 2.186e-12, showing that the registration for rigid parameters of rotation, translation, and scaling and the non-rigid displacement vectors are optimized with a small error. The program was written in matlab code, using image processing toolbox and optimization toolbox.

In this experiment mutual information is optimized using the simplex method. It takes six hours and close to seventy iterations, depending upon the error difference between the source and the target images. The registration method was similar for about 8 sets of source and target image pairs. The time taken was varying depending upon the difference between the source and the target images. The number of iterations also varies accordingly.

It was observed that the difference in translation distance did not cause a significant change in the optimization time but change in rotation and scaling did show some change in terms of the time taken to optimize the registration. Since there is no elastic change in the target image, the displacement vectors were optimized to zero, showing successful registration with a small error.

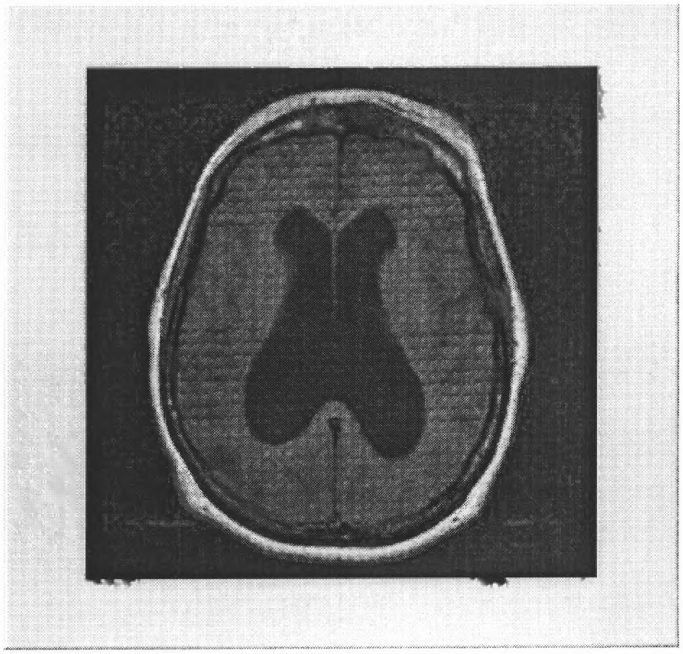

Figure 4.2.1 Source Image

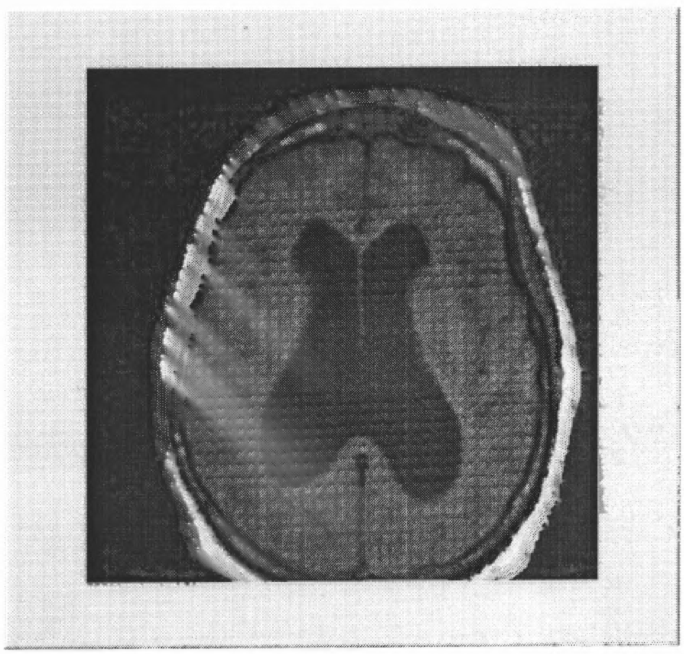

Figure 4.2.2 Target Image

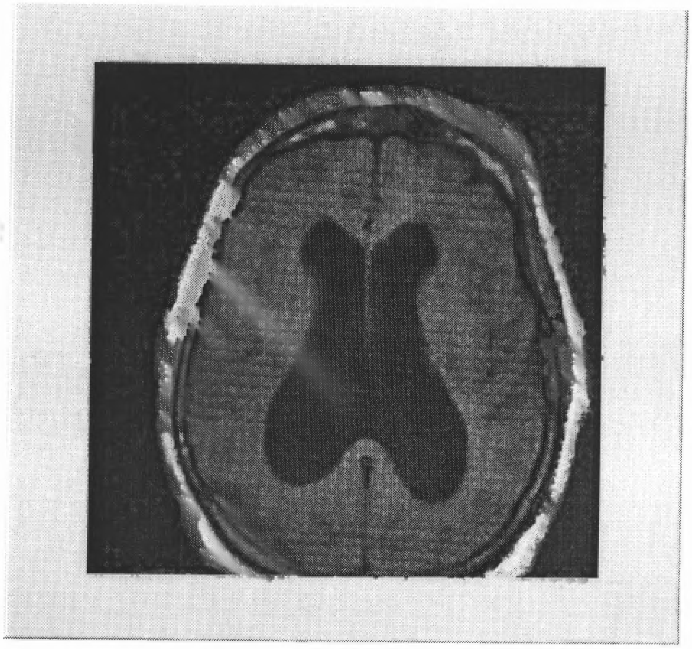

Figure 4.2.3 Registered Image

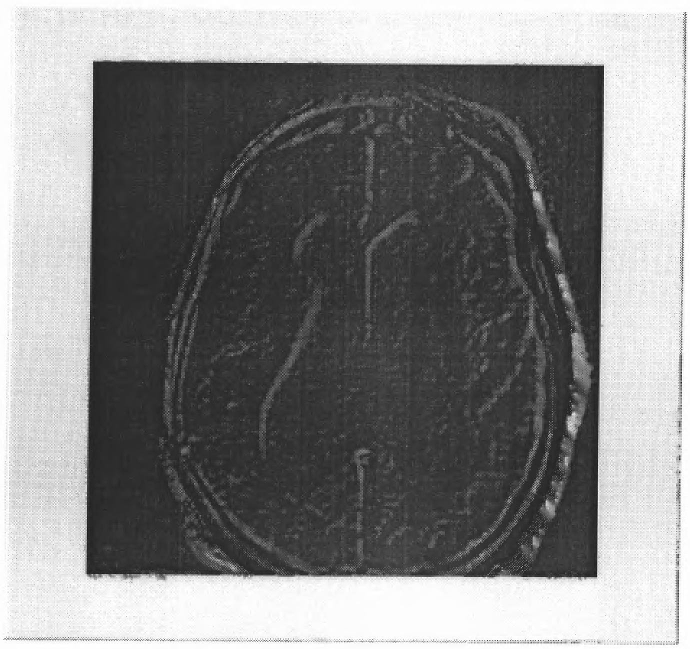

Figure 4.2.4 Registration Error

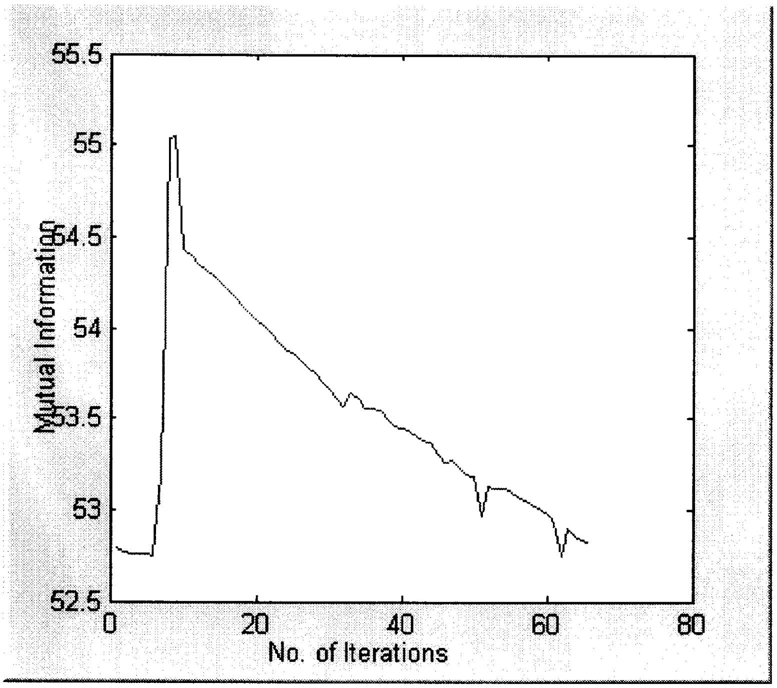

Figure 4.2.5 Optimization Graph

CHAPTER 5

CONCLUSION AND FUTURE WORK

The registration algorithm presented in the previous chapters is performed on two-dimensional images with a control grid of only the minimum number of control points (3x3). The two dimensional target images do not have any elastic deformation. The registration results yield displacement vectors with very small or zero displacements proving that the geometric transformation is quite effective.

The result of registration for the not being zero or negligible is not because of the transformation method used; it also depends on the optimization technique or method used. For the rigid case the optimization gave successful results. The reason for the non-rigid registration not giving similar results might be because of the increase in the number of parameters.

The optimization method used was the Nelder and Mead Simplex method. The Simplex method has certain disadvantages in that, after reaching a certain minimum, there is a possibility in the method to restart the whole optimization from the beginning. This was observed when dealing with the non-rigid registration. Certain parts of the optimization curves were similar or a repetition could be observed.

So, one area of improvement in the registration algorithm is to use a more robust and efficient algorithm. The optimization time while using the simplex method was also too high. For practical implementation, the optimization times have to be considerably fast. While choosing another optimization method the aspect of shorter implementation times and the possible increase in the number of parameters should be taken into consideration.

Optimization methods like Powell's method, other minimization methods using function derivates like Powell's quadratically convergent method, steepest descent are effective choices.

The number of control points taken into consideration was minimum in this implementation since only two-dimensional images are being considered and there is no elastic deformation. But in the typical implementation successful registration is preferred using the three-dimensional structure.

The three dimensional structure is a three-dimensional array. Each slice of the array is a two-dimensional brain image. It is easy to think of this as if many two-dimensional slices from consecutive parts of the brain are taken and stacked together to get a three-dimensional structure.

The two-dimensional brain slices or images are being stored in standard compression form like jpeg or tiff etc. The image data is actually in dicom standard which gives details of the slice thickness, in all the three axes. But when the image is being stored in jpeg we do not have such details. It only has the pixel or intensity values.

To actually get a three-dimensional brain structure the slices in between two image slices have to be interpolated. The interpolation to get a three-dimensional structure was done as a part of this research work. The linear interpolation method was being used. After interpolating the slices in between they are stacked one upon the other in the correct order and this gives the correct three-dimensional structure.

The figure below gives a brief illustration. The boxes with dashed lines are the interpolated slices that are interpolated using the original slices above and below them. The distance is calculated using the header information in the medical image files. The interpolation is one to get a three-dimensional pixel or voxel of the same height, length and width. The number of slices therefore increases to get the whole volume of the desired brain in one three-dimensional array.

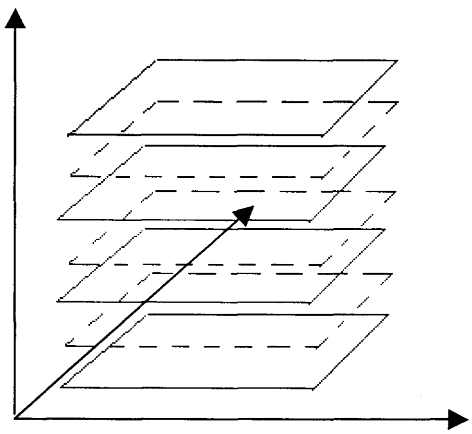

Figure 5.1 Interpolation to get three-dimensional brain volume

The other main aspect of the elastic registration method is to be able to register effectively, the preoperative images and the intraoperative images. The preoperative images are usually full view showing the whole brain structure. The exposing times (time taken to obtain the scan) are higher and hence the images are also quite clear.

In the case with intraoperative images the images are not full view. They show usually the part of the brain that is exposed during the surgery. The imaging times are very less compared to the preoperative images and hence the clarity of the image is poor and there is also a considerable amount of noise.

Registering the full view preoperative brain volume to the partial view intraoperative brain volume using elastic deformation is end goal of the elastic registration method with the help of free form deformation using b-splines. The intraoperative images are also be interpolated just like the preoperative to get the full view intraoperative brain volume. So then three-dimensional registration is done using the full view preoperative brain volume and partial view intraoperative brain volume. The b-spline has to also take the three dimensions into consideration.

It will give three three-dimensional distance vector arrays. For example if a 10 x 10 x 10 control point grid is chosen then the number of parameters for optimization will be 3000, and the rigid parameters of rotation, translation and scaling in all the three dimensions have to also be included.

The resolution of the number of the control points chosen determines the smoothness of the transformation. A tradeoff between the number of control points and the smoothness of the transform is often noticed because the increase in the number of control points causes an increase in the number of control points and optimization time.

The interpolation of the transformed intensity values has to be interpolated in three dimensions. Tri-linear interpolation is used taking into account the eight surrounding intensity locations. The optimizing cost is not only the similarity measure but it also includes a cost for the smoothness of the transform.

The control point locations in this research work are being taken in terms of the pixel locations. Ideally, it is to be taken in terms of the pixel measurement like millimeter etc. From that information the location of the control point on the grid is to be calculated.

The computation time is to be mainly taken into consideration and choice of software used has to give registration and optimization times that can be applied in a practical implementation. The preferred choice is C/C++ in a Unix or Windows environment.

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