CHAPTER-2

LITERATURE REVIEW

Advances in medical imaging technologies have enabled the diagnosis procedures not possible a decade ago. The acquisition speed and the resolution enhancements of imaging modalities have given doctors more information, less invasively about their patients. However, because of the multitude of imaging modalities[1,2,3,4] like Computed Tomography (CT), Positron Emission Tomography (PET), Magnetic Resonance Imaging (MRI) and the sheer volume of data being acquired. An increasing array of diagnostic images will be collected for each patient, either using different modalities (CT, MRI, PET), or the same modality at different times for research purposes and also for the treatment follow-up studies. Utilization of the new data effectively has become a problem. To handle the potentiality of this raw data, these images can be merged into one integrated view through a procedure called image registration [5, 6].

The objective of image registration is to find a transformation [7] to apply to a floating image so that it best aligns to a reference image. The combination of images from different modalities leads to additional clinical information which is not apparent in the separate imaging modality. For this reason, physicians prefer multiple imaging modalities to obtain more details. Image fusion is performed to extract all the useful
information from the individual modality and integrate them into one image. The complete registration with the advanced imaging modalities is shown in Fig.2.1. The images obtained from different scanners, must be aligned into the same spatial location before image fusion and visualization.

![Diagram showing the schematic process of registration involving CT, MRI, PET, Ultrasound, Registration, Fusion, Visualization]

**Fig. 2.1. The Schematic Process of Registration**

In this work registration method is used for the detection of brain tumors. Currently the most accurate methods for defining tumor boundaries are manual tracing. However, since very large data sets need to be compared for multi-year follow-up on individual patients, or for research studies aimed at assessing best treatment option, there is a need to find automated ways of tracing the tumors. A problem that arises in the automated tracing of tumors is that the boundaries for the tumors may not be clear. This requires combination of multiple images
such that they all have the same co-ordinate system [8, 9]. Hence there is a need for the automatic image registration techniques. Automatic image volume measurements of the tumors are also needed for follow up studies. This also requires the image sets to be registered. In this dissertation work radiological imaging modalities are primarily considered. Tomography modalities are the easiest modalities from the point of view of image registration, because they provide pixel datasets in which the sampling is normally uniform along each axis, though the pixels themselves tend to have anisotropic resolution.

This chapter is organized as follows. In section 2.1 the literature corresponding to registration process is reviewed. Section 2.2 reviews the literature corresponding to non-rigid or deformable registration. Section 2.3 discusses the literature corresponding to Level set based active contour segmentation. Section 2.4 presents the literature related to the joint registration and segmentation.

2.1. REGISTRATION PROCESS

Several studies carried out on the registration of medical images. In the several review papers the following procedure is adopted for the global affine registration [2, 7]. Assuming that, the two images of the same
object are available, a structural image and a functional image, the process of registration are composed of the following steps:

   i. Acquiring information from two images
   ii. Pre-processing to improve the quality of images
   iii. Determination of the registration cost function (similarity measure)
   iv. Selecting the same characteristics and finding a mapping between two images to find out transformation functions
   v. Reconstructing images based on above functions
   vi. Optimization of the similarity measure
   vii. Combining reconstructed images by overlapping them with an appropriate transparency
   viii. Verification and validation of registration algorithm

Images of a patient obtained by CT, MRI, SPECT and PET scanning are displayed as a 2-D array of pixels and stored in memory. To find out a transformation between two images precisely, they should be pre-processed to improve their quality. If these images are too noisy or blurred, caused by instruments or patient’s movement while scanning, they should be filtered and sharpened to improve visualization. According to Maintz.et.al [1] registration can be performed using different criteria. The registration can be area based and feature based methods [8, 9, 10, and 11]. According to typical image registration algorithm [30] consists of the following basic components:
2.1.1. Similarity Measure

Similarity measure is a cost function [1, 5, and 6] used as an alignment measure that quantifies the quality of alignment (one over other) i.e. match between the two images. There are two types of similarity measures: geometrical similarity measures (used for feature-based registration) and intensity similarity measures (used for intensity-based registration. Geometrical similarity measures involve minimizing cost functions related to the distance between corresponding features in the two images. Intensity similarity measures involve minimizing cost functions computed using the intensity values (directly or indirectly) in regions of interest in the two images. The most frequently used measures are SSD (Sum of Squares Difference)[5], CC(Correlation Coefficient)[88], and MI (Mutual Information)[16,17,18,19,20,21].

In this Dissertation work information theoretic metric MI is fully automatic and needs no predefined landmarks [8, 9] is used. In addition, unlike other intensity based metrics, it is suitable to be applied on both mono-modal and multi-modal registration.

2.1.2 Finding a Transformation between Two Images

Geometrical transformations [1, 3, 6, and 7] align the corresponding objects in two or more images. The images could be two(2-D) or three dimensional (3-D).
<table>
<thead>
<tr>
<th>Transformation</th>
<th>Matrix</th>
<th>Equations</th>
</tr>
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</table>
| Identity             | \[
\begin{bmatrix} 1 & 0 & 0 \\ 0 & 1 & 0 \\ 0 & 0 & 1 \end{bmatrix}
\] | $x = w$  
$y = z$ |
| Scaling              | \[
\begin{bmatrix} \delta x & 0 & 0 \\ 0 & \delta y & 0 \\ 0 & 0 & 1 \end{bmatrix}
\] | $X = \delta x w$  
$Y = \delta y z$ |
| Rotation             | \[
\begin{bmatrix} \cos \theta & \sin \theta & 0 \\ -\sin \theta & \cos \theta & 0 \\ 0 & 0 & 1 \end{bmatrix}
\] | $x = w \cos \theta - z \sin \theta$  
$y = w \sin \theta + z \cos \theta$ |
| Shear (horizontal)   | \[
\begin{bmatrix} 1 & 0 & 0 \\ \alpha & 1 & 0 \\ 0 & 0 & 1 \end{bmatrix}
\] | $X = w + \alpha z$  
$Y = z$ |
| Shear (Vertical)     | \[
\begin{bmatrix} 1 & \beta & 0 \\ 0 & 1 & 0 \\ 0 & 0 & 1 \end{bmatrix}
\] | $x = w$  
$y = \beta w + z$ |
| Translation          | \[
\begin{bmatrix} 1 & 0 & 0 \\ 0 & 1 & 0 \\ \delta x & \delta y & 1 \end{bmatrix}
\] | $x = w + \delta x$  
$y = z + \delta y$ |

**Fig. 2.2. Transformations of a Registration Process**
Geometrical transformations [1, 3, 6, and 7] align the corresponding objects in two or more images. The images could be two(2-D) or three dimensional (3-D).

A spatial transformation modifies the spatial relationship between pixels in an image, mapping pixel locations in an input image to new locations in an output image by using scaling, rotation. Some spatial transformations are rigid, affine, projective, and curved. The transformations used are shown in Fig.2.2.[1]. A class of admissible geometric transformations perform either point or region mapping that can be applied to the image(s) to warp the image(s) spatially [37, 38].

2.1.3. Optimization

Optimization [18, 20, and 21] refers to the iterative approach of adjusting the transformation parameters (in the intensity-based registration) or the alignment between features (in feature-based registration) in an attempt to improve (maximize) the similarity measure. In the feature-based registration, the transformation is computed directly from the correspondences between features. The optimization procedure starts with an initial estimate of the transform (or correspondence). Based on this estimate, the similarity measure is computed. The optimization procedure then makes a new estimate of the transformation parameters, computes the similarity measure and continues the process
until there is no significant improvement in the value of the similarity measure. Optimization methods are classified as search based [26, 27] and evolutionary kind [90].

2.1.4. Interpolation

Image resizing is necessary to increase or decrease the total number of pixels, whereas remapping can occur under a wider variety of scenarios: correcting for lens distortion, changing perspective, and rotating an image. Even the same image is resized or remapped the results can vary significantly depending on the interpolation algorithm. It is the only an approximation; therefore an image will always lose some quality each time the interpolation [22, 23, 24, 25] is performed.

Fig. 2.3. Example for Interpolation

Finally by using convolution-based interpolation[22], the transformed non-grid samples are realized. Any convolution kernel to actually interpolate the given samples must satisfy the following requirements:
\[ h(x) = 1 \text{ if } x=0 \]
\[ = 0 \text{ if } x \neq 0 \text{ for all } x \in \mathbb{Z}, \]

**2.1.5. Fusion**

There exists various interpolation kernels \([22,85]\) like nearest neighbor, bi-linear, bi-cubic and sinc functions etc. The type of interpolation function is a tradeoff between accuracy and computational time.

It is a process of obtaining a single image from a set of input images. The fused image should have more complete information which is more useful for human or machine perception. With the development of new imaging methods in medical diagnostics, there arises the need of meaningful (and spatial correct) combination of all available image datasets. Examples for imaging devices include Computer Tomography (CT), Magnetic Resonance Imaging (MRI) or the newer Positron Emission Tomography (PET). Fig.2.4 illustrates the fusion of a CT and a MRI image. Figure also depicts that it only fuses complementary information from two sensors (CT and MRI). Image fusion improves reliability and capability.

**2.2. NON-RIGID REGISTRATION**
From the large number of studies of literature, global registration has limited applicability when non-rigid shapes are considered. In contrast to rigid, non-rigid transformations maps straight lines to curves [30,41]. Non-rigid registration is the process of determining such transformations given two images of an object.

(a) CT         (b) MRI         (c) Fused Image

Fig.2.4. Fusion of CT and MRI Images
According to [30] non-rigid transformation models can be divided into physical and functional. The physical models in general, are derived from the theory of continuum mechanics [41] and can be divided into two main subcategories: elastic and fluid flow. Functional representations [41] originate from interpolation and approximation theory. They use basis function expansions to model the deformation. There are many different types of basis functions [38], e.g., radial basis functions, \( B \)-splines\([36, 37] \) and wavelets [30].

Physical model consider the image as the elastic body. Physical deformation in the brain [32, 35] can occur during neurosurgery as a result of factors such as swelling, Cerebro-Spinal-Fluid (CSF) loss, hemorrhage and the intervention itself. Non-rigid registration addresses such misalignments of the physical deformation with the help of techniques like active contours that allow the alignment of datasets that are mismatched in a non-rigid or non-uniform manner. In this work non-rigid models are used for modeling the deformation of brain tissues due to the tumors and lesions.

One approach is to delineate a structure of interest from one image, and use the deformation field calculated by non-rigid registration of that image to a second image to delineate the same structure in the second image. This approach is sometimes called segmentation.
Non-rigid registration [33, 34] can automatically quantify small changes in structures of anatomical structures over time by means of segmentation propagation. In this thesis a non-rigid registration algorithm based on optimizing mutual information to quantify small changes in brain due to tumors is considered. For the registration both intra- and inter-subject [42] scans are used.

First the difference deformation field is estimated and is applied on the target image so that it evolves. Finally whenever it resembles the fixed image, evolution stops. The process of evolution in non-rigid registration is shown in Fig.2.5.

Fig.2.5. Non-Rigid Registration Process
Non-rigid registration is performed as a two stage process [43]. Because of large differences, first global changes and gross differences in size and orientation between the reference image and the subject images were compensated by the affine (12 degrees of freedom) registration algorithm. Secondly, local deformation was calculated using deformable models. The full brain image was used for the global coarse grid registration and the fine grid registration is performed using a region of interest (ROI) as shown in Fig.2.6.

As per the studies, non-rigid registration is local and hence object is to be segmented before the analysis. The dynamic active contour method is used for the segmentation. Active contours and curve evolution methods usually define an initial contour $C_0$ and deform it towards the object boundary. In active contour models [28, 40, 61, 71, 72] one places
a closed planar parametric curve \( C_0(s) = (x(s), y(s)), s \in [0, 1] \) around image parts of interest. Then this curve evolves under smoothness control and the influence of an image force. The active contours can be implemented in two ways namely Parametric Active Contours[28, 29, 40] (PACs) and Geometric Active Contours [43, 45, 56] (GACs).

2.3. ACTIVE CONTOUR BASED IMAGE SEGMENTATION

Deformable models are useful in segmenting, matching, and tracking anatomic structures by exploiting constraints derived from image data. They combine physics, geometry and approximation theory. Deformable models initiated a new approach known as physics based geometric design. One of the popular approaches to image segmentation is curve evolution and active contour models.

2.3.1. Parametric Active Contour (PAC) Segmentation

Kass. et. al. [28] introduced classic parametric deformable models also known as snakes [28,29,41-43] for the segmentation based on energy minimizing snakes and dynamic snakes. Energy minimization is a static problem, whereas dynamic deformable models [40,41] unify the description of shape and motion i.e. shapes evolution through time. Dynamic models are suitable for time varying medical image analysis. 

Snakes, or active contours, are used extensively in computer vision
and image processing applications, particularly to locate object boundaries. Problems associated with initialization and poor convergence to concave boundaries, limited their utility. In parametric methods the external forces can be derived by using various techniques called Gradient Vector Flow (GVF) [31, 32], PoissonInverse Gradient (PIG) [95], and the Vector Field convolution (VFC) [29]. In GVF the field is calculated as a diffusion of the gradient vectors of a gray-level or binary edge map. The GVF framework might be the useful in defining new connections between parametric and geometric snakes, and might form the basis for a new geometric snake.

Automatic initialization approach for parametric active models, termed the PIG [95] initialization method, has been introduced. The PIG technique estimates the underlying external energy field from the external force field via solving Poisson’s equation, which can also be used for vector field visualization. From the estimated external energy field, iso-models are extracted, and the iso-model with the lowest energy is selected as the initial model. To obtain a high quality initialization, both an advanced edge detector and a noise robust external force field are necessary. This method can initialize one or more active models automatically in both 2-D and 3-D. The computational cost is high.
A static external force for active contours, called VFC, has been introduced. The VFC field [29] is calculated by convolving a vector field kernel with the edge map generated from the image. The VFC snakes are less computationally expensive, more robust to noise and initialization than GVF snakes. VFC can also be easily customized and enhanced for different applications.

In the above snake models, the parametric curve is embedded into an energy minimization framework. Apart from energy minimization the parametric curve can also evolve directly under motion equation desired from geometric considerations [45]. However, the parameterization [43] of the curve causes difficulties with respect to topological changes and numerical implementations. Thus to prevent these difficulties, implicit active contour models have been developed.

2.3.2. Geometric (Implicit) Active Contour (GAC) Segmentation

Geometric (Implicit) active contour models [28, 45-57] constitute a very interesting application of levelset ideas with in active contour framework. They embed the active contour as a levelset [47, 49-57] in a suitable image evolution that is determined by a Partial Differential Equation (PDE) [47]. The basic idea is that the user specifies the initial guess of an intensity contour (ex: an organ or a tumor or a person to be tracked). Then this contour is moved by image driven forces to the boundaries of the desired
object. Then final contour is extracted when the evolution is stopped. Here the basic idea is to implement the initial curve $C_0(s)$ implicitly within the higher dimensional functions [56, 57, 58] and to evolve this function under a PDE. Usually $C_0(s)$ is embedded as a zero levelset into a function $u_0: \mathbb{R}^2$

$$u_0(x) = \begin{cases} d(x, C_0) & \text{x is inside } C_0 \\ 0 & \text{x is on } C_0 \\ -d(x, C_0) & \text{x is outside } C_0 \end{cases}$$

where $d(x, C_0)$ denotes the distance between the point $x$ and the curve $C_0$.

is the main advantage of the implicit active contour are the automatic handling of topology changes, high numerical stability and independence of parameterization.

### 2.3.3 Distance Transform

The distance transforms [74] or distance functions are the basic feature of level set. A distance transform is applied to a binary image in which object pixels have the value 1 and other 0. All pixels in this image are labeled with their distance from the surface of the object. By pre-labeling all image pixels in this way the computational cost per iteration can be substantially reduced. Level set methods are mathematical tools for transforming surfaces. These surfaces are described by a signed-
distance-function that returns the distance to the surface given a point. The surface separates the inside and the outside of some object; it is therefore often referred to as the interface. On a computer, one stores an implicit representation of the interface. That is, for each pixel a value is stored, representing the distance from that pixel to the surface. Inside the object, this distance is negative, and outside it is positive, as shown in Fig. 2.7.

**Outside (+ve)**

**Inside (-ve)**

![Image of SDF used in Level Set Evolution]

**Fig. 2.7. SDF used in Level Set Evolution**

During Evolution it will remain as the function, hence implementation on the grid is easier. Discrete image is represented by a vector whose components contain pixel values. The values can be determined by interpolation method. A stopping criterion is indicated by edge indicator function. In each case, the image was initialized to a signed distance function from a mask that covered neatly the complete image domain. However, it is necessary in some applications to maintain the SDF during the curve evolution for stability. In this work, different spatial discretization methods like HJ-ENO1, HJ-ENO2, HJ-ENO3 and
WENO, and for the time discretization Range-Kutta Total Variation Diminishing (RK-TVD) is used and their suitability for different tomographs is tested. The segmentation using level set evolution SDF needs re-initialization [63]. The segmentation using variational methods avoids re-initialization. In this work segmentation on brain tumors is performed using energy and DRLSE [75] variational methods.

The framework for segmentation is to design modeling the evolution of boundaries. The aim is to provide computational technique for tracking moving interfaces. The interface motion can be formulated using the boundary value and initial value formulation [54]. The equation for the motion of a propagating curve is formulated by considering the stability considerations and force functions. The evolution faces the problem at the corners.

Curve propagation may not be smooth all the time. It can develop smooth corners in finite time. The corners are analogous to shocks in the solution of hyperbolic conservation laws [48] and the solution can be naturally constructed beyond the appearance of the corners through the notion of entropy, satisfying weak solution. As the curve moves, the oscillation decay will depend on the sign of force. The total oscillation or the variation of the front measures the “wrinkling”. When corners developed, normal cannot be defined properly hence weak solution can be defined. If
vertical ridges are formed, solution does not exist. Solution can be obtained through entropy condition [55].

The above mentioned curve analysis of shapes can provide strong support to image understanding and all its applications. Shape representation [59] is important in computer vision applications such as registration, recognition, segmentation. Some representations like snakes powerful enough to capture a certain number of shape deformations, but they require a large number of parameters to deal with important deformations and they cannot deal with changes of topology.

An emerging way to represent shapes can be derived using level set representation. This selection is invariant to translation and rotation. Distance maps, have some properties that describe a shape in a powerful way. They refer to structures of higher dimensions, when the information space refers to clones of the original shape positioned coherently in the image plane. This representation in the image plane (iso contours) can account for local deformation. The recently proposed edge flow method is quite effective on large and diverse classes of images, but it requires post-processing to detect closed contours. One of the contributions of this method is to utilize the effective edge indicator function [63] as the prior knowledge within the curve evolution framework to obtain better
segmentation results. The purpose of the edge function is to stop or slow down the evolving contour when it is close to an edge.

Active Contour Evolution through variational level-set-based segmentation formulation [76] uses both shape and intensity prior information [77]. This method solves a large number of image segmentation problems. Early approach to model the shape energy is based on the assumption that the segmentation should prefer a smooth partitioning boundary. This is usually referred to as a shape regularization term, where the curve’s length, curvature or interior area is typically incorporated into a penalty term. Such geometric shape priors are still widely used in general image segmentation when further shape prior information is not available. Region based active contour models are robust to noise and can detect objects with very diffuse boundaries.

### 2.4. Joint Image Registration and Segmentation

The segmentation is obtained by finding a non-rigid registration to the prior shape. Combining registration and segmentation has been motivated by the need to incorporate prior information to guide and constrain the segmentation process. The quality of the images acquired by the various medical screening modalities is often poor due to the presence of multiple noise sources in the acquisition system, degradation
of data content during reconstruction processes (e.g. tomographic reconstruction with Radon transform), motion and respiratory artifacts introduced by motion of the patient and inherent limitations of system acquisition accuracy. The combination of these factors degrade the signal to noise ratio of the data, limit the spatial resolution, introduce inhomogeneities in the tissue appearance across volumetric slices, and deteriorate boundary definitions between specific organs and their surrounding tissues. These issues are encountered with other medical imaging modalities such as ultrasound, MRI, PET and SPECT and CT.

In Medical imaging atlas based segmentation [89] is preferable due to the presence of noise. To detect the object shape precisely multiple images of that shape are used. The reference image is to be registered with the target image in order to extract the desired shape. Hence, it requires simultaneous registration and segmentation. Two methods 1. Pure PDE formulation and 2. Variational formulation are used.

A joint segmentation and registration methods [79-82] have been developed through active contours. In the context of brain MRI segmentation for example, incorporation of atlas information to assist the segmentation task of a particular data set has been a very successful and popular approach for many years. For organs with very characteristics shapes such as cardiac ventricles, the corpus callosum in
the brain, or cartilages of the knee, shape priors (including active shape models, active appearance models and statistical shape descriptors) have been used with great success in the context of constrained segmentation.

The use of an atlas (or a shape model) to assist the segmentation process requires that the target image data and the atlas (or the models) is being aligned via either pre-registration or via a new concept of combined registration and segmentation. When considering registration as a pre-processing step, common atlas-based segmentation methods use warping of the atlas to the target data via maximization of mutual information of image pair. Vemuri. et al. that derived a novel curve evolution approach in a level set framework for image intensity morphing and non-linear associated PDE for the corresponding coordinate registration between an atlas and an image. Applications of the method include a clinical study on segmentation of the corpus callosum via morphing of a shape model defined in the atlas space, after registration of the data with the proposed method.

The chapter focuses on methods that explicitly combine segmentation and registration in a variational framework. By combining registration and segmentation, one can recover the image region that corresponds to the organ of interest, given a model of this structure. Level set deformable models offer a very flexible framework to propagate a moving front with segmentation-driven constraints while registering the
segmentation result (i.e. the level zero curve) to a given model. Distance transforms have been successfully applied in the past to registration problems. In a level set framework, Paragios [71, 72] has published several papers recently focusing on matching geometric shapes in a variational framework for global as well as local registration. The first attempt at combining segmentation and registration in a single geometric deformable model framework might be attributed to Yezzi et al. Their key observation is that multiple images may be segmented by evolving a single contour as well as the mappings of that contour into each image.

The main trend of the reported efforts uses a shape model and incorporates a constraint in the energy of the geometric deformable model that forces the evolving contour to fit to the shape model. In an effort to derive a rigorous and complete scheme, Paragios and Rousson focused on the integration of a shape model, defined directly in a level set space, to derive a shape prior in an energetic form and integrate it with a data-driven variational segmentation framework. Applications of their combined registration and segmentation framework focused on the segmentation of physically corrupted or incomplete natural images.

A new variational Distance Regularized Level Set Evolution PDE based level set method for a simultaneous imagesegmentation and non-rigid registration using prior shape and intensity in formationis
presented. The segmentation is obtained by finding a non-rigid registration to the prior shape. The non-rigid registration consists of both a global rigid transformation and a local non-rigid deformation. In this model, a prior shape is used as an initial contour which leads to decrease the numerical calculation time.

2.5. Conclusion

Level set methods for segmentation and registration of medical images have been the focus of intense research for the past decade producing very promising results. Major advantages of the method include its robustness to noisy conditions, its aptitude in extracting curved objects with complex topology and its clean numerical framework of multi-dimensional implementation. Despite their success, these methods still need to be refined to address two limitations:

(1) Computation time needs to be further reduced, for viability of the method in clinical application where interactivity (and therefore close to real time computation) is critical. This optimization will have to handle the constant increase in data size observed in medical imaging applications with improvements of spatial resolution, temporal resolution and now the introduction of combo scanners such as PET/CT machines.
(2) Robustness to variation in image quality and organ anatomy needs to be studied. Unfortunately, the methods described in this chapter are only rarely validated in clinical studies. On the other hand it is well known that these methods require tuning of their parameters to adapt to the nature of the image data to segment. In that view, it is therefore critical to evaluate robustness of the performance on a set of data that covers the range of quality encountered in clinical practice for a particular examination. For methods based on shape models, it is also critical to test the method on a variety of abnormal (e.g. disease) cases that differ from the average anatomy that they typically represent. Such validation for medical application should always clearly specify the context of the problem at hand in terms of anatomy of interest (e.g. endocardial surface of myocardium muscle), imaging modality (e.g. three-dimensional real-time ultrasound) and clinical application targeted (e.g. quantification of volume). Only in this context can a segmentation method be really tuned, tested and validated for clinical application. The results were obtained through Matlab and the computational time in each iteration was about 1 second utilizing a Pentium 4 CPU running at 2.4 GHZ with 512MB of RAM. Windows XP Home Edition was used as the operating system.