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Research Article

Deformable Registration Methods for Medical Images: A Review Based on Performance Comparison

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Abstract: Deformable registration methods are widely used for the accurate registration of objects with large-scale deformation. In this paper, we present a detail review on performance analysis of deformable registration methods. We comprehensively review each registration method and describe its features, advantages, issues and challenges. Deformable registration methods are further quantitatively compared and evaluated based on a set of criteria, which estimate the performance of each method. The performance of registration methods is estimated using root mean square error (RMS), mutual information (MI), computational time complexity and memory requirement. It is found in our analysis that every registration method has its own strength to register deformable objects. However, due to large-scale variations in deformable objects most of the registration methods are not still a perfect choice in clinical applications. Therefore, advanced and powerful registration methods are needed to develop in future, which can precisely, efficiently, and automatically register medical images with large-scale deformations.

Keywords: Medical image processing, image registration, deformable registration, imaging modalities

1. INTRODUCTION

In the last two to three decades, tremendous growth has been observed in the area of medical image analysis due to the development of automated, efficient, accurate, and non-invasive devices. Medical imaging [1-4] is used in several applications in the clinical setting such as diagnostic setting, planning and procedures. The role of medical imaging is now not only limited to simple visualization and inspection of anatomic structures but it is also used as a tool for surgical and radiotherapy planning, inter and intra-operative navigation and for tracking the progress of disease [5].

The rapid advancement in this challenging area has driven the need for sophisticated pre-processing techniques. Image registration [6-18] is the most important step in medical image processing in which one to one geometric correspondence between source and target images is established. The source image is fixed image, which remain unchanged during registration process while the target image is the moveable image super-imposed on the source image. In image registration, both images represent the same organ/tissue obtained from either a same modality but with different time frames/ angles or by different imaging modalities. The basic purpose of establishing geometric correspondence between source and target image is to obtained useful and complementary information. This is done by quantitatively comparing their features using sets of parameters which includes feature detection, feature matching, transform model estimation and image re-sampling and transformation [19-21].

Recent developments and wide spread use in imaging modalities [9, 10, 22-24] provides an easy to use platform for the radiologists and surgeons to obtain useful information from human anatomy. However, each modality show different types of information i.e. either anatomical (showing mainly morphology) or functional (showing mainly information on the metabolism of the

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fundamental anatomy). Modalities such as X-rays, magnetic resonance imaging (MRI) , computed tomography (CT) and ultrasound (US) [25] are used to obtain anatomical information while single-photon emission computed tomography (SPECT) and positron emission tomography (PET) are used to extract functional information. However, both MRI (DWI, DCE-MRI, and MRSI) and US (Elastography, contrast enhanced US) can also be used to obtain functional information. The proper integration of useful information from two separate images taken with different types of modalities is often required in the clinical tracks of events. This is done by the registration process which brings the separate images obtained from different modalities into special alignment and integrates useful information from them.

Deformable registration is widely used in computer assisted surgery and radiotherapy for the accurate voxel by voxel mapping of medical images with large-scale local and global deformations. Deformable registration also enhances the planning, execution and evaluation of surgical procedures [26]. In deformable registration, a special association between source and target image is established during transformation. The correspondence between transformations signals are usually performed locally in a non-linear and dense fashion [27].

Deformable registration is one of the best choices for the analysis of medical images obtained either by the same or by different imaging modalities having high degree of functional and anatomical variability. Deformable registration algorithms either operate on images features such as lines, counters and points/ landmarks or on their gray levels i.e. directly on pixel or voxel data [28]. Algorithms belong to deformable registration can successfully determine the local differences in the anatomy and accordingly resolve them.

One of the main challenges today for deformable registration methods are how to properly validate them on clinical data. The lack of adaptation in clinical workflow is due to their limited availability and high computational requirements [29]. Several other challenges includes recovering a local transformation that align two signals that have a non-linear relationship, proper alignment of tissue having sudden change in volume, registering poor and non-diagnostic quality images, and designing image similarity for multi-model scans.

The importance and popularity of deformable registration have led to several survey papers, which are listed in Table 1, together with the publication years and topics. In general, each paper covers only a subset of the topics in deformable registration. For Example, the work of Sotiras et al. [27] is one of the comprehensive review on

Table 1. Surveys on deformable registration.

Year	Reference	Topic
1996	[5]	Deformable Models in Medical Image Analysis: A Survey
2008	[97]	Objective assessment of deformable image registration in radiotherapy: A multi-institution study
2010	[90]	Implementation and evaluation of various demons deformable image registration algorithms on a GPU
2011	[98]	Deformable Medical Image Registration: Setting the State of the Art with Discrete Methods
2013	[99]	Evaluation of various deformable image registration algorithms for thoracic images
	[27]	Deformable Medical Image Registration: A Survey
	[10]	Survey of Medical Image Registration
2015	[30]	Evaluation of various Deformable Image Registrations for Point and Volume Variations

deformable medical image registration in which they attempt to give an overview on the recent advances in the field and evaluate each component of deformable registration. Although the work of Sotiras et al provide in-depth systematic review but they not cover the quantitative evaluation of deformable registration methods. Similarly the review of Mani et al. gives a short overview and the pros and cons of several types registration methods including deformable registration [10]. The study of Han et al. [30] evaluated accuracy of various DIR algorithms using variations of the deformation point and volume. Mclnerney and Terzopoulos [5] present a detail review on the development and application of deformable models to problems of fundamental importance in medical image analysis, such as segmentation and registration.

We have performed the experiments on the datasets of two 2D rat lung images, the one after inspiration of air into lungs (source image) and the second after exhalation (target image). The size of each image is 128 * 126 and the physical spaces are one millimeter along x axis and one millimeter along y axis. The datasets and parameters are obtained from [31].

The main scope of this paper is focused on the quantitative evaluation on deformable registration methods. Furthermore, recent developments and challenges are also analyzed. The evaluation parameters are outlined in Fig 1 which includes mutual information (MI), root mean square error (RMS), computation time and memory space occupied during execution. We have found the accuracy and efficiency of each deformable registration method with the help of these parameters.

The main contribution of this review are as follows.

- Deformable registration methods which includes finite element model (FEM) based, BSplines, level set motion, BSplines multi-grid, warping with kernel Splines, warping with BSplines, asymmetric demon and symmetric demon deformable registration methods are discussed in a clearly organized manner, and their performance are shown.
- To examine the state of the art, each registration method involved in medical image processing are discussed in detail. The merits and limitations of each method is summarized. Our main focus is on the detail estimation of accuracy and efficiency because the performance of deformable registration is not been surveyed previously using these parameters.
- We discuss the future work on deformable image registration methods
- This work attempts to provide a theoretical foundation and compact platform for researchers by evaluating the important aspects of deformable image registration methods.
- It will also help clinicians by providing relevant and quantitative information on diagnostic, surgical and treatment planning which will eventually improve their knowledge on this challenging area of research.
- The above mentioned contributions clearly distinguish our survey from the existing surveys on deformable registration methods. To our knowledge, our survey is the broadest.

The remainder of this paper is organized as follows: Section 2 briefly reviews the work related to image registration. Section 3 categorize and presents the methods for deformable registration in detail. Section 4 analyzes the performance of each method. Section 5 summarizes this paper.

2. MEDICAL IMAGE REGISTRATION

Image segmentation and registration are the two main areas of medical image processing. Image segmentation divides an image into different segments of interest while image registration establishes a one to one correspondence between two different images of the same organ. Literature study dictates that image segmentation and registration are the most challenging areas of medical image processing and a lot of research work is available on it [5, 8-10, 19, 20, 22, 32-39]. Fig 2 show the process of registration of human head 3D images acquired using CT and MRI scanners. In the registration process, source CT image which is the most suitable to represent anatomical information i.e. bones is mapped on MR

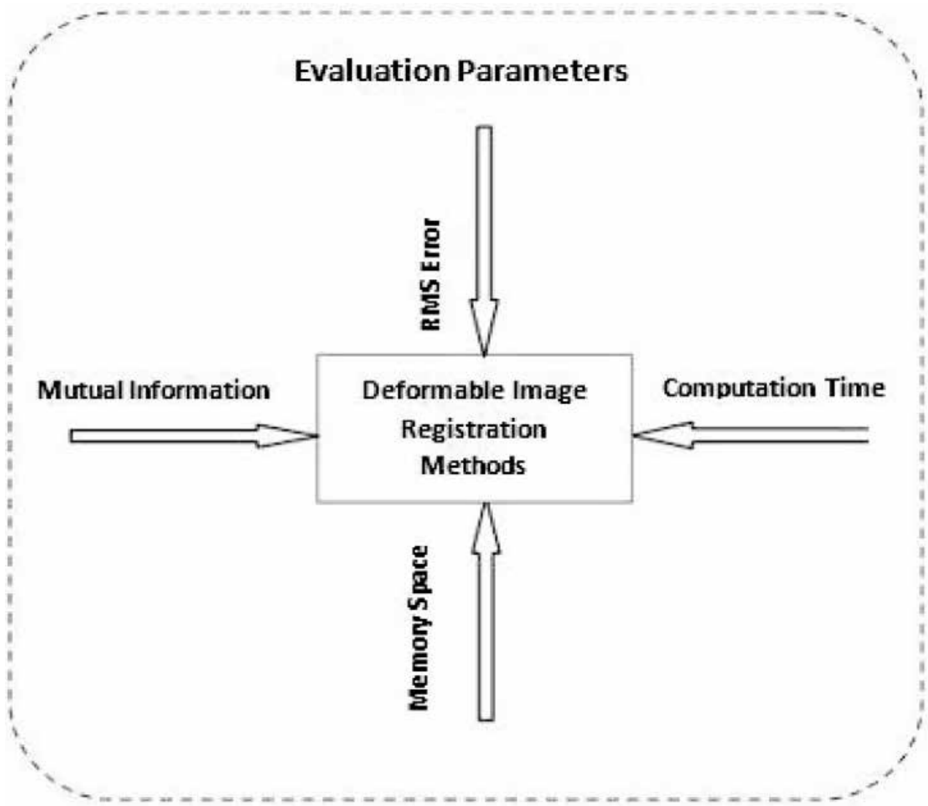

Fig. 1. Evaluation parameters for deformable registration methods.

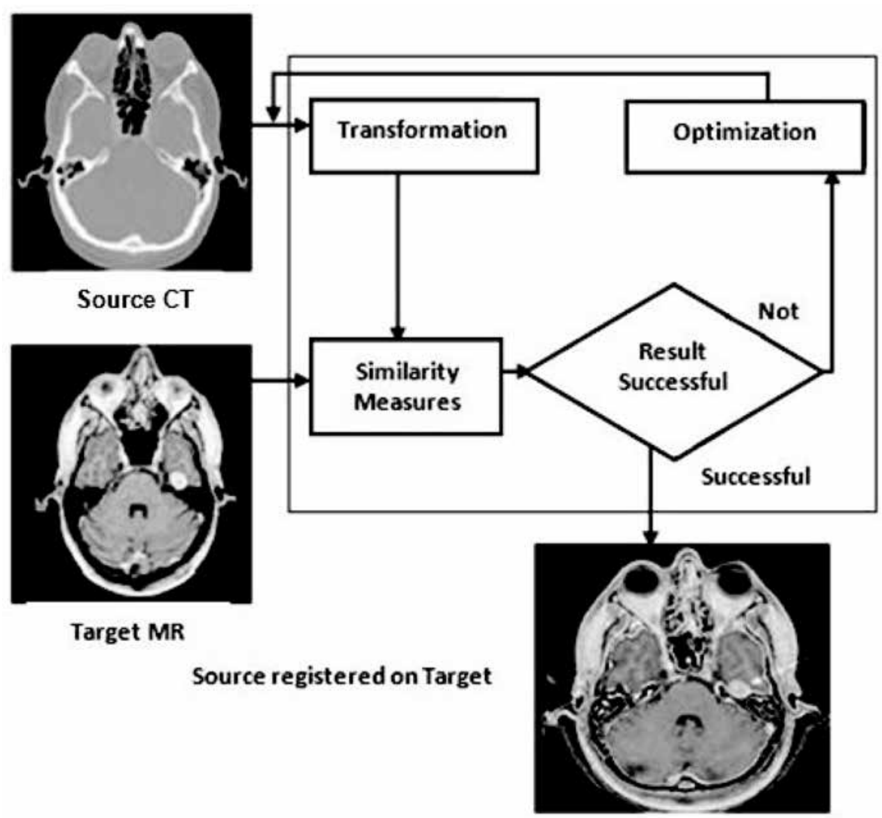

Fig. 2. CT and MR registration of brain images.

image which shows functional information such as soft tissues and tumor [40, 41]. It is shown in Fig 2 that the registered image provide more useful information not only about the tumor but also about the soft tissues and bony structures.

It is also shown in Fig. 2 that the process of registration is based on three important steps i.e. transformation, similarity measures and optimization techniques. The steps involved in registration processes are interrelated and iterative. In the transformation step the points or landmarks in source image space is mapped to the corresponding target image space [42]. A transformation function maps source image to target image considering image dimensionality, accuracy, and computational speed [43, 44]. Similarity measure, is another important step in image registration because it can precisely estimate the correspondence between source and target images. Similarity measure estimate the degree of matching between source and target images and it is based on pixel intensities and patterns, cross-correlation, anatomical structures and mutual information [20, 43, 45-47]. Angle of view, time interval and sensor used are the essential parameters for estimating the similarity measure of input images. It is important to choose best similarity measures while dealing medical images taken from human organs with constant variation and movements during the course of time.

As mentioned earlier that registration is an iterative process, at every iteration similarity is checked between source and target image. If the similarity is not according to the requirement of successful registration then the process is optimized [42, 43, 48-50] to further find the best alignment between source and target image as shown in Fig 2. In this procedure, similarity parameters obtained from the earlier steps are updated (either increased or decreased) tell the optimum values. Several types of optimization methods with pros and cons are available for the registration of medical images. The popular among them includes quasi-Newton optimization, evolutionary strategy, genetic algorithm, stochastic approximation, iterative closest point, powell's method, downhill simplex method, steepest gradient descent and the conjugate gradient method [43, 44, 51-55].

3. DEFORMABLE REGISTRATION METHODS

Deformable registration is a fundamental technique for the analysis of mono and multi-modal images of deformable organs such as heart, lungs, breast and kidney. Deformable organs naturally show consistent deviations due to breathing and movement. Therefore, the precise identification and localization of potential tumor tissue is difficult and challenging. Furthermore, several other issues such as the proper identification of both anatomical and functional contents and automatic voxel-by-voxel transformation are also successfully done using the advance methods of deformable registration. Fig 3 [26] shows the registration of multi-modal CT and PET images of unresectable pancreatic cancer. In the Fig , the anatomical contents e.g. bones and hard tissues are apparent in the CT image (A) while functional contents such as metabolism are clear in the PET image (B). However, the pancreatic tumor is not clearly visible in both A and B. The registered image (C) at the bottom contains the properties of both CT and PET and thus the tumor is more visible as indicated by the arrow.

Beside multi-modality images, the analysis of pre and post interventional images obtained from mono modality is also important for treatment success. Such types of mono modal images obtained at different time are also precisely analyzed with deformable registration methods. However, all the methods use different types of operations to perform registration on the set of 2D and 3D images, which might be good for some situation but not necessarily suitable for others [56].

Deformable registration methods use several types of complicated models to estimate the internal behavior of deformable tissues. Among them, some of the popular models are finite element model (FEM), elastic model, viscous fluid model and radial basis function [57, 58]. FEM decomposes images into several desirable regions containing soft tissues, create volume meshes for particular tissue and allocate a precise tissue property for volume meshes. FEM is a powerful computational tool applicable to several types of deformable registration algorithms. Elastic model is also a useful physical model for the proper transformation

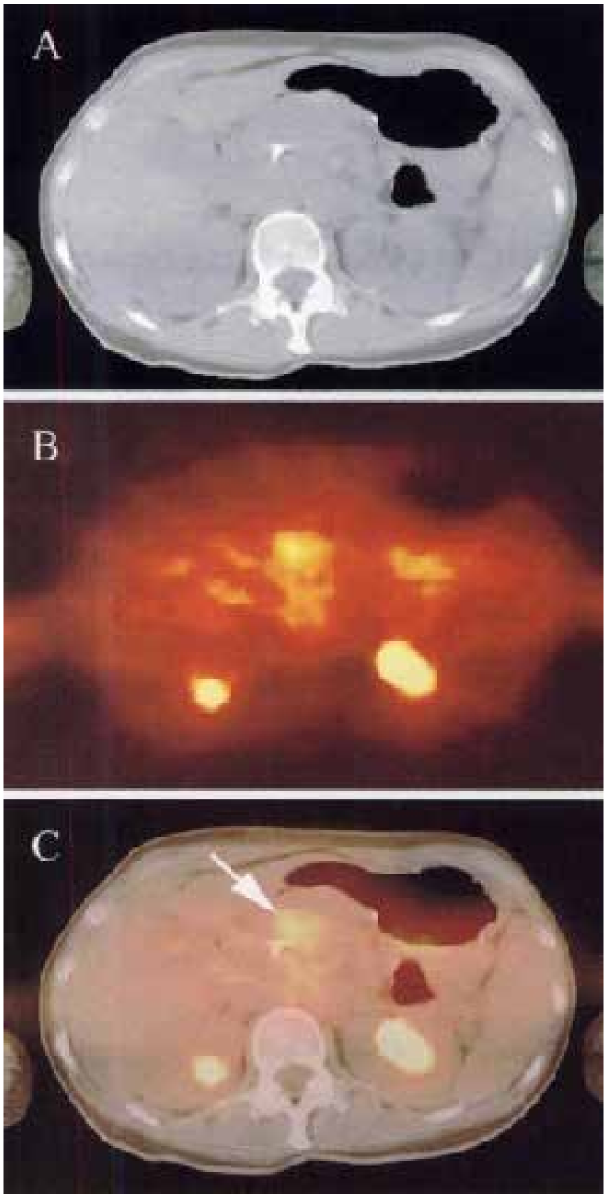

Fig. 3. Deformable registration of multi-modal CT and PET images of the abdomen.

of detailed local deformations during registration process [27, 59]. This model considers images as deforming elastic objects and estimates the small differences between them using external body forces. Deformable registration using elastic model can give robust and fast results and can also efficiently describe multimodal deformation. Contrast to elastic model which is best suited for small deformation in the tissues, viscous fluid model is the right choice for image transformation when the number of deformation is more in the tissues [60]. However, high computational time complexity of viscous fluid model is the main reason behind its less widespread use and popularity. Radial basis function is another model for the estimation of local differences and point correspondence in deformable registration. Radial basis function is mostly used for the interpolation of images with local distortion and differences [61]. This function minimizes dissimilarity between source and target image and provide a smooth resultant image with more clear information.

Registration methods belong to deformable models are more complex as compared to registration methods based on rigid models. Therefore, to further improve the performance and reduce computational complexity, researchers are trying to develop more effective deformable registration methods from time to time. Therefore, there is a need to further investigate deformable registration methods with high performance and that might be suitable in almost every type of scenario. Recently several types of deformable registration methods have been developed as shown in Fig 4. These registration methods are further discussed in the subsections below and their quantitative evaluation and comparison is described in section 4.

3.1 FEM-Based Image Registration

Several types of physical and biomechanical models are available for the analysis of deformable registration. Finite element method (FEM) is the most popular model among them which successfully compute the biomechanical properties of human tissues and special positions of anatomy [62]. FEM effectively estimates large local deformations in the various tissues during registration process. This model treats human organs images as elastic bodies and applies non-uniform meshes to the important features in them which improve the accuracy of registration [62-64]. In order to generate registered image and solve linear system of equations, FEM uses linear elasticity and static analysis assumptions. Efficient modeling of material properties in object and providing better global solution to the entire image domain are also the main features of FEM. However, the accuracy of registration should be considered while estimating material properties of object because using FEM in deformable registration the accuracy rely on material properties.

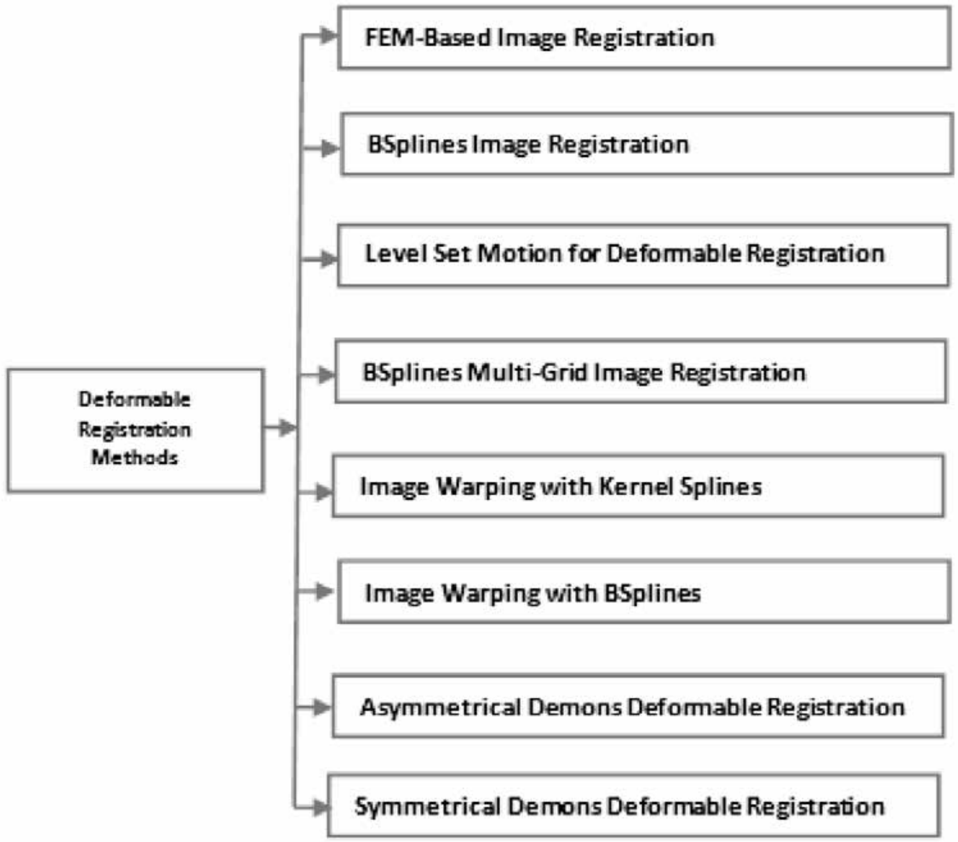

Fig. 4. Deformable registration methods.

The basic idea behind finite element method is to discretize image domain in groups and apply mechanical or physical forces on them. It is due to these forces that the relations between different types of tissues are formed which help to estimate deformations and obtained tissue properties from the estimated deformations. The important applications of FEM are in brain modeling and simulation during image guided surgery, physical integration of deformable registration methods, analyzing mechanical deformations during biopsy examinations and testing, reconstruction and improvement of elastic properties in deformable tissues such MR breast, lung and prostate images. Configuration of boundary conditions is another important feature of FEM in deformable registration [65]. However, due to complexity in the geometries of human anatomical structures FEM faces several difficulties while estimating boundary conditions during image-guided radiation therapy. Therefore, the computational complexity is more that affect the speed and efficiency of registration method. FEM based deformable registration methods are mostly used in a situation where the high accuracy is desired. Registration results are also better in case of low contrast tissues because FEM provides several mechanisms based on elasticity and biomechanics to align low contrast tissues with high one.

3.2 B-Splines Image Registration

Sampling frequency changes, proper estimation of un-known pixel values from known pixel values, transformation of a digital image to analog image and increase in the resolution are the necessary steps in image processing. These important steps in image processing are performed by the techniques of interpolation. Basis Splines (B-Splines) are widely used piecewise continuous interpolation functions for the analysis of digital images. B-Splines functions are based on polynomials and are spread over an interval of unit width in which the number of pieces is preoperational to the order of splines [66-68]. These functions efficiently detect and compute image shapes, curves and contours having large variations and transform them into continuous images. Registration using B-Splines model also generate several types of non-linear elastic deformations. B-Splines execute images locally and with multi-scale processing due to their excellent localizations and multi-resolution properties.

Deformable image registration provides flexible mapping of local key points between source and target images due to high degree of freedom in transformation. The transformation become more smoother when used with B-Splines functions because of their fast interpolation schemes , generation of a vector field on interested volume and provision of compact support [69, 70]. In deformable transformation using B-Splines interpolation, several coefficient values are defined and distributed on a grid at continuous interval due to which wide variety of deformation become possible. However, the use of more coefficient values increases the running time of transformation and effect the efficiency of registration.

3.3 Level Set Motion for Deformable Registration

Level set motion is another important and widely used framework to represent deformable objects. Level set uses global regularization of its shapes while dealing with 3D interfaces and automatically detect the boundaries of interested regions during image segmentation and registration [71]. Level set methods give promising results while dealing with deformable models because it represents the models as 3D images. In the 3D images, the intensity at each voxel is considered as distance measurements to object surface. In the distance measurements, object internal values are negative and the outer values are positive [72-74]. In deformable registration using level set motion algorithm, the histogram of source and target images are matched with user specified number of quantile values. In other words, during registration, intensity values are same at both images while representing the same homologous points on an object with pixels.

Medical image registration and segmentation with level set motion give successful results and are more popular than other types of techniques such as mesh. Robustness in noisy conditions, changing and extracting curved objects with complex topology and multidimensional implementation/ computation of motion of the interface with simple and compact mathematical notation [73, 74]. However, level set motion framework has several limitations and need more improvements. Mesh framework such as FEM has built-in ability to track vertices but level set motion framework is no capability to do so. More features are lost in level set motion framework because resembling is performed at each time step with low pass filter. Moreover, high computation time, less stability to multi-resolution images and organs anatomy with high variations are some other limitations of deformable registration using level set motion which requires further improvement.

3.4 B-Splines Multi-grid Image Registration

Modifying grid of control points and increasing similarity measures are the main steps in registration using B-Splines approach to deform an image. In order to obtain more intensity values and improve the robustness of registration, a multi-resolution approach is followed. In this approach, a grid containing multiple resolution levels i.e. low and high are placed on the images [75-77]. Registration process based on B-Splines multi-grid interpolation is performed in two steps. In the first step, images with low resolution levels are estimated and transformed. In the second step, the transformation is again performed on the images with high resolution values propagating estimated parameters to them which are obtained in the first step.

Registration methods based on B-Splines multi-grid/ multi-resolution approache perform better then single-grid/ resolution approach. The speed and efficiency of registration method is enhanced by mapping the spatial resolution of the underlying image model to the step size of the registration method. Performing maximum iterations on coarsest resolution is also the unique property of B-Splines multi-grid registration. Avoiding local minima due to smoothing effect of pyramid and well handling of local and global errors and invert-ability in deformable objects are some other features of B-Splines multi-grid registration. On the other side, B-Splines multi-grid registration gives weak results while operating on images with high distortion and rotational deformations [78-80]. Moreover, this method is also unsuitable in mesh refinement procedures with large scale adaptive procedures due to its high setup cost.

3.5 Image Warping with Kernel Splines

In image warping, a mapping function is applied on digital image which make distortion in it and as a result a new position is created for each landmark point in the image. The basic purpose is to create a possible similarity between set of images. Several types of filtering operations such as smoothing, edge detection, elimination of noise/blur and intensity enhancement is performed on digital images through the processes of convolution [81]. Convolution is performed through several types (i.e. size 2*2, 3*3 and 4*4) of matrices also called kernel. Kernel consists of mathematical values which are applied to pixel values resulting modified image with different properties is formed. The resultant image greatly depends on the values used and on the size of kernel. Kernel spline is popular and widely used method for image warping and it uses a 3D mapping function to find out information about landmark points or pixel intensities in both source and target objects [82, 83]. This is done by localizing a mapping area of pixel intensities in which the size of area under consideration is find out by increasing the distance into twice between the source and target point.

Kernel spline interpolation functions can effectively model deformation field in landmark based image registration. A smooth global transformation is performed with kernel spline by computing local controlled deformation of landmark points [84, 85]. Image deformation model is created by joining spline kernel over the area of image under consideration in the form of rectangular grid.

3.6 Image Warping with BSplines

Beside computer vision and multimedia application, image warping has also got importance in the fields of medical image processing such as image morphing and deformation. Several powerful warping methods are developed in the recent years for the precise analysis and matching of medical images. BSplines warping is the popular and widely used among them because it precisely deforms medical images with its significant property of local control and global mapping. BSplines mapping functions perform free form deformation on the control points and establish a one to one correspondence between them to generate a warp image. Images having local distortion, irregularly spaced samples in them and have nonlinear distortions are successfully warped with BSplines interpolation [86-88]. Medical images with large local deformation such as coronary arteries/ cardiac images are also successfully warped with BSplines interpolation functions. However, accurate image warping with BSplines needs more computational time which makes it less desirable in a situation when the time constraints are important.

Image warping with BSplines is performed by defining local domain which contains many control points [88]. Subsequently, the local domain which is divided into several blocks is shifted to a new region. The warping is performed again and again on the shifted domain till the recovery of all pixels in the image. Images with inconsistent contrast between them are therefore precisely warp with BSplines. Furthermore, BSplines also provide one-to-one mapping property due to which there is no chance of distorted image to fold back upon itself.

3.7 Asymmetrical Demons Deformable Registration

Demons methods also called gray-scale automatic deformable algorithms are efficient and robust registration methods for medical images [28, 77, 89-91]. These algorithms are mostly used for intensity based image registration and perform operation on prominent and distinctive features of images. Demons algorithms greatly depend on the intensity or color change (image gradients) in the source and/or target images. Therefore, changing the gradients of input images strongly affects the accuracy of registration. Several types of demons algorithms are available with high capability to describe critical structure and trace potential differences/ similarities in source and target images during radiotherapy and image guided surgery.

Uniform one-to-one mapping of corresponding point landmarks in both directions is very important for the consistent and smooth registration of medical images [27]. However, majority of the available registration methods are asymmetrical and unidirectional because registering source image to target image does not show the same associations as registering target to source. Furthermore, most of the transformation functions such as linear and non-linear elastic functions, thin plate functions, cubic kernel and quadratic regularization functions are also perform asymmetrically during registration [92]. The difference in coordinate frames between source and target images due to the difference in the deformation field also gives better registration result when the transformation is asymmetric. To represent a valid probabilistic model on the basis of atlas based registration, the asymmetric approach provides more simplicity than symmetric registration. In image-guided surgery, image to atlas based registration using asymmetric transformation is mostly used for the precise analysis of tumor in human organs.

In asymmetric approach, registration relay on the choice of target domain because the estimation and mapping of point lands-marks is unidirectional. Therefore, unidirectional transformation of deformable images provides more efficiency than bi-directional transformation, particularly in the case of mono-modal image registration. However, the performance of bi-directional (symmetric) registration is much high on the basis of running time and estimation of total errors in the registration of multi-modal deformable images due to the availability of regional symmetric similarity measures [93].

3.8 Symmetrical Demons Deformable Registration

Pair-wise and bi-directional mapping of homologous point land-marks between source and target image are widely used methods for the accurate and consistent image registration. The pair-wise and bi-directional mapping of point landmarks in one coordinate to another coordinate is also called symmetric registration [94]. In symmetric registration both images are treated in the same manner and the mapping of similarity measures is performed from source image direction to target image direction and vice versa. Such type of two ways mapping provides more consistency and accuracy during image registration because the possibility of detecting different transformation components will be more. Furthermore, symmetrical registration also show robustness against local minima because in the optimization process it uses the gradients of both images

Contrast to symmetric image registration, asymmetric image registration maps point land marks between two images in a non-uniform and unidirectional way due to which the choice of target image usually influences the results of deformable image registration. Symmetric registration also eliminates the chance of inverse consistent errors which usually occurs due to the inconsistent voxel-by-voxel wise association between source and target images in both directions [95]. The inverse consistent function computes transformation information from source and target images and converts them into a common intermediate image. This function also ensures that the transformation from source image side is the inverse of the transformation from the target image side. On the down side, the two way transformation require more computational time and is difficult to implement especially in case of image registration with iterative optimization. Furthermore, symmetrical registration cannot perform well in the registration of image to template (atlas) based registration [96] because in this type of registration the mapping is mostly performed in a single direction for the template to exhibit a suitable probabilistic model.

4. PERFORMANCE EVALUATION

The performance evaluation of different deformable registration methods is always a difficult task faced by the researchers. The main reason is the unavailability of related pixel information between source and target images. We have evaluated the performance of deformable registration methods by implementing them in C++ based on the Insight Segmentation and Registration Toolkit (ITK) [72]. The computer system used for testing the performance of registration methods is Core i5 with 4GB RAM. The performance i.e. accuracy and efficiency was evaluated by testing the eight variants of deformable registration methods. We have implemented the registration methods on the datasets of two 2D lung images of living rat obtained from ITK software package [72]. For experimental analysis, images were taken at different times, the one after inspiration of air into lungs (source image) and the second after exhalation (target image). In the quantitative analysis, mutual information, root mean square error (RMS), computation time and occupied memory were used as evaluation metrics. Since deformable images hold high local variation, therefore, for each method we have performed three types of registration for rat lungs images: registering normal images, registering the same images by inducting 0.001% and 0.002% Gaussian noise. Table 2 shows the overall quantitative analysis of each method on different levels. The basic aim was to estimate the effect of change or noise on the accuracy and efficiency of each registration method.

Accuracy evaluation in deformable registration is a challenging task due to variations in every voxel points. In our experiment, this is performed by estimating mutual information and root mean square errors between source and target images. On the other hand, efficiency of each method is calculated based on computation time and memory space occupied by each method.

To find out the accuracy of each registration method, the values of mutual information and RMS errors estimated in Table 2 at noise levels (0%, 0.001% and 0.002%) were further listed in Table 3 and Table 4. On the bases of data obtained in Table 3 and Table 4, accuracy of deformable registration methods are graphically shown in Fig 5 and Fig 6 respectively. Mutual information (MI) and RMS are the two essential parameters to estimate the accuracy of registration method. These two parameters are widely adopted by a large number of researchers in the medical image processing community. MI estimates the similarity measures between source and target images through pixel-by-pixel correspondence while RMS error is a standard statistical metric for error prediction. The registration method is more accurate if the values of MI are maximum and RMS values are minimum.

It is shown in Fig 5 that in most registration methods, the introduction of noise has little effect on the values of mutual information. However, in the experiments, we obtained high mutual information values for FEM based registration method. Similarly, we estimate good results while testing level set method for mutual information. Therefore, FEM based and level set registration methods provide more accuracy as compare to others deformable registration methods. On the other hand, the accuracy of warping with kernel splines is much low in our experiment due to small mutual information values obtained from the registration of source and target images at different noise levels.

We have also tested the accuracy of each registration method based on RMS error at different noise levels. Accuracy based on RMS error is shown in the Table 4 which is further plotted in Fig 6. In this experiment, we obtained minimum RMS error values for FEM based registration and high values for warping with kernel splines. Therefore, the accuracy of FEM based registration based on MI and RMS error is much high than other types of deformable registration methods. However, the accuracy of warping with kernel splines is low compared to other methods due to low MI and high RMS error values obtained in our experiments.

In order to determine the efficiency of deformable registration methods, they are tested on the basis of computation time and occupied memory space. Registration method is more efficient if it takes minimum time and less memory space during execution. The computation time estimated for all registration methods in our case at different levels of Gaussian noise are listed in Table 5 and graphically shown in Fig. 7. It is shown in the Fig that the warping with kernel splines is the most efficient method at 0% and 0.001% Gaussian noise because it takes less time than others methods. Similarly, asymmetric demon registration also provides consistent efficiency at different noise levels. On the other hand, the efficiency of FEM based method is much low due to excessive time it takes during registration of source and target images. We have also estimated the efficiency of each registration method on the bases of occupied memory space. Values obtained for memory space occupied by each method at different noise levels are listed in

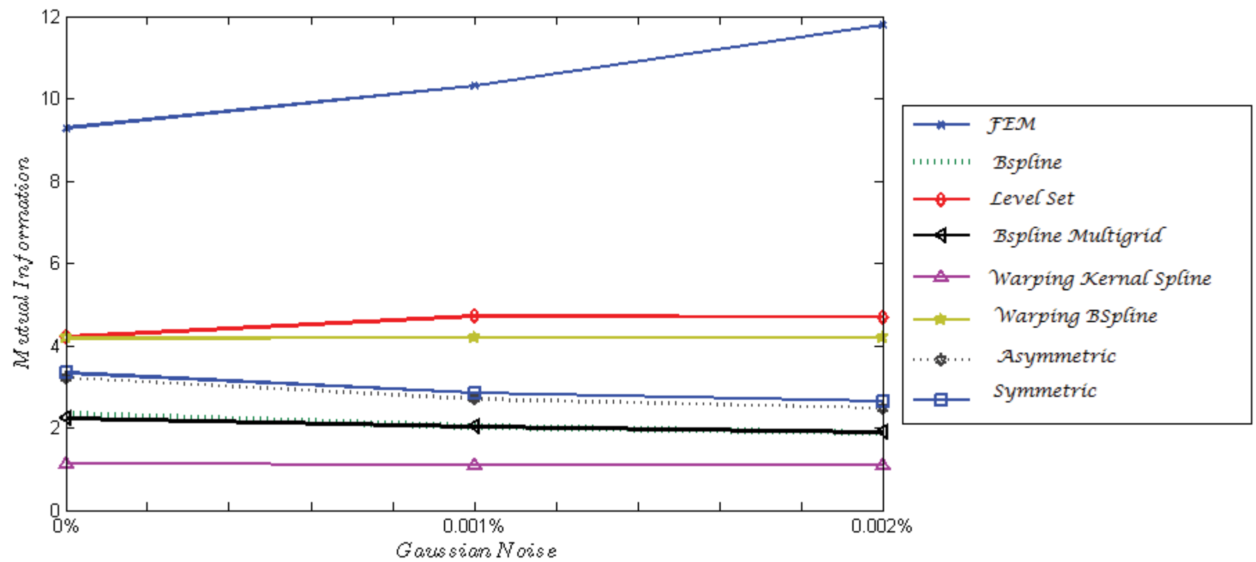

Fig. 5. Graphical representation of MI at different levels of Gaussian noise.

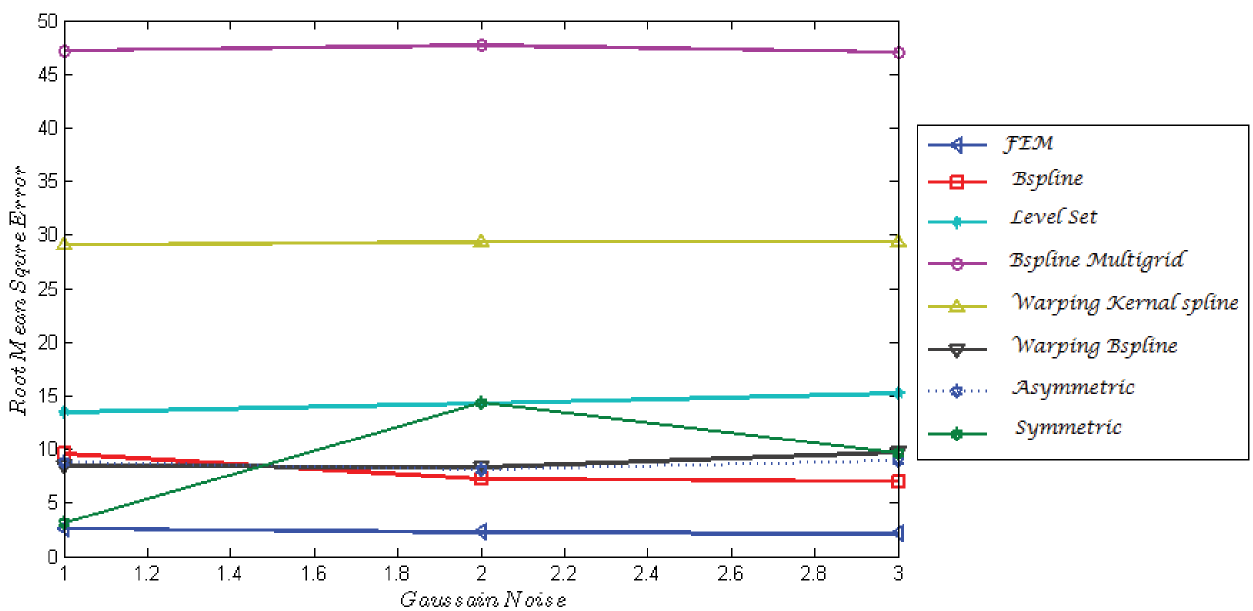

Fig. 6. Graphical representation of RMS errors at different levels of Gaussian noise.

Table 6 and their graphical representation is shown in Fig 8. In this case, the efficient methods are BSplines multi-grid and FEM based registration due to the minimum memory space occupied at different noise levels. However, the memory spaces occupied by BSlines registration, warping with kernel and BSplines methods are much high due to which they are less efficient.

After the detail evaluation and testing of deformable registration methods we came up with certain conclusions. In our experiments, the performance of FEM based registration is high than other types of registration methods. This is due to the sharing of excessive amount of mutual information, less number of RMS errors in registration and taking less memory space during execution. We also estimate high computational time during execution for FEM registration, which negatively affect image registration. Minimizing the computational time for FEM based registration will make it a perfect

Table 2. Experimental evaluation of deformable registration methods.

Parameters	FEM based registration			BSplines registration			Level set registration			BSplines multi-grid registration			Warping with kernel splines			Warping with BSplines			Asymmetric demons registration			Symmetric demons registration		
	Noise (0%)	Noise (0.001%)	Noise (0.002%)	Noise (0%)	Noise (0.001%)	Noise (0.002%)	Noise (0%)	Noise (0.001%)	Noise (0.002%)	Noise (0%)	Noise (0.001%)	Noise (0.002%)	Noise (0%)	Noise (0.001%)	Noise (0.002%)	Noise (0%)	Noise (0.001%)	Noise (0.002%)	Noise (0%)	Noise (0.001%)	Noise (0.002%)	Noise (0%)	Noise (0.001%)	Noise (0.002%)
Mutual Information	9.276	10.305	11.785	2.3286	2.021	1.87	4.212	4.7103	4.7043	2.221	2.028	1.886	1.142	1.105	1.109	4.170	4.189	4.189	3.219	2.694	2.473	3.332	2.855	2.640
Root Mean Square Error (mm)	2.590	2.270	2.125	3.087	14.320	15.981	9.602	7.221	7.044	13.46	14.28	15.23	47.2	47.67	47.074	29.124	29.337	29.337	8.442	8.321	9.674	8.785	8.081	8.911
Computation Time (Seconds)	1.024	1.065	1.018	0.453	0.532	0.535	0.397	0.435	0.596	0.532	0.453	0.543	0.315	0.463	0.478	0.643	0.745	0.764	0.386	0.547	0.452	0.642	0.7032	0.796
Memory (kb)	788	1048	1096	5656	4360	4432	3320	2065	1896	136	136	136	3922	4037	4054	3912	3991	4193	3206	1960	1960	3160	1760	1920

choice for the successful registration of deformable images. It is also observed that the performance of warping with kernel splines in terms of accuracy is low due to high number of RMS errors arises during registration and sharing of low mutual information. However, the efficiency in terms of computational time is high for warping with kernel splines method. Likewise, BSplines multi-grid registration provides more efficiency in terms of computational time and occupied memory space. Therefore, the improvement in terms of accuracy can also make this method a perfect choice in clinical applications.

Deformable registration methods are widely used for the accurate registration of objects with large deformation. Therefore, several registration methods are available which automatically register medical images. After a thorough analysis of each method, we find out that every method provide their own strength and flexibility for the precise and efficient registration of medical images. However, due to complex and difficult to calculate deformation field, most of the registration methods cannot perform perfectly in clinical applications. Therefore, generic and powerful registration methods are required to be developed in the future, which can precisely, efficiently and automatically register medical images with large-scale deformations.

5. CONCLUSIONS

Deformable image registration is a challenging task in medical image analysis due to different imaging conditions, variability in anatomical structures and elasticity of the body and organs. In this article, we have experimentally evaluated the existing deformable registration methods on the images of rat lungs to estimate their performance. Although several automatic deformable registration methods are available applicable for single modality, linear and small local deformation, universal and generic methods are still a problem in clinical applications. To perfectly register medical images obtained through multimodality with uncertain and complex features of deformable objects further research is needed. However, in our analysis, we came up with a conclusion that FEM based registration method obtained excellent performance in terms of

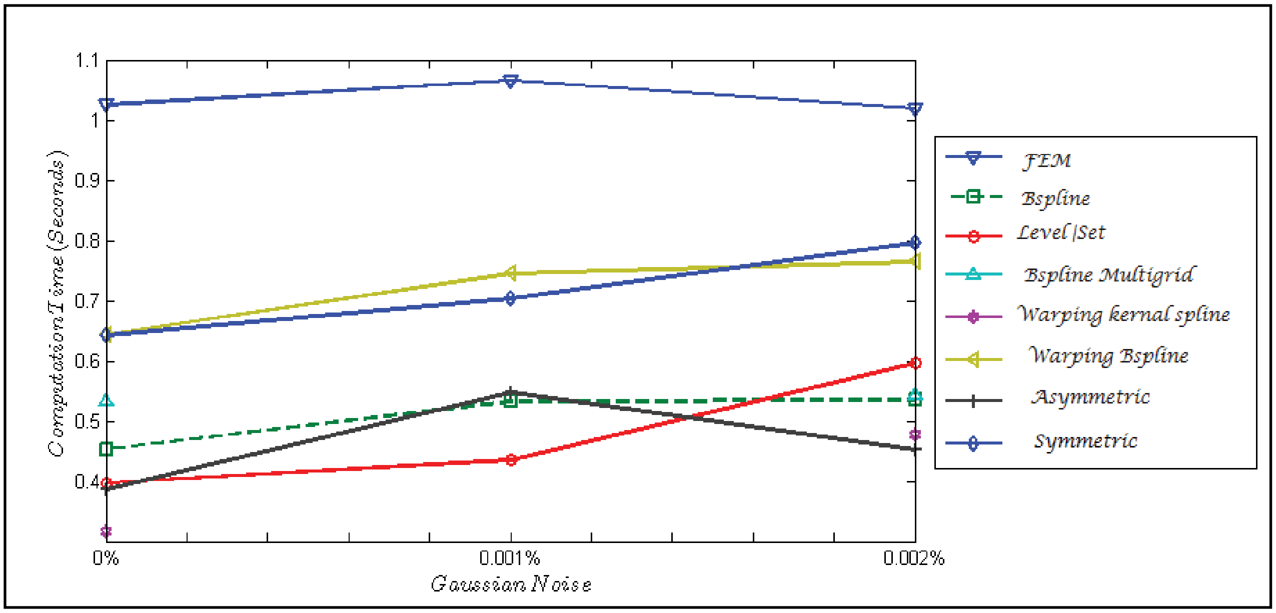

Fig. 7. Graphical representation of computation time at different levels of Gaussian noise.

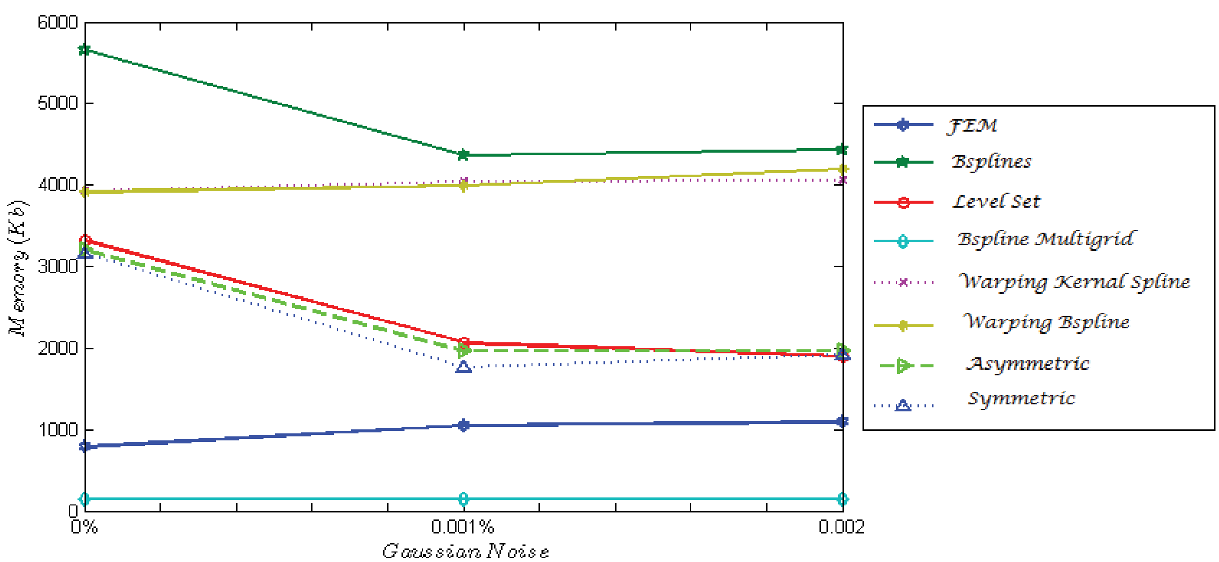

Fig. 8. Graphical representation of memory space occupied by deformable registration methods at different levels of Gaussian noise.

Table 3. MI of deformable registration methods at different noise levels.

	FEM based registration	BSplines registration	Level set registration	BSplines multi-grid registration	Warping with kernel splines	Warping with BSplines	Asymmetric demons registration	Symmetric demons registration
Noise (0%)	9.276	2.328	4.212	2.221	1.142	4.170	3.219	3.332
Noise (0.001%)	10.305	2.0211	4.7103	2.028	1.105	4.189	2.694	2.855
Noise (0.002%)	11.785	1.872	4.7043	1.886	1.109	4.189	2.473	2.640

Table 4. RMS error of deformable registration methods at different noise levels.

	FEM based registration	BSplines registration	Level set registration	BSplines multi-grid registration	Warping with kernel splines	Warping with BSplines	Asymmetric demons registration	Symmetric demons registration
Noise (0%)	2.590	3.087	9.602	13.46	47.23	29.124	8.442	8.785
Noise (0.001%)	2.270	14.320	7.221	14.289	47.678	29.337	8.321	8.081
Noise (0.002%)	2.125	9.602	7.044	15.235	47.074	29.337	9.674	8.911

Table 5. Computation time for deformable registration methods at different noise levels.

	FEM based registration	BSplines registration	Level set registration	BSplines multi-grid registration	Warping with kernel splines	Warping with BSplines	Asymmetric demons registration	Symmetric demons registration
Noise (0%)	2.590	3.087	9.602	13.46	47.23	29.124	8.442	8.785
Noise (0.001%)	2.270	14.320	7.221	14.289	47.678	29.337	8.321	8.081
Noise (0.002%)	2.125	9.602	7.044	15.235	47.074	29.337	9.674	8.911

Table 5. Computation time for deformable registration methods at different noise levels.

	FEM based registration	BSplines registration	Level set registration	BSplines multi-grid registration	Warping with kernel splines	Warping with BSplines	Asymmetric demons registration	Symmetric demons registration
Noise (0%)	1.0245	0.453	0.397	0.532	0.315	0.643	0.386	0.642
Noise (0.001%)	1.065	0.532	0.435	0. 453	0. 463	0.745	0.547	0.703
Noise (0.002%)	1.0186	0.535	0.596	0.543	0.478	0.764	0.452	0.796

Table 6. Memory Space Occupied by Deformable Registration Methods at Different Noise Levels.

	FEM based registration	BSplines registration	Level set registration	BSplines multi-grid registration	Warping with kernel splines	Warping with BSplines	Asymmetric demons registration	Symmetric demons registration
Noise (0%)	788	5656	3320	136	3922	3912	3206	3160
Noise (0.001%)	1048	4360	2065	136	4037	3991	1960	1760
Noise (0.002%)	1096	4432	1896	136	4054	4193	1960	1920

accuracy and memory space. Our experiments also confirm that in terms of efficiency, the performance of BSplines multi-grid and warping with kernel splines is excellent compared to other methods.

The future work is to further improve the performance of deformable registration methods we obtained in our experiment and to develop an advance registration method applicable for the registration of several types of deformable objects. In the next work, we will also evaluate the performance of deformable registration methods on larger datasets containing 3D and 4D deformable image and for a broad range of medical image registration methods according to the criteria we adopted in this work.

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