INTRINSIC REGISTRATION TECHNIQUES FOR MEDICAL IMAGES: A STATE-OF-THE-ART REVIEW

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ABSTRACT

Medical image registration is the process of mapping two or more medical images into a single more informative image for the purpose of receiving precise and complementary information. The precise mapping of medical images obtained in different time- frames and by the same or different modalities is now possible due to the availability of large number of registration techniques. The purpose of this paper is to present and analyse intrinsic registration techniques for medical imaging in a comprehensive manner. Our approach of analysis is unique from already published work because we have performed detailed investigation on each registration techniques, and analyse similarity measures and assessments according to various parameters. The knowledge on the work that has been developed in the area is presented in a compact form. This work is expected to provide a useful platform for the researchers in the field of medical image registration in general and in intrinsic registration in particular.

Key Words: Medical image registration, Image guided surgery, Intrinsic registration, Medical imaging modalities

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INTRODUCTION

Image registration techniques have been extensively studied in the computer assisted surgery by the medical imaging community for the last two decades[1,2]. Registration techniques are used for mapping two or more similar images taken with same or different modalities or through different time-points and angles. The basic purpose is to obtain more precise image by quantitatively comparing them with their corresponding features. Matching set of images in registration processes involves feature detection, feature matching, transformation of source image into target image and the optimization procedure. In feature detection, image features such as edges, lines, curves and points are detected while in feature matching steps a cost function is used to find the similarity measure in source image and in reference image. Image transformation allows translation, rotation and scaling while the optimizer finds the degree of appropriateness in transformation.

The importance and use of image registration is in several fields including medicine, remote sensing and computer vision. Medical field is among one of them which grab more attention recently due to the rapid development and use of sophisticated computer-assisted surgical techniques in image guided surgery. In medical field, images of the same organs are taken with different imaging modalities such as magnetic resonance imaging (MRI), computed tomography (CT), ultrasound (US), single-photon emission computed tomography (SPECT) and positron emission tomography (PET). These modalities have their own property to show images e.g. CT and MRI mostly used for showing anatomical structure while PET shows functional contents.

Registration techniques can perform the similarities and differences among multi-modal images of the same organs according to different properties such as pixel-by-pixel and voxel-by-voxel. Integration of related information obtained from multimodal images is more reliable and can assist the clinicians to take accurate decisions. Therefore, it is now easy for the clinicians to easily monitor and get complete information about the tumor of the patient by applying the techniques of image registration to mono-modality and multimodality 3D-2D or 3D-3D images. Although the early use of medical image registration were mostly done in the analysis of brain images but now it is a core tool in the analysis of several other medical treatments such as the reliable analysis of heart images, implant dentistry, neurosurgery, hip and knee surgery and for the treatment of other organs such as retina, chest/lung, abdomen, breast, prostate, whole thorax, cervical, pelvis and whole body[3-10].

Several types of techniques have been developed for the registration of medical images and each have their own way to perform registration process[11-16]. Intrinsic registration techniques are the most popular among

them successfully used in several clinical applications. Although each technique in intrinsic criteria performs independently and on different behavior but the goal is the same, which is to registered medical images for diagnostic purpose. All the techniques related to intrinsic category need patient generated content for registration[17,18]. Registration of medical images in case of intrinsic techniques requires the use of points, curves, landmarks, surfaces and gray levels of images.

Intrinsic registration techniques are categorized into point based (landmark based), surface based and voxel based. Point based registration techniques can perform global transformation of medical images with optimum speed and efficiency. These registration techniques include anatomical and geometrical landmarks for the registration of medical images with constant variability. Surface based registration is another variation of intrinsic techniques, which divide important features of images into segments and integrate the corresponding segments into a single more informative image. Surface based techniques are further divided into rigid models and deformable models, which can map, locate and divide medical images into appropriate segments. Intrinsic registration based on voxel or intensity measure deals with images in two ways: either directly operates on image gray levels or uses whole image contents for registration. In these techniques, there is no need of image segmentation for registration because feature space of the image to be registered is extended from points to segments to complete features. These features increase the set of corresponding information of related points in two or more images. Reduction to scalars/vectors also called movements and principle axes and using full image content are the two types of voxel-based registration. The former reduces image gray value and directly operate on it while the later uses whole image gray value information in registration processes.

This paper is aimed to provide a comprehensive review of intrinsic registration used for medical images. Although the proposed categorization and evaluation is inspired by the work of Maintz and Viergever[19], in which medical image registration techniques are classified based on nine basic criteria. These include dimensionality, nature of registration basis, nature of transformation, domain of transformation, interaction, optimization procedure, modalities involved, subject based registration and object based registration. Maintz and Viergever also further sub-divided the image registration techniques into more specific categories, which provide compact knowledge for the researchers in this field. The work of Maintz and Viergever almost describe every medical registration method but in very brief. There is also the lack of comprehensive analysis on each technique according to different parameters, which we used in this work such as accuracy, efficiency, reliability, robustness/ stability, optimization procedure, transformation, error detection, target localization, computation/automation, clinical use/applications, modality and the support/availability of software tools.

The work presented in this paper analyzes intrinsic registration techniques in a comprehensive manner and based on the above-mentioned parameters. Furthermore, almost every possible aspect of the most popular intrinsic registration techniques was covered including their pros and cons. We have also organized and compile the available knowledge on this challenging area of research in a concise manner. We hope that this review paper will provide a compact platform for both researchers and clinicians in the area.

METHODOLOGY

In this paper, to give insight knowledge and understanding of the available intrinsic registration techniques, they are evaluated against a set of parameters including accuracy, efficiency, reliability, robustness/ stability, optimization procedure, transformation, error detection and calculation, target localization, computation/automation, clinical use/applications, modalities involved, software tools availability and the major drawbacks of each technique. In order to evaluate the different techniques according to the above mentioned parameters they are presented in Table 1. The Table provides state-of-the-art information to the users and researchers in the image registration field. The most important parameters we used in the analysis of intrinsic registration techniques are briefly describe as follows. .

Accuracy: Useful clinical applications and improved health care require an accurate image registration with high speed and simple algorithms and sophisticated evaluation techniques. Registration with automatic preprocessing segmentation also needs high level accuracy for improved health care[20,21]. Registration and segmentation are complementary for each others because a registration technique with high accuracy can easily solves segmentation problems and vice versa. The registration technique is called inaccurate if errors either actual or timely occurred at any time in image during registration. Therefore, to achieve high accuracy in the image registration, weaker and inaccurate techniques should be replaced with stronger and sophisticated one[22]. Medical image registration can be validated by both quantitative and qualitative accuracy in that the former requires a ground truth that is consistent in clinical applications while the later type of accuracy can be obtained using simple visualization tools and spectrum. Several types of techniques such as non-rigid deformation and composite wrapping have been developed which can enhance the accuracy of registration.

Efficiency: Efficiency of registration techniques be-

come a key issue with the development of complex algorithms based on iterative nature, computation of complex similarity measures and with re-sampling procedures[23]. Such problems greatly reduce the speed and efficiency of registration process. Therefore, several types of registration algorithms with high efficiency have been developed. These algorithms play an important role in image guided surgery with efficiency and without compromising reliability[24]. The speed and efficiency of registration technique can be improved by optimizing interpolation and transformation parameters, developing fast template based tracking approaches, using parallel and multi-resolution approaches, reducing number of similarity measures and by the use and selection of subsets of pixels.

Reliability: Reliability is an important validation parameter for registration technique because expected results are always required in the range of possible clinical input. Registration technique is more reliable if it is tested on several combinations of input images providing the same results as expected.

Robustness/stability: Medical images are always affected by the noise, blur and organs movements. This change strongly affects the consistency of registration process. Registration process is robust/stable if a small amount of change in the source image results the same amount of change in the target image [25]. On the other hand, registration processes is unstable if a small variation in the source image results large variation in the target image.

Optimization procedure: Optimization is an important metric in image registration because it affects and measures the accuracy, preciseness and robustness during image transformation[26]. Optimization procedure is applied iteratively till the merger of similarity measure obtained from scene image and model image during image registration process. Or in other words, this iterative procedure continue until the exploration of the space of possible transformations i.e. feature based classification, appropriate segmentation, and finding similarity measures and objects enhancement. Although optimization always remains a problem in medical image registration but still there are several techniques available which have improved the registration process. These techniques include gradient decent, non-linear conjugate gradient, multi resolution techniques, evolution strategy and simultaneous perturbation.

Transformation: Transformation in image registration is the matching of points in one image space also called coordinate system with another image space. Image registration strongly relies on appropriate transformation of points in target image space to the points in source image space[27]. Several types of transformation are available for image registration such as rigid and non-rigid, the former involve translation and rotation while the later involves scaling along with translation and rotation.

Error detection: Error detection is an important step in image registration process because it increases the accuracy of image transformation. Errors during image registration usually occur due to the change and movements in medical image[28]. Error detection was a big problem in the early registration techniques because the accuracy of image transformation directly depends on it. The missing of errors from registration techniques and algorithms often creates problems for researchers and clinicians. Homogeneity of images during mapping process always creates errors in image registration. Several types of testing techniques have been developed which can easily and automatically detect errors in image registration.

Target localization: Target localization is the separation of tumor from normal tissues and it allows better local control of tumor volume in image guided surgery and treatment planning. In modern radiotherapy, target loclization is performed by the use of modern registration techniques and image fusion. Precise target determination and localization is critical and difficult step in image guided surgery without using the modern techniques of image registration and fusion[29]. The registration and fusion of different modalities such as CT-MRI now clearly demarcate tumor from normal tissues and provide better target localization.

Computation/automation: Several types of automatic and semi-automatic registration techniques have been developed which require less or no interaction from the users. These registration techniques have the capability to register medical images with high speed and taking less computational time and resources. Functional and structural features in images belongs to different modalities are now easy to identify with accuracy due to their automatic advanced mapping approach. Therefore, such types of automatic techniques are now a suitable choice for researchers and clinician due to their precise and fast mapping mechanism.

Clinical use/applications: Modern image registration techniques are currently less adopted in clinical practices. The usefulness and success of registration technique is subject to its widespread adaptation and use in clinical practices. Currently the use of rigid registration in clinics is more than non-rigid registration techniques. However, for any registration techniques to be useful in clinical practices, its accuracy should be validated.

Modality: The development of successful registration techniques in recent years is possible due to the availability of sophisticated imaging modalities such as CT, PET, MRI and SPECT. The accuracy and quality of registration depends on these modalities. Image registra-

tion is now performed with mono-modal or multimodal techniques in which the former registered images with single device/ sensor while the later registered images with multiple devices/sensors. Each modality has their own characteristics to represent medical images i.e. the anatomical information of brain images can be best shown by MRI while PET can show functional information in more detail. Furthermore, registration of multimodal images such as CT-MRI and PET-CT are widely used in medical field for tumor localization, segmentation of organs and prostate localization. In image-guided surgery, the precise alignment of preoperative images with intra-operative images is also now possible using multimodality registration.

Software Tools support/Availability: For a registration technique to be accepted by clinicians and other technical users, needs strong support and availability of software tools. A software tool provides an environment for users to create, store, edit, maintain, and visualize image information in registration process. The more a registration technique is supported by the software tools, the higher will be its use and value.

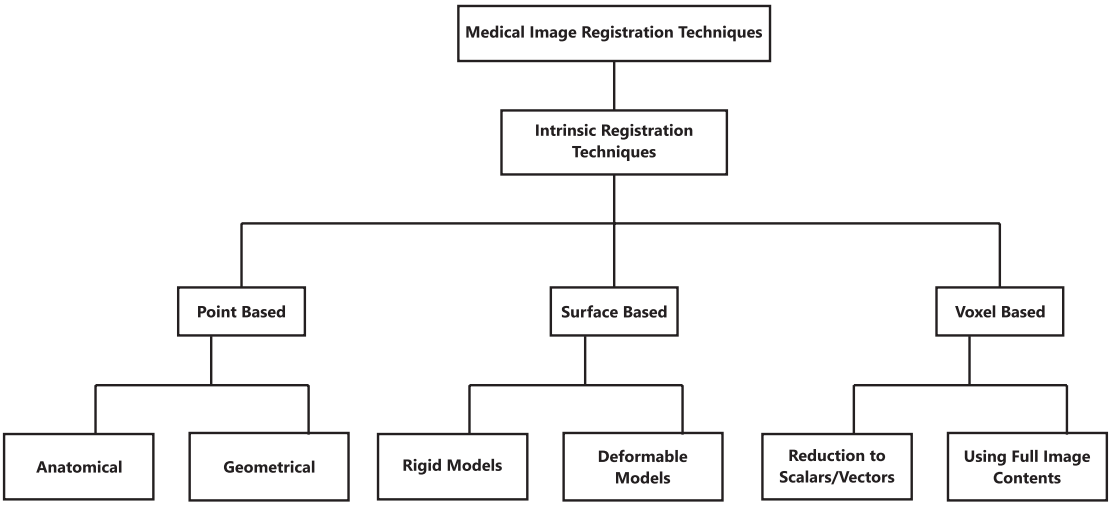
Medical image registration techniques

In medical imaging research community, image registration has been accepted as a highly vibrant area due to its broad range applicability and importance in human anatomy. Therefore, huge amount of investment has been made in the last 20 years by the academia and industry around the globe for the development of image registration techniques. The purpose was to take medical images from multiple modalities, in different time-frame and angle and creating the correspondence of similar features in them[30]. The frequent variations in human body organs due to breathing and movement can results dissimilarity in images, although the images are taken from the same sensor but at different time, or at the same time but at multiple sensors or by changing the angles of a sensor. Such type of variations in the images of human anatomy, which are highly sensitive to operate need transformation of multiple images of the same scene to a single more informative image. Such type of transformation is performed with the help of image registration techniques. These techniques relate corresponding significant points in each image, extract similar features, perform optimal transformation and measure similarity and dissimilarity measure in multimodality images[1].

Each modality has their own characteristic to represent medical image e.g. MRI for better visibility of tumor and soft tissues and CT for better representation of bone structure[31,32]. Therefore, precise representation of similarity measure obtained from different images into single one is essential which is only possible by using the appropriate technique of medical image registration[33]. Furthermore, medical image registration also improve surgical and treatment planning by providing more clinically relevant diagnostic information.

Several types of research articles have been published on the categorization of medical image registration techniques. These categorizations covers some of the important aspect of the medical image registration techniques but in very brief and without any detail, pros and cons and other aspects such as accuracy, efficiency, reliability, error detection and calculations, target localization, optimization and computational complexity. In this paper, we have narrowed down the categorization of medical image registration into intrinsic criteria. The primary goal is to evaluate these techniques, cover a comprehensive literature review about them and describe their use and importance in research and clinical practices. Diagrammatic representation of the categori-

Figure 1: Medical image registration techniques



zation we have proposed is shown in Figure 1 and their detail is given in the subsection below.

Intrinsic registration techniques for medical images

Intrinsic registration algorithms are commonly used techniques in medical image processing. It refers to the process of extracting and mapping features and anatomical information from the subject image itself[34]. In intrinsic registration, image features and anatomical information are determined through different geometric means such as points, curves, snakes and principle axes. Flexibility, reliability, non-invasiveness and automatic segmentation are the important features of intrinsic registration[35]. Intrinsic registration techniques for medical images are further categorized into landmark based, segmentation based and voxel-based. Table 1 analyzes and compares the available intrinsic registration techniques using a set of evaluation parameters and their detail is discussed in the sub-sections below.

1.1. Landmark based (point based) registration

Landmarks (both anatomical and geometrical) are useful points obtained from patient images. In landmark-based registration, the corresponding landmark points, which represent the same feature in multiple images are determined and mapped. In the next step, image transformation is estimated from the locations of the landmarks. In image registration, landmarks selection and extraction are performed either by manual method, semi-automatic and fully automatic method. The manual method for image registration is simple but require intensive user interaction to determine points selection and extraction from different images. Therefore, the accuracy of registration process highly depends on the experience of user. On the other hand, automatic methods globally transform images with high efficiency. However, the accuracy of these methods greatly depends on the precision and optimization of algorithms. Similarly, in both manual and automatic methods the proper selection of landmarks is also necessary for accurate registration of medical images. Figure 2[36] shows the registration of CT-PET images based on landmarks in which small scattered points or landmarks are compared to the original image contents. Furthermore, fast optimization algorithms are applied which calculate the average distance between each point, find the related landmarks and its neighbors in the image dataset[36]. Landmark based registration is further divided into anatomical registration and geometrical registration.

In computer assisted surgery and radiotherapy, the accurate mapping of anatomical structures is an important pre-processing step. However, this step requires many efforts because in different patients, the anatomical structures vary significantly[37]. The accurate detection and matching of corresponding landmarks

Figure 2: CT-PET image registration based on landmarks

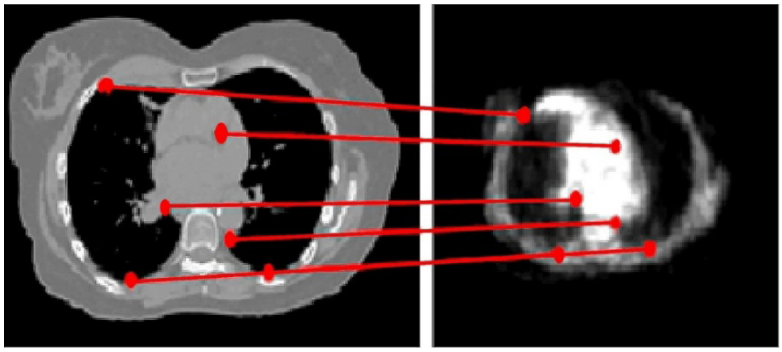


Figure 3: Anatomical landmarks in human pelvic bone

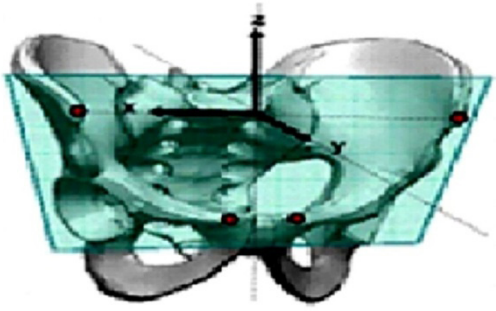


Figure 4: Geometrical landmarks on facial geometry

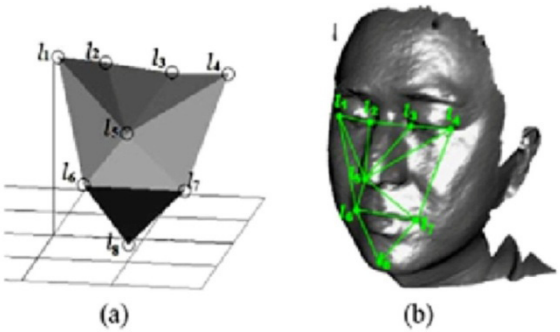
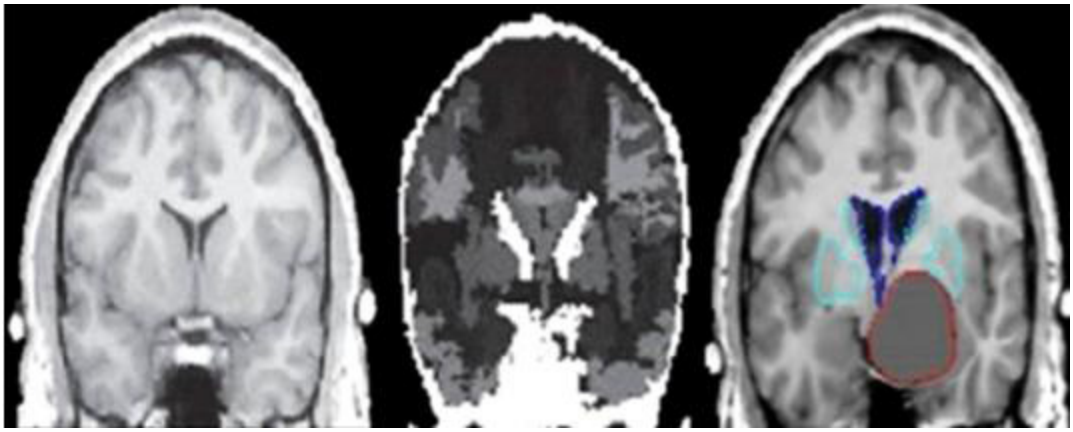


Figure 5: Segmentation/surface based registration of brain image



Atlas image Atlas label map Segmented

in medical images with high variability are mostly performed with anatomical landmarks based registration. Automatic identification of anatomical features in multimodal images at various levels is another important feature of anatomical registration. However, in case of less number of defined landmarks for selection and identification may produce inaccurate registration results. Brain MR surgery, bimaxillary surgery, lateral skull based and temporal bone surgery are the main areas in which anatomical registration is used effectively. Figure 3 shows some anatomical landmarks in human pelvic bone i.e. on anterior superior iliac spine, pubic tubercle and pubis[38].

Another type of landmark-based registration is geometric registration in which the process of registration is performed based on the measurement of key points and their positions in medical images. This registration technique is mostly used in multidimensional and multimodality images[39]. Estimation of global and local differences in multidimensional images is perfectly done with geometric registration. The accuracy of geometric registration highly depends on the proper selection of key geometric points and features. The identification of key points and features are easily done in normal images while in noisy images, require a lot of care and efforts[29]. Figure 4[40] shows the diagrammatic representation of geometrical landmarks which is based on individual facial geometry. Registration processes based on patient geometry is usually performed in four steps: identification of landmark points, development of mesh model, image transformation and interpolation[41,42].

1.2 Segmentation based (surface based) image registration

In segmentation-based registration, the objects of interest in both images have been segmented on the bases of related landmarks and then transformation function is applied on one image until the alignment of related landmarks[43]. A repetitive process is applied at the end to reduce the distance between the two segments. Segmentation-based registration converts images of different nature into a single more informative image. However, in some cases accuracy is compromised when there is continuous splitting in either one or both images. The essential requirement in image-guided surgery is the availability of high number of information but some time different types of images contains low or missing information of human anatomy[44]. In such type of situations, segmentation based

Figure 6: Rigid registration based on feature points matching

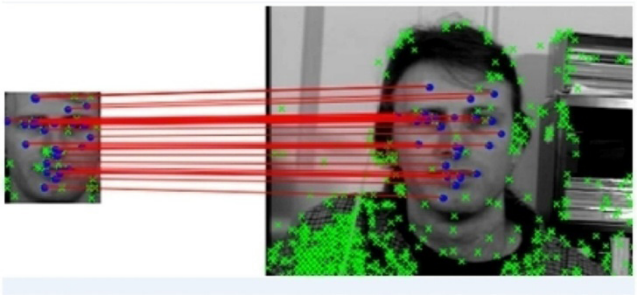
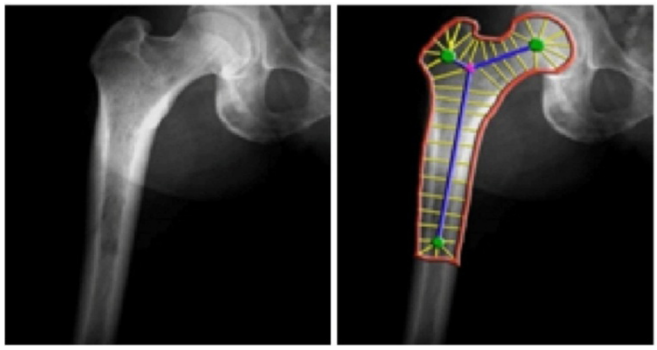


Figure 7: Deformable model based registration



registration work successfully than other types of registration methods. Figure 5[45] shows registration of brain image based on segmentation techniques. The Figure is based on two deformable models in which the left one is an atlas image, the centre is atlas label map and the right one is segmented brain image. In Figure 5, the atlas image at the left is modified to reproduce the tumor-induced deformation which is further segmented and transferred to the patient image by deformable segmentation based registration. Segmentation based image registration is further categorized into rigid models and deformable models, discussed below.

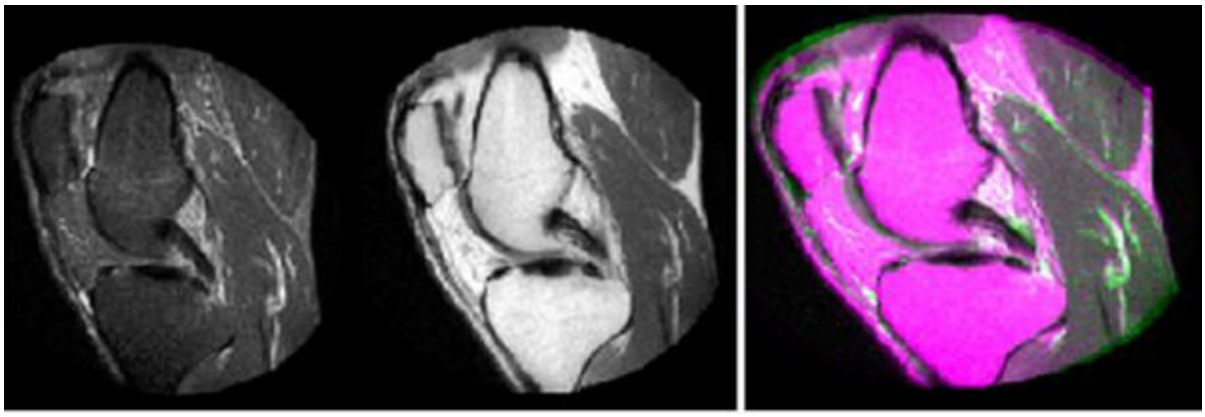
Registration of medical images with rigid transformation is performed by the translation and rotation of objects in the images. In other words, rigid model based registration translate and rotate feature points (point, curves, and surfaces) in one image and mapped them into their corresponding information in the second image. The transformation in rigid registration preserves the shape of subject images, distances and angles among points. In this type of transformation, the shape of subject images, distances and angles among points remain the same. Figure 6[46] shows feature point matching between a template and the current input image. In the Figure, detected feature points represented by green cross and matched feature points represented by blue dots are shown in both template image and input image. In this rigid model registration, the point matching algorithm is applied on the two surfaces, which greatly help and guide clinicians to detect distinctive feature points in images.

Deformable registration is a fundamental technique in medical image processing and is a suitable choice for the analysis of images of deformable organs such as heart, lungs, breast and kidney. Because it can easily make a distinction between deformable shapes in objects. Human organs naturally show continuous variations due to breathing and movement and the proper identification of tumor is a difficult task. Deformable registration not only precisely identify and match tumor in two are more images of same organs but also isolate both anatomical and functional contents. Deformable registration also precisely estimates the internal behavior of deformable tissues. On the other hand, efficiency of deformable registration is low while its computational cost is high as compared to rigid registration. Registration based on deformable model is shown in the Figure 7[47]. In the Figure, the left image show patient data before registration and the right one is the registered image obtained as a result of non-rigid deformation during segmentation process. Applying active contours to this registered image we can get more precise and exact position of the data.

Intensity (voxel) based registration

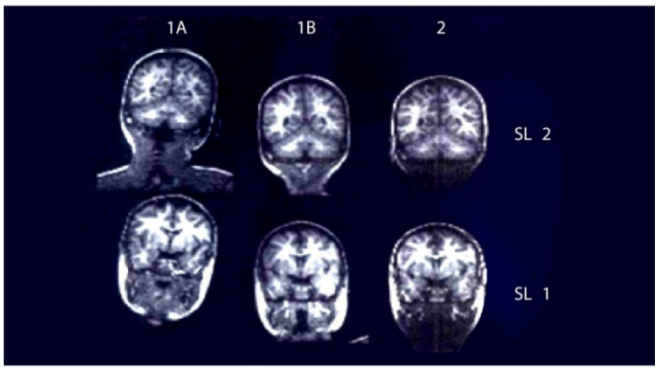
Intensity based registration optimizes similarity measures which determine the degree of shared information of the image intensities. These similarity measures

Figure 8: Intensity based registration of two MRI images



Fixed spine echo image | Moving spine echo image with inversion | Registered image

Figure 9: Principle axes registration of two volumetric MR scans of the brain



are important for accurate registration of medical images. The registration is performed by either using entire content of images or only image gray scale values [48]. Image features estimation and their correspondence with other image features are simple and strait forward in intensity based registration. Figure 8[49] shows the sagittal view of two MRI images of knee using intensity based registration. Image on the left side is fixed one while the center one is moving image obtained at the same time but with changed of alignment to some extent. Image on the right side is the registered image in which the similar intensity values of fixed and moving images are indicated by gray areas. Similarly, the difference between two images according to brightness levels is indicated with magenta and green areas. It is obvious that intensity based registration operate on the whole image gray values and these techniques cannot requires prior data reduction by the user or segmentation. Reductive registration and using full image content-based registration are the two popular types of intensity based registration.

Reductive registration operates on image gray levels and uses center of gravity, angular mass and the principle moments for registration[50]. Reductive registration is performed in rigid manner i.e. only translate and rotate images. In image-guided surgery, reductive registration matches the corresponding volumes or points or surfaces of medical images. Atomicity, speed and easy implementation are the main features of reductive registration. Figure 8[51] shows registration of two volumetric MR scans of the brain image of the same patient in 3D form. Registration technique used in this figure for two brain images of the same patient through different scanner is principle axes rigid transformation, which covers the whole brain volume. In Figure 9 both images of column 1A are aligned with column 1B with rotation and translation, as a result registered images are obtained in column 2.

Another type of intensity-based registration uses full image contents for mapping two or more medical images. The main difference in reductive and full image content based registration is that in the earlier prior reduction of image gray value content is performed while the later one uses whole image gray value information during registration process. Similarity measures, image uniformity, square intensity differences and intensity

Table 1: Analysis of intrinsic registration techniques for medical images using a set of evaluation parameters

Parameters	Intrinsic Registration Techniques					
	Landmark based (point based) registration		Segmentation based/surface based registration		Intensity (voxel) based registration	
	Anatomical	Geometrical	Rigid models	Deformable models	Reductive registration	Using full image contents
Accuracy	Accuracy depends on precise correspondence between landmarks	Accuracy relies on the accurate localization of a sufficient number of corresponding landmarks in all modalities.	High accuracy is only possible if the pre-segmentation step is performed precisely.	Provide very high accuracy when the images are precisely pre-processed and well suited for inter-subject registration.	Low accuracy due to strong dependence on the intensity variations	Low accuracy due to strong dependence on the intensity variations
Efficiency	Require more processing time due to the physical contact with multiple points and the creation of large number of exposure by the surgeons	Require more processing time due to the physical contact with multiple points and the creation of large number of exposure by the surgeons	Show high efficiency when registered structures are clearly visible and easy to segment.	Less efficient due to internal energy constraints	High, because it can directly operate on image gray values and does not require preprocessing and user interaction	High, , because it can directly operate on image gray values and does not require preprocessing and user interaction
Reliability	Excellent reliability and validity	Excellent reliability and validity	Precise pre-segmentation step is essential for reliable registration.	More reliable then rigid models	Robust and versatile	Robust and versatile
Robustness/ stability	Main advantage of using landmarks is robustness	Main advantage of using landmarks is robustness	Gives robust results	Robust and elegant	Highly stable and robust of all registration methods	Highly flexible and robust
Optimization procedure	Simple and efficient due to the availability of limited number of points in the registration process	Simple and efficient	Difficult due to several alteration in image parameters	Computationally efficient due to separate alteration in image parameters	For optimization need a priori knowledge of the nature of registered images	For optimization need a priori knowledge of the nature of registered images

Transformation	- Non rigid and low dimensional - Good feature alignment - Faster to compute the mapping transformation then surface based or intensity based registration	- Rigid and low dimensional - Good feature alignment - Faster to compute the mapping transformation then surface based or intensity based registration	Rigid transformation, with only six degrees of freedom.	Non rigid	Rigid, non-rigid and global transformations,	Rigid, non-rigid and global transformation
Error detection and calculation	Point based algorithms can easily identify and calculate errors such as Target registration error (TRE and fiducial localization error (FLE) due to the availability of well known points	Point based algorithms can easily identify and calculate errors such as Target registration error (TRE and fiducial localization error (FLE) due to the availability of well known points	Easy due to small amount of change in angle	Difficult error detection, measurements and comparisons due to high degree of freedom	Detection and computation of mean square error is difficult due to low resolution and small variations in image intensities.	Detection and computation of mean square error is difficult due to low resolution and small variations in image intensities.
Target localization	Difficult, due to improper visibility of target lesion	Difficult due to surrounding critical organs and normal tissues	Simple due to dependence on less number of points for correspondence	Easy but has some limitations in a situation such as patient motion and breathing	Difficult and subject to inaccuracies, uncertainties and measurement errors	Difficult and subject to inaccuracies and measurement errors
Computation/ automation	Intensive computation and automatic landmark selection is a challenging task	Intensive computation	-Commonly automated but presegmentation step is usually executed semiautomatically -Intensive computation	-Commonly automated but presegmentation step is usually executed semiautomatically -Intensive computation	Computationally expensive as they operate on the full image content but Implemented in an automatic fashion	Computationally intensive but Implemented in an automatic fashion

Clinical use/ applications	Bimaxillary surgery	Used for brain, breast, chest, liver, kidneys diagnoses	Lung cancer radio-therapy	-Track them on-rigid motion of the heart, the growing tip of neuritis, motion of erythrocytes. -Used to locate structures in the brain, register imag-es of the retina, ver-tebra and neuronal tissue	Mainly used in the re-alignment of scintigraphic cardiac studies	Spline surgery, cor-onary angiography, morphometry
Modality	CT, MR, PET, CT-MR	CT, MR, PET, CT-MR	CT,MR, PET, SPECT	X-Rays, CT, MR and ultrasound	CT, MR, PET	Mostly restricted to mono-modality
Software tools availability	Photoshop and Matlab landmark/fiducial based registration toolbox	Photoshop and Matlab landmark/fiducial based Registration toolbox	Drop, VRMesh soft-ware	Virtual Grid, Bellevue city, WA	Virtual Grid, Bellevue city, WA	Maxilim software
Drawbacks	- Difficult registra-tion of point match-ing constraints - Produce errone-ous results due to the fewer definable points. - Local discontinu-ities - Require automatic and high-accuracy matching of a large number of land-marks	- Time consuming identification of landmarks. - Less robust under severe geometric distortions or Incomplete match-ing. - Local discontinu-ities - Landmark ex-traction is always prone to error.	- Number of 2D views, angle be-tween views, view angle relative to anatomical objects, co-registration error between views, noise in the images, and image distortion. -Registration ac-curacy is limited to the accuracy of the segmentation step.	-Very sensitive to parameters -poor convergence to boundary concav-ities -Unable to capture object curves in some medical image segmentation - Infinite number of possible non-rigid transformations of the templates - Cannot handle topological changes during model gener-ation or evolution	- Sensitive to miss-ing image data - Limited to image to image registration - Often susceptible to any physical dif-ferences in the imag-es being matched	- Cannot cope with large geometric deforma-tions -Very limited use in time constrained applications such as intra-operative 2D and 3D registration

variance are the different types of function used by the full image content-based registration for the transformation and creation of correspondence between two or more images. Both inter-subject and atlas based registration is performed precisely and with improved visualization of the subject voxel with full image content based registration. The computation cost of full image content-based registration is high in some clinical application such as 3D-3D. Moreover, in time constrained applications such as intra-operative 2D-3D registration this registration technique has not been introduced yet.

After thorough analysis it is not difficult to decide that each type of intrinsic registration is a good example of human's efforts for the accurate registration of medical images. To further refine the vision, researchers and clinicians contributed their massive efforts in developing techniques, which are powerful and applicable for every type of registration problems[52]. Furthermore, the main motive was to ensure accurate registration of medical images along with high level of flexibility, efficiency, reliability and automation. In the preceding sections of this article, the available registrations techniques belong to intrinsic registration are highlighted in extreme. To further refine the idea and increase the strength of understanding, the discussed intrinsic registration techniques are evaluated using the criteria describe in section 2.

A detail analysis of the main features of the intrinsic registrations is presented in table 1. It is obvious from the table that every technique can register medical images effectively using its own mechanism. However, landmark based registration techniques such as anatomical and geometrical landmarks are the most appropriate registration techniques to represent medical images. The superiority of landmark-based registration techniques over its companions is due to a number of its reasons including: (1) less complexity/cost (2) excellent reliability and validity (3) good optimization (4) easy mechanism to detect errors and find out coordinates (5) wide clinical application and software tools availability[53].

After analysis of the facts about the intrinsic registration techniques presented expressively in the above sections, it is found that intrinsic registration techniques can be used to successfully register medical images upto some extent. Each type of discussed registration technique can process medical images using its own mechanism. These registration techniques have majority ratio of similarities and therefore, can be used for any type of medical registration problems subject to the introduction of sophisticated technology and algorithms in the field[53,54]. The list of similarities among the techniques includes efficiency, reliability, wide spread clinical applications, applicability to mono and multi-modalities open based software tool availability and easy and quick transformation mechanism. The drawbacks related to intrinsic registration such as difficult target localization and intensive computation can be easily eliminated with the development of advanced tools and algorithm.

Tremendous work has been done in recent years in the field of image-guided surgery and its related technologies. All this work leads to the development of sophisticated techniques in medical image registration. The importance of image registration in the field of image-guided surgery is obvious because the precise matching between features in sets of images is the primary goal of successful surgery. Therefore, to achieve such goal, research communities developed a number of techniques in the past several years in medical image registration. It is due to these efforts that clinician and patient now takes lot of benefits in medical diagnoses and surgeries.

CONCLUSION

Intrinsic registration techniques can be used to successfully register medical images upto some extent. Each type of discussed registration technique can process medical images using its own mechanism. These registration techniques have majority ratio of similarities and therefore, can be used for any type of medical registration problems subject to the introduction of sophisticated technology and algorithms in the field. Most of the intrinsic registration techniques provide good performance i.e. efficiency, accuracy and reliability. However, the main factors effecting the performance intrinsic registration is the physical associations between two images, complex optimization procedures, intensive computation, transformation mechanisms (rigid and non-rigid), invasiveness, compatibility issues, missing or partial data and difficult target localization. Therefore, more work is desired from the research community to address these issues.

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CONTRIBUTORS

FA conceived the idea and drafted the manuscript. SUR drafted and critically revised the manuscript. All authors contributed significantly to the submitted manuscript.