AN INVESTIGATION TOWARDS ISSUES AND CHALLENGES IN MEDICAL IMAGE REGISTRATION

Fakhre Alam[1], Sami Ur Rahman[2], Muhammad Hassan[3], Adnan Khalil[4]

[1-4] Department of Computer Science & IT, University of Malakand, Dir (L), Khyber Pakhtunkhwa - Pakistan.
Address for Correspondence:
Fakhre Alam
Department of Computer Science & IT, University of Malakand, Dir (L), Khyber Pakhtunkhwa - Pakistan.
Email: fakhre.uom@gmail.com
Date Received:
December 19, 2016
Date Revised:
May 25, 2017
Date Accepted:
June 05, 2017

ABSTRACT

The continuous development and innovation in medical imaging techniques provide clinicians new ways for improved health care services. Despite improvement in health care services, several issues and challenges in medical image analysis are still present. Image registration is one of the most important tasks in medical image analysis and is the most critical step in several clinical applications. In this paper, medical image registration, which effectively integrate complementary and valuable information from multiple imaging resources and represent them in a single more informative image, is introduced. This paper covers the most prominent state-of-the-art issues and challenges in medical image registration and suggests some possible solutions. Moreover, the factors affecting the accuracy, reliability and efficiency of registration techniques are presented. An improved health care service is difficult to achieve until all the issues and challenges in medical image registration are identified and subsequently solved.

Key Words: Medical image registration, Image registration techniques, Computer-assisted surgery

This article may be cited as: **Alam F, Rahman SU, Hassan M, Khalil A. An investigation towards issues and challenges in medical image registration. J Postgrad Med Inst 2017; 31(3): 224-33.**

INTRODUCTION

Over the last few decades, medical imaging techniques has brought several changes in the way patients are treated and operations are performed. The advancement in medical imaging techniques lead to the advancement in computer-assisted surgery (CAS) and radiotherapy. CAS uses medical imaging techniques for diagnosis, treatment planning, disease monitoring, minimally and non-invasive surgeries. The availability of these techniques provides several benefits to the patients such as reduced surgical trauma, fast recovery and reduced hospital stay and cost[1,2]. Nowadays, medical imaging techniques assist clinicians in qualitative diagnosis and resect the tumor based on image information. The availability of precise real time image information during CAS is due to the integration of intra-operative imaging with navigation technology.

Real time visualization of images of interested anatomical regions during the surgical process is an essential requirement for CAS system[3]. The required images of the interested anatomical regions are obtained through high resolution 2D and 3D scans such as X-rays, computed tomography (CT), magnetic resonance imaging (MRI), functional MRI (fMRI), ultrasound (US), positron emission tomography (PET) and serial positron emission tomography (SPECT). Similarly, multiple images are obtained in different time-frames or from different angles of the same subjects. Generally, information in the individual images is not enough for accurate diagnoses and need to be integrated to reveal high information. In medical imaging, information integration from multiple images is performed through the process of registration[4-6]. Surgeons use these integrated information for analysis and visualization in computer-assisted surgery. The process of image registration is performed by geometrically aligning/mapping corresponding points (image pixels or voxels) from two or more images (pre-operative and intraoperative images of a patient). As a result a registered image is obtained which contain more information than single image[7]. Figure 1 shows the mapping of coordinate frames and anatomical structures in one image of the same organ to their corresponding positions in another image of that organ.

Successful CAS greatly depends on the registration of pre-operative images of the patient and intra-operative images of a patient. In CAS, it is not a good practice to rely on a single image obtained in the same time-frames or with a single modality. Therefore, images of the interested regions are taken either at multiple time-frames or with multiple scanners. The obtained images are further aligned with image registration techniques, which improve their quality. These high quality and more informative images help surgeons to accurately locate region of interest while the surgery is in progress.

Inspite of numerous research development and

clinical use, image registration techniques undertaken in CAS still need further improvement. It is therefore necessary to develop more advanced techniques in the area of registration having the capability to accurately and efficiently align medical images. In this regard, researchers and clinical practitioners need to come forward and work on some of the prominent issues and challenges in the area of medical image registration, which are being presented in this survey paper. The objective of this paper is a): to present the background knowledge and techniques about medical image registration. The purpose is to provide an idea to novice researchers in the field. b): to identify and present some of the most important issues and challenges in the field c): to analyze the issues, challenges and present possible solutions and research guidelines.

CORE KNOWLEDGE

In medical imaging, registration is performed by aligning images of the patient with normal subject, or of different patients, or a subject to an atlas. The purpose is to carry out accurate diagnosis and perform successful treatment. Although several types of imaging modalities are now available but each have their own features to extract different types of information from human organs. Modalities, such as MRI and CT are used to obtain anatomical structures while PET and SPECT are used to access functional information[8,9]. The integration of both functional and anatomical information is always required in CAS and greatly helps the surgeon in diagnosis and treatment planning. Multi-modal registration is shown in Figure 2. In the Figure, MR image (a) of human brain is integrated with SPECT (b) image

Figure 1: Mapping of same coordinate frames and anatomical structures in two images of a same orga

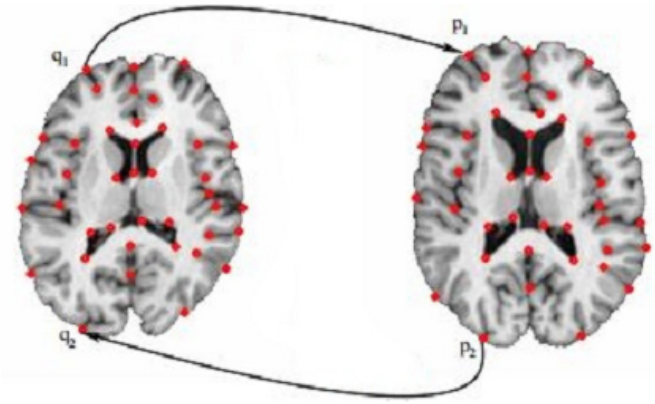
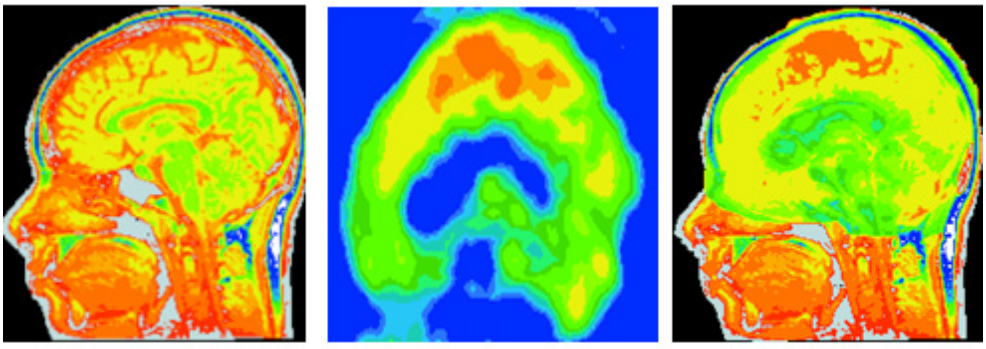
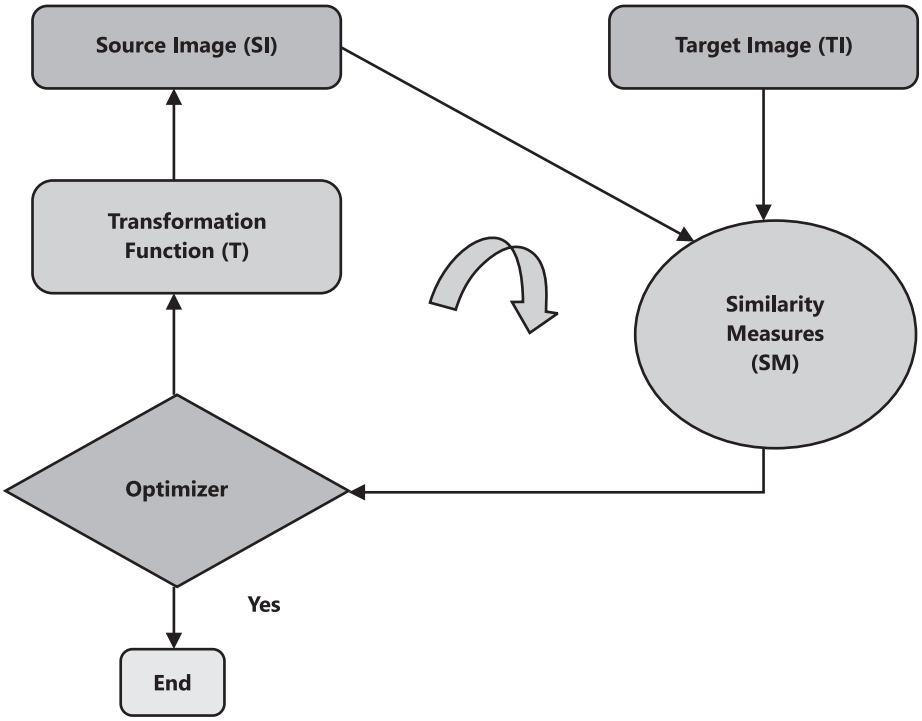


Figure 2: MR and SPECT image registration. In the Figure, human brain images obtained from different modalities are mapped and the resultant registered image is shown which provide more visibility and information of tissues. Anatomical image (a) is obtained with MR scanner while functional image (b) is taken with SPECT. The registered image (c) simultaneously shows functional and anatomical information.



a b c

Figure 3: The process of registration using similarity measure



of the same patient. The registered image (c) provides both anatomical information (obtained through MR) and functional information (obtained through PET). The integration of functional and anatomical information provides useful and accurate clinical diagnosis and surgical procedures. Furthermore, safety of the patient is insured and the quality of treatment is improved.

The main aim of registration is to find the geometrical transformation between separate images and accordingly map them in order to obtain maximum information. Registration is an iterative process, source image is transformed to target image, similarity measures between them is computed and the resultant image is generated if the similarity measures are fulfilled. The process is repeated for the optimization of transformation parameters, if the measure of similarity between source and target image is not perfectly aligned. Registration process can be expressed in the following equation and its graphical representation is shown in figure 3.

$$T' = \arg_T \max SM(T(SI(x,y,z)), TI(x,y,z)) \quad (1)$$

As shown in equation (1) and subsequently in figure 3, the registration is achieved by finding the transformation T/ that optimally aligns a source image SI and target image TI under a similarity measure SM. In the equation, x,y, and z are the coordinates of source and target images where T is image transformation function that maps the source image features into the corresponding target image space. In the registration process, the coordinates of source image is transformed to the corresponding coordinates of target image iteratively. At each iteration, the optimizer check maximum similarity measure and if it is not achieved, the process is repeated. This process is continued until the transformation function optimally aligns source image features into their corresponding target image space. Let "s" be the moving source image and "t" be the fixed target image, and let "T" and "g" be the special transformation and intensity mapping function, then the mapping between two images can be expressed as:

$$t(x',y') = g(T(s(x, y))) \quad (2)$$

Where x/ and y/ denote the coordinates of target image t while x and y denotes the coordinates of source image s. In case of 3D images, the coordinates are x/, y/,,z/ and x, y, z for source and target image respectively and the mapping can be expressed as:

$$t(x',y',z') = g(T(s(x, y, z))) \quad (3)$$

TECHNIQUES

The existing image registration techniques are categorized into feature-based, intensity-based and segmentation-based, the detail is given in the sub-sections below.

2.1 Registration techniques based on image features:

Landmark points, lines, edges and curve are image features which its behavior. Image features are extract-

ed from raw pixel values in the image because they are more robust and easily processed than raw pixel values[10]. Different types of cues such as color, shapes and texture are used to represent image features. Images contains local and global features in which the earlier covers a large portion of the image while the later one focuses on the specific portion. Local and global features are extracted with different types of techniques for the analysis and registration of medical images.

Feature-based techniques are fundamentally used in medical image registration. In these techniques, the corresponding features (points, landmarks) in source and target images are specially matched and accurately transformed. In feature-based registration, corresponding landmarks and features are transformed on the bases of similarity measures. Similarity measures define how well two images are registered[11] and the actual comparison is performed on datasets through iterative transformation. Feature-based registration approaches are computationally efficient because transformation is based on the analytical values of geometric points landmarks. Furthermore, these approaches also show high robustness to illumination changes and are better suited for large displacements. However, the extraction and matching of corresponding features in the preprocessing step and the manual and semi automatic specification of landmarks made these approaches less accurate. Images with large homogenous areas and appearance variations are mostly registered with feature-based techniques.

2.2 Registration techniques based on image intensity:

Intensity-based registration techniques are now a day widely used in CAS and radiotherapy. In these techniques, image intensity i.e. scalar values in the image pixels or voxels is considered for registration. Registration techniques based on image intensity directly operate on image pixel or voxel values (image gray values) without considering sparse feature landmarks[12]. Within certain space of transformation, these techniques search for maximum similarity measures between the source and target images. Intensity based registration uses parameters such as mutual information (MI), Normalized mutual information (NMI), normalized correlation (NC), mean squared difference (MSD) and sum of square differences (SSD) for similarity measures. These statistical parameters play an important role in intensity-based image registration by maximizing intensity similarity measures and by reducing cost function.

Intensity based registration methods operate on image intensity values and the transformation is performed iteratively. At each iteration, the similarity measures between voxel intensities of source and target images are optimized. This iterative transformation of image intensity values involve interpolation between sample points and map both the position and related intensity value at that particular position[13]. In feature-based methods, the delineation of feature landmarks is important for accurate registration which some time affect the accuracy of registration. On the other hand, intensity-based registration methods provide high accuracy by taking into account more image information.

Performing retrospective registration with intensity-based methods need minimum amount of preprocessing or user interaction[14]. As a result, the automation of these methods are easy when compared to point-based or surface-based registration algorithms. However, the lack of human supervision in intensity-based methods may also produce inaccurate registration results. Registration of single and multi-modal medical images, registration of same or different dimensional images (2D-2D, 2D-3D, 3D-3D) and registration of rigid and deformable models are the widely used application areas where intensity-based registration methods are successfully applied.

2.3 Registration techniques based on image segmentation:

Image segmentation is a fundamental task in medical image processing for the delineation of anatomical structures and other regions of interest. In image segmentation, the demarcation is performed on the bases of voxels of the same anatomical structures[15]. Segmentation is achieved by identifying boundaries of the structure or by categorizing every voxel based on its intensity properties. In medical image analysis, segmentation is used for the localization of pathology, quantification of tissue volumes, study of anatomical structure, computer-aided diagnosis and treatment planning, and computer-integrated surgery[16].

Registration methods based on image segmentation are widely used in CAS for the accurate mapping of different types of images into a single more informative image. In these methods, the anatomical structures and other regions of interest in the input images are segmented before actual transformation[17]. Segmentation is performed on the basis of corresponding landmarks in the input images. Transformation function is repeatedly applied on the input images till the alignment of corresponding landmarks. Segmentation-based registration techniques are more successful than feature-based and intensity-based registration techniques when the medical images contain low or missing information about human anatomy. However, the continuous splitting in input images sometimes compromise accuracy.

Rigid models and deformable models are the two popular techniques for the implementation of segmentation-based registration. Segmentation-based registration using rigid models are simple and are widely

used techniques in clinics. Deformable models, on the other hand, are complex but are successfully used for the organs with large deformation. Furthermore, rigid models only translate and rotate the objects of interest in the source and target images while deformable models provide many degrees of freedom (translation, rotation, scaling and shear) to the objects of interest. Segmentation-based registration techniques using rigid models extract surfaces from input images while in deformable models, the surfaces of source image are segmented and are elastically deformed to fit the target image[18].

ISSUES AND CHALLENGES

The development of highly sophisticated data scanning devices and advancement in imaging techniques raises more challenges in the area of medical image registration. The main challenge is the development of more accurate and efficient registration techniques in a clinically acceptable time-frames. This section investigates issues and challenges in medical image registration and presents different solutions provided by researchers to handle these issues. However, in order to be an effective instrument for the clinical practice, registration algorithms must be computationally efficient, accurate and most importantly robust to the multiple biases affecting medical images.

3.1 Efficiency, accuracy and robustness:

Computational efficiency (performance) , accuracy in the alignments of images and robustness against multiple biases affecting medical images are the three main issues in non-rigid registration[19]. The performance of registration method is an important parameter in computer-assisted surgery (CAS) because timely respond with accurate alignment is always desired. The natural behavior of medical images is not consistent due to the effect of noise, blurr and organ movement. Therefore, highly robust and consistent registration is required to manage small amount of variations in the source and target images during CAS. Similarly, without high accuracy in medical image registration method, it is not possible to obtain successful results[17]. Accuracy is always affected by the introduction of errors (either actual or timely) in the medical images during the registration process. Similarly, robustness is greatly affected by the variation of intensity and missing of required data in the input images[19].

The performance, robustness and accuracy in medical image registration methods depends on several parameters including modality, effects on image contents, similarity measures, transformation, optimization and implementation mechanisms[20]. These complex parameters are interdependent and it is difficult to assess the effect of each one on the registration method. However, the initial assessments up-to some level about the influences of these parameters is important prior to registration.

3.2 Similarity measures:

Similarity measures are statistical concepts used for the correct alignment of source and target images during registration. These measures determine registration level of images through a given location. Similarity measures between source and target images are estimated on the bases of image intensities or features. Mutual information, correlation and joint entropy are the commonly used techniques for the implementation of similarity measures.

Mutual information (MI) is an intensity-based similarity measure, which automatically estimates the similarity in multi-modal images[21]. However, in high volume multi-modal images the corresponding points greatly varies which results the differences in intensities. These differences require the estimation of joint histogram, which alternatively increases the computation time of registration. Moreover, in the registration of multimodal images, local intensity variations also degrade the performance of mutual information because the joint histogram computation is adversely affected. Another issue related to estimation of similarity measure in multimodal image registration is the exclusion of spatial and geometrical information about the voxel. Like that of intensity information, the estimation of spatial and geometrical information are also important because they may provide additional cues about the optimal registration.

Correlation coefficient is another similarity measure for medical image registration. It symmetrically measures the linear dependence between the image intensities of corresponding voxels in both images. Correlation coefficient accurately and efficiently evaluates the accuracy of mono-modal medical image registration. For the registration of multi-modal images, however, correlation coefficient is not a favorable similarity measure because of poor statistical and computational efficiency[22]. Registration of medical images with correlation coefficient as similarity metric provides several advantages including easy implementation, no need to estimate probability densities at every iteration, insensitivity to geometric distortion, intensity inhomogeneity and data missing. On the other hand, correlation coefficient is greatly affected by the outliers, which consequently degrade registration performance. Moreover, local extrema and large errors in registration also affect the performance of correlation coefficient. In order to avoid such problems in registration, appropriate techniques are required for sampling and visual inspection.

Combining medical images with mis-aligned structure results an image with duplicated information. The

basic purpose of registration is to reduce the duplicated information and make it more simple and informative. Registration uses several types of matrices for information measure in multiple images. Joint entropy is commonly used information measure in digital image processing[23]. The measurement of uncertainty in both joint distribution and conditional distribution of a pair of random variables is performed with joint entropy. The relative transformation of source image to target image is always occurred when the joint entropy is minimum[24]. During transformation, the volume of overlap between source image and target image also changes as they are transformed relative to one another. The relative transformation and volume overlap greatly affects the reliability of alignment and registration. However, the solution for this problem is already done by Collignon et al[25] and Wells et al[26] using mutual information (MI) as registration metric.

In entropy-based image registration, only pixel intensity values are used for alignment and image histograms are used for computation[27]. The use of pixel intensity values only as alignment measure neglect the spatial information in the images which may affect alignment accuracy. Similarly, entropy-based measures are more complicated than simpler measures and are therefore computationally expensive than simpler one.

3.3 Registration of multimodal medical Images:

Each modality exhibit different characteristics i.e. CT and MRI are used for structural imaging while PET and fMRI for functional imaging. Proper alignment of diverse features (functional and anatomical contents) in multiple input images is important for successful registration. However, such alignment is still an issue because images obtained from multiple modalities differ in spatial resolution. In multi-modal medical image registration, the association between intensity values of related pixels is also complex and unknown. The missing of features in one image and presence in another image, mapping of single intensity value in one image to multiple values in another image are the challenging issues in multi-modal image registration[28]. These issues greatly affect the proper computation of similarity measures based on their intensity values in medical image registration[29].

3.4 Detection of reliable landmarks

The reliable identification of anatomical landmarks in mutli-modal (CT, MR, PET etc) 3D images are essential and one of the important first step in medical image registration. Landmarks are detected either with manual method or with automatic method[30]. The manual method for the identification of landmarks requires medical expertise and takes more time. The available automatic methods for landmarks identification are fast and could reliably detect landmarks in medical images. The automatic methods for landmarks selection are mostly depending on machine learning approaches. Therefore, quality of training data sets plays an important role in the reliable identification of anatomical landmarks. In computer vision, it is easy to obtain large training data sets but in medical field creating a large database of images are challenging and requires a lot of efforts and time.

3.5 Outliers rejection:

The basic aim of medical image registration is to find the optimal transformation between two images by maximizing similarity measures such as mutual information (MI), entropy and correlation-coefficient. However, mutual information is always affected by the presence of outliers (objects in one image but not in another) in source and target images. In medical image registration, the presence of unpredictable outliers in pre-operative and inter-operative images greatly affects mutual information[31]. Therefore, several approaches have been used for the rejection of outliers in medical image registration. The most prominent among them include consistency test[32], intensity transformation[33], gradient-based asymmetric multifeature MI[34], graph-based multifeature MI[35], joint saliency map (JSM)[31] and normalized gradients[36].The rejection of outliers is a challenging task in medical image registration because a large number of outliers are present in the image guided surgery applications. Therefore, more efforts are required to improve the robustness of available similarity measures towards outliers.

3.6 Convergence of optimization methods to local maxima:

In medical image registration, optimization method plays an important role in the proper extraction of landmarks and searching of other similarity measures i.e. mutual information in sub-images. However, optimization method compromise registration accuracy in the presence of local maxima of similarity measure. Similarly, in elastic transformation, the inaccurate extracted landmarks also produce registration error in the presence of local maxima[37]. In this regard, several optimization methods have been developed for medical image registration to avoid local maxima and improve similarity measures such as mutual information and cross correlation. However, further investigation is needed to develop advanced optimization methods for medical image registration.

3.7 Guidance to clinicians:

In computer-assisted surgery and radiotherapy, clinicians face several problems while taking pre-operative and intra- operative measures. The main problem is the accurate mapping of contrast information in

multi-modal images i.e. organ scanned multiple times with different scanners. In such type of scenario, it is difficult for the clinicians to know exactly the location and orientation of patient with respect to different imaging systems. Image registration and fusion in treatment room provides more guidance and help to the clinicians while operating on patient data. With image to patient registration, data is associated precisely and the treatment is given to the patient according to pre-operative plan[13].

In surgical guidance system, registration techniques processes information obtained from physical devices. Information is processed with an algorithmic procedure for optimal transformation images. Most of the transformation is optimal due to the advancement in medical image registration techniques but it is not ideal. As a result, the chances of error called target registration error (TRE) is high. Similarly, the role of image registration is also highly important when the surgical guidance is based on pre-operative images. Here, accurate registration is required for the surgical guidance system. Inaccuracy in the surgical guidance system will be useless and dangerous to the patient life. In typical computer-assisted surgery (CAS), the anatomy of the patient captured in the pre-operative image remains rigid from image acquisition to surgical procedure. Non-rigid registration, which is successfully used for image-to-image registration need further research and improvement in image-to-patient registration[38]. For accurate registration and transformation of corresponding points from image to patient, further improvement is required in surgical guidance system especially in case of non-rigid registration.

3.8 Relating contrasting information:

Relating contrasting information in different types of medical images is a challenging task in multimodal image registration. In CAS, the patient's organ is scanned multiple times with different types of imaging modalities which create difficulties for the identification/ fixation of patient location and orientation with respect to different imaging systems. Therefore, it is necessary to developed more advanced registration techniques which can easily remove the differences in patient positioning and relate information from different types of images.

3.9 Parameters determination and their correspondence:

Parameters such as points, landmarks and curves are the components of an image and their proper determination and mapping are essential for accurate registration. Image registration algorithms determine the corresponding parameters in both source image and target images and aligned them properly[39]. The correspondence between two images is either functional or structural. The former relates the equivalent anatomical structures in the two images while the later line up the same functional regions. Image registration algorithms, which determine high number of corresponding parameters are more flexible. However, the efficiency of such algorithms is slow and requires more computation time. Rigid and affine registration algorithms are computationally efficient because the take less parameters for correspondence. On the other hand, non-rigid registration algorithms are mostly slow because they determine a large number of parameters by matching voxel intensities in images. Moreover, the transformation in non-rigid registration algorithms is asymmetric and there is no guarantee of mapping each landmark/ point in the source image to its corresponding position in the target image.

3.10 Automatic image registration:

Automatic registration in medical images aligns the common detected features in pre-operative and intra-operative images without user interaction. Automatic registration techniques are widely used in medical image processing and several types of image-guided surgeries are successfully performed with automatic medical image registration techniques. The performance of automatic image registration is high because it requires less time and minimum efforts from the user while aligning the subject images. Moreover, the point/ landmarks in automatic registration method transform globally and with high efficiency[17]. The accuracy of automatic image registration methods is also high but greatly depends on the precision and optimization of algorithms. Automatic image registration is still an open problem in medical imaging and some of the challenges include the proper selection of 3D landmarks, extraction of same features in multi-modal images, variable/limited anatomical coverage and low contrast to noise.

ANALYSIS AND DISCUSSION

Medical image registration is a mature field that has been extensively studied. A lot of research work has been done for its improvement in computer-assisted surgery and radiotherapy. In this review paper, we have made an effort to provide a comprehensive knowledge on medical image registration. The existing issues and challenges in the field are investigated in extreme and research guidelines are presented. To our knowledge, the issues and challenges in medical image registration have not been investigated comprehensively in previous reviews. Moreover, our approach was based on three core aspects: 1) Describing background knowledge and techniques used for medical image registration, 2) presentation of main issues and challenges and their possible solutions in medical image registration and 3) description of guidelines that would be helpful for the development of new advanced registration techniques.

The adaptability and inclusion of these guidelines can be helpful in developing better registration techniques that will perform better in mitigating issues such as accuracy, computational efficiency, reliability and robustness. These guidelines include:

- One of the most important questions concerning medical image registration is its use in real clinical settings. Clinical data is always affected by intensity consistencies such as noise, motion and intensity in-homogeneity. The currently available registration algorithms provide limited capability to efficiently and accurately cope with these issues in real clinical setting. In order to increase the use of registration in clinical practice and make it an effective instrument for the above issues, accurate, robust and computationally efficient algorithms are desired.
- In medical images, landmarks provide anatomy specific constraints and
- Guide the deformation process in regions with uneven information. However, the detection and extraction of significant landmarks to perform an accurate registration remains a very challenging task.
- In multimodal registration, features in the same images obtained from different scanning device are aligned. Due to different scanning devices, images of the same subject show different feature characteristic i.e. functional and anatomical. Therefore, accurate correspondence of features between source and target images in multimodal registration remains a challenge in computer-assisted surgery. Although, several types of image registration methods based on mutual information are available which create statistical relationship among the features in source and target images. Although, mutual information is a standard similarity measure for multimodal image registration but its performance degrades when the images contains local intensity variations. Moreover, mutual information only considers intensity information in the images and ignores spatial information. Therefore, the development of advance techniques in which mutual information can easily cope with local intensity variations and fully consider spatial information along with intensity information will bring a great change in multimodal medical image registration.
- Correlation coefficient is another similarity measure which accurately and efficiently evaluates the accuracy of mono-modal medical image registration. However, in multi-modal registration, the performance of correlation coefficient is greatly affected by the outliers, local extrema and large errors. In order to avoid such problems in multi-modal registration, appropriate techniques are required for sampling and visual inspection.
- Joint entropy is another similarity measure which estimates the amount of information in the two or more combined images. However, image registration based on joint entropy are complicated, computationally expensive and consider only pixel intensity values in the images. Considering only pixel intensity values and neglecting spatial information in images greatly affect the alignment accuracy. Therefore, more research is needed in the area of image registration with joint entropy to overcome the above issues.
- The alignment of functional images of low quality and the determination of functional abnormality is often a difficult task in medical image registration. Therefore, resolution of functional images and the accuracy of functional analysis techniques need further improvement.
- In medical image registration, the identification of reliable landmarks is performed with either manual or automatic method. The former requires medical expertise and takes more time while the latter is fast but depends on machine learning approaches. In other words, automatic methods depends on the quality of training data sets which are easily obtained in computer vision but requires more efforts and time in medical field. Therefore, the development and availability of large databases of images in the medical field will easily solve reliable landmarks identification problem in automatic methods.
- In medical image registration, optimal transformation is performed by maximizing mutual information in the source and target images. In case of pre-operative and intra-operative images, mutual information is greatly affected by the presence unpredictable outliers. Although, several types of approaches have been developed for the rejection of outliers but it is still a challenging issue in computer-assisted surgery. The development of new techniques for the minimization of large number of outliers in CAS will reduce their effect on MI.
- Most of the optimization methods in medical image registration converge to local maxima which is not desired. Further research is needed for the development of advanced optimization methods for medical image registration, which can easily avoid local maxima.

- In surgical guidance system, transformation of corresponding points is usually optimal but not ideal. However, ideal transformation (i.e. maps every point in the image space onto its correct counterpart in physical space and vice versa) is only possible if the target registration error (TRE) is very low. Therefore, further research is required to minimize the chances of TRE in image to physical space registration.
- In computer-assisted surgery, it is difficult to relate contrasting information in multi-modal images due to differences in images and patient positioning. The main reason is the identification/ fixation of patient location and orientation with respect to different imaging systems. Therefore, it is necessary to developed more advanced registration techniques, which can easily remove the differences in patient positioning and relate information from different types of images.
- Parameters determination and their correspondence in non-rigid registration is not computationally efficient as compared to rigid registration. The efficiency in non-rigid registration is affected by the identification of large number of parameters and asymmetric transformation. The computationally efficiency in non-rigid registration can be improved by using symmetric algorithms for transformation and the introduction of techniques which uses minimum number of parameters for correspondence.
- Despite the wide spread use, accuracy and performance, automatic image registration methods is still an open problem. Some of the challenges in automatic image registration include the proper selection of 3D landmarks, extraction of same features in multi-modal images, variable/ limited anatomical coverage and low contrast to noise. Moreover, the accuracy of automatic image registration methods also depends on the precision and optimization of algorithms. The investigation of new optimization algorithms for automatic image registration, as well as the development of advanced schemes for 3D landmark selection, feature extraction, anatomical coverage and contrast to noise will improve the performance of automatic image registration.

CONCLUSION

In the few decades, tremendous development and exploration have been done in medical image registration. Medical image registration have been used, among the many available solutions, for patient diagnosis and care treatment by providing more facilities to the clinicians. In this regard, a lot of efforts have been made for the development of advanced techniques in medical image registration. Nevertheless, clinicians face several prominent issues and challenges in the operating rooms. Although, researchers from the medical imaging community have been working to cope with these issues and have devised solutions that have mostly resolved these issues, however we need much to do in order to get to more advanced techniques and achieve the desired goal. We suggest future directions for developers in the area toward more robust and accurate registration algorithms for clinical applications.

REFERENCES

1. Cleary K, Peters TM. Image-guided interventions: technology review and clinical applications. Annu rev biomed eng 2010; 12:119-42.
2. Lindseth F, Lango T, Selbekk T, Hansen R, Reinertsen I, Askeland C et al. Ultrasound-based guidance and therapy, advancements and breakthroughs in ultrasound imaging 2013; 28-82.
3. Castro-Pareja CR. Real-time 3D elastic image registration. The Ohio State University, (2004).
4. Alam F, Rahman SU, Khalil A, Khusro S, Sajjad M. Deformable registration methods for medical images: a review based on performance comparison. Proceedings of the Pakistan Academy of Sciences. A Physic Comput Sci 2016;53:111-30.
5. Alam F, Rahman SU, Khalil A, Ullah S, Khusro S. Quantitative evaluation of intrinsic registration methods for medical images. Sindh Univ Res J 2017;491:43-8.
6. Alam F, Rahman SU, Ullah S, Khalil A, Uddin A. A review on extrinsic registration methods for medical images. Tech J Univ Engineering Technol Taxila 2016;21:110- 9.
7. Bali RK. Clinical knowledge management: opportunities and challenges: Idea Group Pub 2005.
8. Alam F, Rahman SU, Khusro S, Ullah S, Khalil A. Evaluation of medical image registration techniques based on nature and domain of the transformation. J Med Imag Rad Sci 2016; 47:178-93.
9. Dogra A, Patterh MS. CT and MRI brain images registration for clinical applications. J Cancer Sci Ther 2014; 6:18-26.
10. Deng H. Image feature detection and matching for biological object recognition: Oregon State Univ 2007:1-137.
11. Feng DD. Biomedical information technology. California: Elsevier Science; 2011.
12. Chou YY. Transitive and symmetric nonrigid image registration. Citeseer; 2004.

13. Hajnal JV, Hill DLG, Hawkes DJ. Medical image registration: CRC Press; 2001.

14. Beutel J. Handbook of medical imaging. Medical image processing and analysis. Soci Photo Optical; 2000.

15. Xie Z, Tamez-Pena J, Gieseg M, Liachenko S, Dhamija S, Chiao P. Segmentation by surface-to-image registration. Med Imag 2006; 6144:614405-7.

16. Guo Y. Medical image registration and application to atlas-based segmentation. Kent State Uni 2007.

17. Alam F, Rahman SU. Intrinsic registration techniques for medical images: a state-of-the-art review. J Postgrad Med Inst 2016; 30:119-32.

18. Mani VRS, Rivazhagan DS. Survey of medical image registration. J Biomed Eng Technol 2013; 1:8-25.

19. Liu Y. On the real-time performance, robustness and accuracy of medical image non-rigid registration. Coll William Amp. Mary 2011:316.

20. Neri E, Caramella D, Bartolozzi C. Image processing in radiology: Current Applications. Springer 2008.

21. Keyvanpour MR, Alehojat S. Analytical comparison of learning based methods to increase the accuracy and robustness of registration algorithms in medical imaging. Int J Adv Sci Technol 2012; 41:63-9.

22. Kim J. Intensity based image registration using robust similarity measure and constrained optimization: applications for radiation therapy. Uni Michigan Citeseer 2004:1-77.

23. Bankman I. Handbook of medical imaging processing and analysis. Elsev Sci; 2000.

24. Bailey DL, Townsend DW, Valk PE, Maisey MN. Positron emission tomography: basic sciences. Secaucus NJ: Springer-Verlag; 2005.

25. Collignon A, Maes F, Delaere D, Vandermeulen D, Suetens P, Marchal G. Automated multi-modality image registration based on information theory. Inf process med imag 1995:263-74.

26. Wells WM, Viola P, Atsumi H, Nakajima S, Kikinis R. Multi-modal volume registration by maximization of mutual information. Med image anal 1996; 1:35-51.

27. Sabuncu MR. Entropy-based image registration. Citeseer; 2006.

28. Kim YS, Lee JH, Ra JB. Multi-sensor image registration based on intensity and edge orientation information. Patt recog 2008; 41:3356-65.

29. Liu X, Lei Z, Yu Q, Zhang X, Shang Y, Hou W. Multi-modal image matching based on local frequency information. J Advan Signal Proc 2013;2013:1-11.

30. Riegler G, Urschler M, Ruther M, Bischof H, Stern D. Anatomical landmark detection in medical applications driven by synthetic data. Int Conf Comput Vis Workshop 2015:85-9.

31. Qin B, Gu Z, Sun X, Lv Y. Registration of images with outliers using joint saliency map. Signal proc letters 2010; 17:91-4.

32. Auer M, Regitnig P, Holzapfel GA. An automatic nonrigid registration for stained histological sections. Transac Image Proc 2005; 14:475-86.

33. Likar B, Pernuš F. A hierarchical approach to elastic registration based on mutual information. Image vis comput 2001;19:33-44.

34. Tomazevic D, Likar B, Pernus F. 3-D/2-D registration by integrating 2-D information in 3-D. Trans Med imaging 2006; 25:17-27.

35. Staring M, Van Der Heide UA, Klein S, Viergever MA, Pluim JP. Registration of cervical MRI using multifeature mutual information. Trans Med Imaging 2009; 28:1412-21.

36. Pszczolkowski S, Zafeiriou S, Ledig C, Rueckert D. A robust similarity measure for nonrigid image registration with outliers. 11th Int Sympos Biomed Imag 2014:568-71

37. Yang X, Pei J. Elastic image registration using attractive and repulsive particle swarm optimization. Springer-Verlag 2006; 4247:782-9.

38. Fitzpatrick JM. The role of registration in accurate surgical guidance. Proc Inst Mech Eng 2010; 224: 607-22.

39. Crum WR, Hartkens T, Hill D. Non-rigid image registration: theory and practice. Br J Radiol 2014; 77:S140-53.