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MEDICAL IMAGE REGISTRATION: CLASSIFICATION, APPLICATIONS AND ISSUES

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ABSTRACT

The objective of this paper is to provide a detailed overview on the classification and applications of medical image registration. Issues in medical image registration are also presented along with their promising solutions and research guidelines. In this review, general concepts, classification, applications and issues in medical image registration is presented and analyzed in a comprehensive manner. The methods used for analysis is unique from already published work because we have performed detailed investigation on the classification, applications and issues in medical image registration. The knowledge on the work that has been developed in the area is presented in a compact and systematic form. This work provides contribution to field of medical image registration by providing a useful platform for both researchers and clinicians in the field.

Key Words: Medical image processing, Medical image registration, Registration techniques

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INTRODUCTION

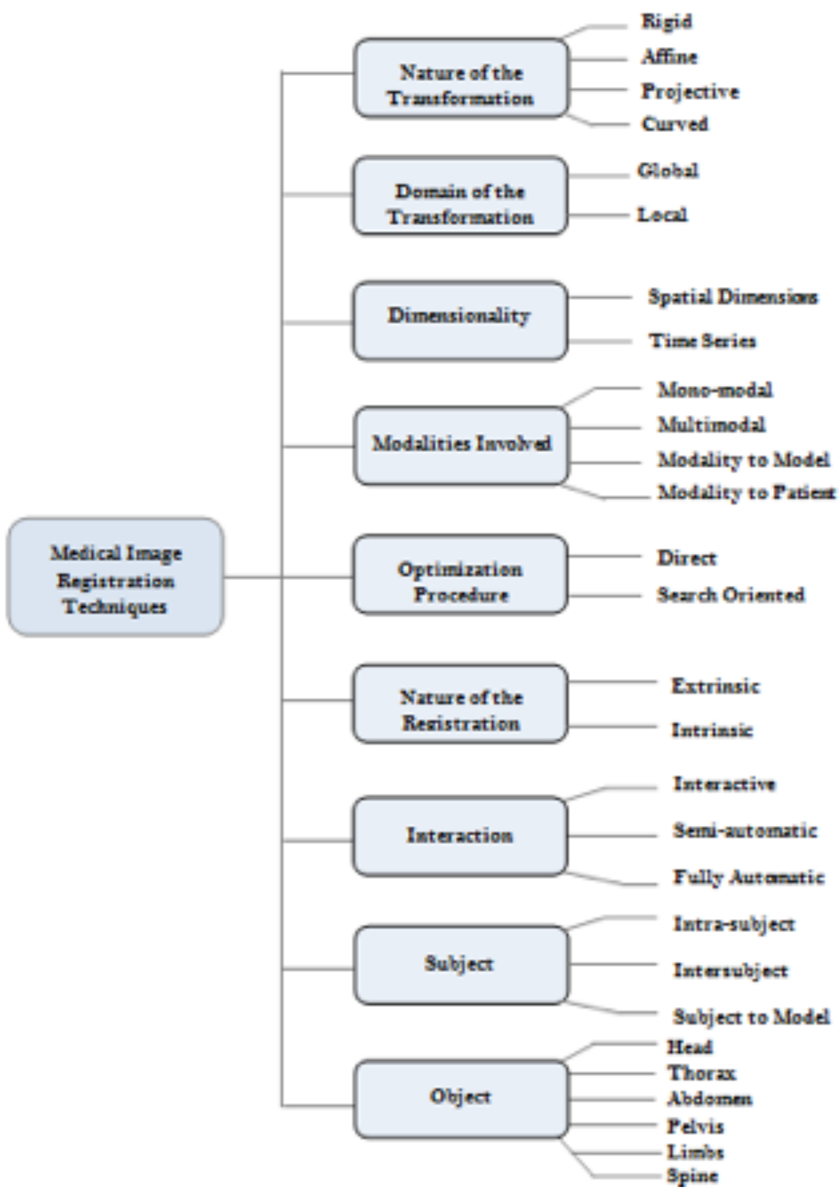
Medical image registration (MIR) is a fundamental processing step in medical image processing. It is the process of aligning two or more input images into a single image which provide more information. Registration process involves the estimation of optimal transformation that best aligns the objects of interest in the input images[1]. In registration, one image (source image) is specially modified (translated, rotated, scaled, and deformed) relative to another fixed image (target image)[2]. MIR provides an environment for the new research in the field of medical image processing due to which the proper detection and diagnosis of tumor in the organ is now possible. Registration of medical images obtained with the same modality in different time-frames is usually required because of possible movements of the object (motion of a patient; changes in the positioning of the patient; cardiac or involuntary motion; growth of a structure; and soft tissue displacements due to breathing)[2,3]. Similarly, registration of medical images that have been obtained from different modalities may be extremely useful and is essential because one and the same structure of the imaged object is represented differently in such images[4].

Information in a single image (obtained from a single modality, at different time-frames and from different angles) is not sufficient for proper diagnosis and surgical planning and need to be integrated to provide more information. Although, recently developed multi-modality devices such as CT-PET and CT-SPECT provide structural and functional information in a single examination. However, these devices cannot perform accurate quantitative comparison and integration of structural and functional information for the diagnosis and patient treatment. Information integration from multiple image datasets obtained through different types of modalities, at diverse times frames and angles create significant challenges[5]. MIR techniques are classified into nine basic criteria formulated by Antoine et al[6]. The nine criteria are: nature and domain of the transformation, dimensionality, modalities involved, optimization procedure, nature of registration basis, interaction, subject and object. Image-guided surgery (IGS), radiotherapy and cancer detection are the popular areas where MIR is widely used.

One of the many issues in current MIR is the unavailability of highly precise, computationally efficient, clinically acceptable and robust registration techniques. Although, the available registration methods provide useful information from separate images, but often the accuracy and efficiency are compromised. An important aspect of MIR in the clinical practice is its computationally efficiency, registration accuracy and robustness to the several types of other biases affecting medical images. Some others open issues includes automatic image registration, detection of reliable landmarks, registration of multimodal images and rejection of outliers in medical images[7].

The purpose of this paper is to present a comprehensive review on MIR in terms of current work and future direction. This paper provides the fundamental knowledge on registration in the domain of medical image analysis. Furthermore, a comprehensive knowledge on the application areas and the current issues in MIR are also highlighted in extreme. The paper also suggests several possible solutions and research guidelines for resolving some of the issues such as computational efficiency, accuracy and robustness. To our knowledge, the registration techniques along with application areas and prominent issues 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 MIR, 2) the use of image registration in different medical fields and 3) the description of issues along with future 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 techniques for the performance improvement of MIR.

Figure 1: The Classification of Medical Image Registration (MIR) Techniques



CLASSIFICATION

Registration techniques are categorized into nine basic methods, each method is further subdivided into one or two levels, as shown in Figure 1.

1. Nature of the Transformation Based Image Registration:

In the nature of transformation based registration, the interested points obtained from source image (moving image) are mapped into target image (template/fixed image) with various transformation methods i.e. rigid and non-rigid. Registration is mostly done on a global basis (mapping similar objects in moving image and fixed image with global geometric transformation)[8]. Nature of the transformation based image registration methods provides accuracy and robustness in the presence of outliers and other artifacts in the input images. Moreover, images from multi modalities are easily aligned with help of these techniques. The mapping of input images is performed through the transformation parameters in this type of registration[9,10]. Rigid transformation is performed with the translation and rotation of moving image (source image) according to the coordinates of fixed image (target image). In rigid transformation, the shape of input images remains the same. Moreover, angles and distances among points also remain unchanged. Affine, projective and curved[11,12] are another types of MIR techniques which involve more transformation parameters. In affine transformation, scaling, shearing, translation and rotation are performed. In projective transformation, registration is performed on geometric objects. Curved transformation is also called elastic transformation and is used in deformable registration.

2. Domain of the Transformation Based Registration:

In domain of the transformation based method, registration is performed by performing transformation on image domain[13,14]. Transformation is either performed on the entire image or its subparts. Domain of the transformation based image registration plays a crucial role in extracting significant features from images. Domain of the transformation based techniques also remove blurring and add sharpness to the input images. Information obtained from image pixels in one domain are directly transformed to another domain in this type of registration. The purpose is to obtain more detailed and significant information. Moreover, mean pixel intensities of an entire image or subregion are reformed on the basis of either adjacent pixel values or on the basis of entire image contents. These techniques also manage signal processing operation in the registration process because accurate analysis of signal often becomes crucial while moving pixel values of an image from one domain into other domain. Domain of the transformation techniques are further divided into local registration and global registration.

In local registration, transformations are implemented on the local geometric features of source and target images. All the local features and significant points are locally transformed, which properly changed each level of the deformation field[15]. In global registration, transformations are applied on whole image parameters. In this type of registration, any change in any parameters affects the whole image[16]. Moreover, local transformation in the registration process can also be regard as as global transformation with respect to that particular domain of the image. Global transformation can also be successfully implemented with local transformation parameters in images with local noise and distortions because some of the irregularities are mostly disregarded in the registration process.

3. Registration Based on Dimensionality:

Image dimensions are critical in the registration process because transformation between moving image (source image) and fixed image (target image) is done either on the image coordinate system or between an image and physical space. On the basis of dimensionality, registration techniques are divided into spatial dimensions and registration of time series. In spatial dimensions, the numbers of geometrical dimensions of the image space are estimated. Based on spatial dimensions, registration techniques are further divided into 2D/2D, 2D/3D and 3D/3D[17]. Registration of medical images obtained at different time intervals is used for the examination of disease progress such as tumor growth, bone growth in children and post-operative monitoring of healing. Based on the monitoring results obtained from the registration, a treatment response is suggested. Single and multimodal 2D and 3D images acquired at different time intervals in preoperative and postoperative procedures can improve treatment accuracy and precision.

4. Registration Based on Modalities:

Registration techniques based on modalities align medical images based on different modalities such as monomodal, multimodal, modality-to-model and model-to-modality. Monomodal registration involves the mapping of two or more images obtained from a single modality. On the other hand, multimodal registration involves the mapping of input images acquired from different types of modalities such as PET and CT. Registration based on modality-to-model and model-to-modality involve one image and a model or patient. Intraoperative registration is mostly performed with model-to-modality registration while gathering statistical information from tissue morphology can be done with modality-to-modal based registration.

5. Registration Based on Optimization Procedure:

Registration of medical images is performed iteratively, moving image is transformed according to the coordinates of fixed image, similarity between the two images is estimated and the final registered image is obtained[18]. The registration process is performed repeatedly to optimize transformation parameters till the acquirement of final image. In general, the basic aim of registration is to maximize the similarity or minimize the cost between two same images. In registration, the coordinate transformation that relates the fixed target and moving source image is estimated by iteratively minimizing the cost function[19]. In image registration process, optimization methods estimate and adjust the differences in parameters between source and target images[20]. In the registration process, optimization starts iteratively and continues till the computation of best parameters for alignment. The performance of registration is measured on the accuracy of optimization procedures. The aim of optimization function is to determine the parameters which are most suitable and similar parameters. The obtained parameters are further used to achieve the best image mapping provided by the similarity metric[21]. Several types of rigid and non-rigid registration algorithm use optimization procedures for the best alignment of monomodal and multimodal images. Registration techniques based on optimization is further categorized into parameters computed and parameters search for. Optimization procedures estimate the optimum location provided any possible-starting estimate.

6. Nature of Registration Basis:

Extrinsic and intrinsic are the two popular registration methods on the basis of nature of the registration. The first one involves the foreign objects introduced into the imaged space while the second technique is based on the image information obtained from the patient himself[17,22-24]. In extrinsic registration techniques artificial objects are usually attached to patient's body. These registration methods always remain the best option in IGS and radiation therapy. In the last decade, registration methods based on extrinsic criteria have been extensively studied in IGS and radiation therapy[25,26]. The aim is to acquire more efficiency, accuracy and reliability by analyzing their corresponding features. Registration methods belonging to extrinsic category rely on external objects i.e. artificial markers and frames attached to the patient's body[27,28]. Intrinsic registration techniques are commonly used in medical image processing. It refers to the process of extracting and mapping features and anatomical information from the subject image itself[29]. 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[30].

7. Registration Based on Interaction:

Registration process on medical images may be performed by using three techniques, interactive technique, semi-automatic technique and fully automatic technique. Interactive image registration techniques are required in medical applications where pre-operative image space need to be accurately correlated to a real time physical space. Interactive image registration techniques are also used in some other clinical applications, such as minimally invasive surgeries and image-guided radiotherapy (IGRT)[31]. The procedure of interactive registration is performed in several steps; firstly, preoperative images are obtained by scanner (PET, MRI and CT etc.) and then a surgical region of interest (ROI) is selected based on some expert knowledge. In the next step, interaoperative images are obtained and registered to the preparative image. Using this procedure, the location of the ROI is tracked dynamically. In semiautomatic image registration technique, the user interaction involves the initialization of algorithm or the rejection/acceptance of suggested registration hypotheses. In the initialization, the data is either segmented or the algorithm is steered[6]. Automatic registration of multimodal functional and structural images by semi-automatically selecting region of interest (ROI) is currently an ongoing area of research. In automatic registration, interested and similar regions from pre-operative and intra-operative images are detected without human interaction[7]. Automatic medical image registration techniques are now successfully used in several medical procedures.

8. Registration Based on Subject:

Subject refers to the patients, whose images are to be registered. Techniques based on subject are intra-subject, inter-subject and atlas. These techniques have been the subject of extensive study in the medical imaging literature. Registration of medical images obtained from same patient anatomy is often required for visualization and quantitative analysis. Similarly, medical images obtained from different patients anatomies can be properly aligned only after accurate registration[32]. Registration of atlas images to patient data can also be used for automatic detection of brain anatomy and for lesion localization. Intra-subject registration, on the other hand, involves the mapping of medical images obtained from the same patient[17]. Registration in which medical images are taken from multiple patients is called inter-subject registration. It is mostly used in the estimation of changes occurred in patient's shape and size as well as grosser changes in topology[17]. Patient to atlas registration involves the mapping of medical images obtained from patient anatomy with the images obtained from imaging database of multiple subjects[17].

9. Registration Based on Object:

Registration techniques based on object involve part of the human anatomy. Registration is mostly performed on head, thorax, abdomen, pelvis and spine. Registration process can be applied to images of human head and brain. Commonly used techniques for the registration of human head include mono-modal, multimodal, modality-to-model and modality-to-patient. Registration of thorax images is a more challenging problem than registration of head images because of the complex internal structure of different organs, natural movement and breathing. Similarly, registration of thorax images obtained from different types of scanner i.e. PET and CT is also challenging because of inconsistent body positioning and inadequately controlled motion artifacts due to respiration[33].

APPLICATIONS

The development of advanced techniques in medical-image analysis leads to the easy availability of distinct information of the patient[34]. The clinicians can now easily diagnose and monitor disease development in the body of patient. Registration plays an essential role in medical image analysis, because it helps the clinicians to observe the developing trend of the disease and accordingly make proper measures. Medical image registration (MIR) has many applications both in diagnostics and in therapeutics[35]. Some of the important applications are in radiation therapy, cancer detection, template atlas application and IGS.

1. Radiation Therapy:

The aim of radiation therapy is to treat tumor and other diseases of the body. Radiation therapy/radiotherapy provides clinically useful dose to the target tumor while minimizing dose to the surrounding normal tissues[36]. Diverse advanced MIR methods have been developed for radiotherapy during the last two decades in order to successfully use this technology for better health care. In radiation therapy, registration is used in patient position verification, treatment planning and treatment assessment[37]. Both rigid and deformable registration has been used in the area of radiation therapy. Rigid registration, which involves only translation and rotation of object, has long been used in radiotherapy. For example, in the registration of CT and MR image obtained from patient with no anatomic changes in the body, rigid registration is very effective. In case of anatomic change in the body of patient due to tumor expansion or shrinkage, weight loss and organ shape variation, deformable registration is successfully used in radiotherapy. The major role of deformable registration in radiotherapy includes automatic segmentation, dose accumulation, mathematical modeling and functional imaging.

2. Cancer Detection:

Medical image registration plays a vital role in cancer detection and in the monitoring of cancer therapy[38]. In early cancer detection, registration techniques are used to detect useful information about the tissue under examination[39]. In cancer detection, registration translate the segmented areas of interest from the hematoxylin and eosin (H&E) images to the infrared (IR). This process reduces the segmentation of the stained images. In the early detection of cancer, it is often difficult for the clinicians to properly locate the cancerous tissue. Even the use of structural-information obtained from MR and CT cannot properly help them due to the low contrast between normal tissues and cancerous tissue in MR and CT images. On the other hand, it is possible but difficult to obtain useful information about cancer tissue and its proper location from the images obtained from PET and SPECT scanner. Image registration is further enhanced by image fusion which significantly help radiologist in the detection of cancer at the early stages and improve the accuracy of diagnosis. Registration is effectively used in prostate cancer, liver cancer, breast cancer and head & neck cancer.

3. Template Atlas Application:

The organs of people are usually different in shapes and sizes, therefore, the images obtained from individuals differ significantly. Due to this variability, the representation of medical images in the form of model is always required. Atlases are the commonly used technique for the representation of medical images[40,41]. Through atlas, populations of medical images with parameters that are learned from a training datasets are modeled. A template is a common example of atlas in medical image analysis. Registration play a crucial role in atlas construction because it maps an image to an atlas, which is further, used to address variability in images. Registration is widely used in template-based medical image analysis for the evaluation and interpretation of data in a standard template or reference atlas space. In computational anatomy, inter-subject registration is used for the construction of atlas to statistically model the anatomy of organs across subjects.

4. Image-guided Surgery:

In image-guided surgery (IGS), preoperative images are registered with intraoperative patient data. In the registration process, the mapping of similar anatomical structures in both preoperative and intraoperative image data is performed. It is also required in IGS to conduct a procedure which obtain images of region of interest (ROI) at different-time frames or with multiple scanners. The quality of obtained images from multiple scanners and at different time frames is improved with registration process. These registered images provide accurate information due to which surgeons can precisely locate ROI during the surgical procedure. A lot of work has been done for the use and implementation of registration techniques in IGS. However, further research and development are required due to the importance of registration in image guided surgery.

ISSUES

Recently, advanced data scanning devices and imaging techniques have been developed. These improvements raise more challenges in MIR techniques used in IGS and radiotheraphy. The prominent challenges are the development of computationally efficient and accurate registration techniques in a clinically acceptable time-frame[1]. Moreover, it is also important that the registration techniques must be reliable and robust regarding the multiple biases affecting medical images. Atomicity in the registration techniques is also required for the proper detection of ROIs in medical images. However, automatic detection of ROI is difficult and prone to errors in multimodal registration of complex and high volume functional and structural images i.e. PET-CT. It is due to the different and non-linear nature of images and the unavailability of sufficient features for the registration. Similarly, in automatic registration of ROIs, it is difficult to accurately estimate mutual information in sub-regions due to high sensitivity to noise and the unavailability of sufficient statistical information. Moreover, region of interest (ROI) based registration techniques are mostly affected by complex nature and non-linear relationship between overlapping regions, intensity in-homogeneity, blurred-object-boundaries and the presence of artifacts. ROIs are usually detected and registered either manually or with pre-defined parameters which are both time consuming and slow.

The most important issues in MIR are accuracy, computational efficiency, robustness and reliability[42]. The performance of image registration plays an essential role in the IGS process. In IGS, timely response with accurate alignment is always required. Medical images are always affected by organ movement, noise and blur. In this type of situation, robustness and consistency is required in the registration techniques to handle small amount of change in input images. Similarly, without high accuracy in MIR techniques, it is difficult to obtain successful results[22]. The accuracy of registration technique is mostly affected by the errors occurring in the medical images. These errors are either actual or timely which usually occurs during the process of registration. Similarly, intensity variations and required data missing from input images also affect the robustness of registration[42].

Imaging modalities shows different characteristics, for example, MR and CT scanners are used for structural imaging while fMRI and PET are used for functional imaging. Proper alignment of multiple features obtained from different types of an organ image is essential for successful registration. However, due to the differences in spatial resolution in images obtained from multiple modalities, it is difficult to properly align these features. In multi-modal MIR, the relationship between intensity values of corresponding pixels is also complex. The mapping of single intensity value in one medical image to multiple values in other medical image and the absence of features in one image and presence in another image is another major issue in multi-modal MIR[43]. The aforementioned issues highly affect the accurate estimation of similarity measures based on their intensity values in MIR[44].

The basic aim of the registration process is to estimates the optimal transformation between moving image (source image) and fixed image (target image) by maximizing similarity measures. The popular similarity measures are mutual information (MI), sum of square difference (SSD), peak signal to noise ratio (PSNR) and correlation coefficient. The accuracy of registration method is evaluated on mutual information measure. However, it is mostly affected by the existence of outliers (presence of objects in one image but not in the other image)[45]. In order to eliminate outliers, MIR techniques has been developed. Consistency test[46], gradient-based asymmetric multifeature MI[47]; intensity transformation, joint saliency map (JSM) & normalized gradients[48]; and graph-based multifeature MI[48] are the popular techniques for the rejection of outliers in medical images. Despite the availability of these techniques, further developments are needed to enhance the robustness of available similarity measures towards outliers.

In MIR, optimization method plays a crucial role in the accurate 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. The local maxima of similarity measure also affect registration accuracy in the elastic transformation due to extraction of inaccurate landmarks[49]. In this regard, several optimization methods have been developed for MIR to avoid local maxima and improve similarity measures i.e. MI, SSD, CC and PSNR. However, further research and developments are required for the improvement of optimization techniques in MIR. In multimodal registration, the mapping of contrasting information in functional and structural images is a challenging task. The patient's organ is scanned several times with different scanners in image guided surgery (IGS) for proper diagnosis. Due to movements, it becomes difficult for the surgeon to properly identify/ fixed the location and orientation of a patient with respect to different imaging systems. Therefore, further improvement are required in the registration technique to easily eliminate the differences in patient positioning and map corresponding information from different types of images. Points, curves and landmarks are the components of images and their accurate detection and alignment are important for the proper registration. MIR techniques detect the corresponding parameters obtained from input images and properly aligned them[50]. The association between two images is either structural or functional. In structural association, the equivalent anatomical structures are mapped while in functional association, the same functional regions are aligned. MIR technique is more flexible if it detects maximum number of related parameters. However, sometimes the computationally efficiency is compromised in the detection of high number of parameters. Rigid and affine methods use minimum number of parameters for correspondence and are therefore computationally efficient. Non-rigid registration techniques, on the other hand, use maximum parameters for correspondence and are therefore slow in computation. Furthermore, the transformation mechanism in non-rigid registration is asymmetric and the mapping of each landmark/point in one image to its corresponding position in the other image is difficult.

CONCLUSION

In today's health care, image analysis techniques such as registration and segmentation play a vital role in the clinical process from diagnostics and treatment planning to surgical procedures and follow up studies. 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. It must be addressed in order to make IGS and radiotherapy a practical reality. In this paper, we have made an effort to provide a comprehensive knowledge on MIR, its popular techniques, application areas and the prominent issues in detail. In clinical applications, further improvement in MIR techniques will satisfy the clinical demands. Therefore, future research is required for the development and advancement of medical image registration techniques and their suitable implementation in clinical applications.

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