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Coarse-to-fine lungs PET-CT image registration

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ABSTRACT

For the problem of image registration based on mutual information ignore global spatial information of the two images, and the lungs PET image is so fuzzy that has fewer correlations with the lungs CT image. This paper proposed a coarse-to-fine image registration method based on region information and mutual information. Experimental results show that this method can effectively to achieve lung image registration which globally aligns the chest region in PET and CT images and locally overlaps nodule lesion anatomical structure region in CT image and nodule highlighted functional area in PET image.

Keywords: Coarse-to-fine, Mutual Information, ROI of Lung

INTRODUCTION

With the development of modern medical imaging, medical image analysis is becoming an important part of the computer-aided diagnosis. Images from modalities such as computer X-ray radiography (CR), X-ray computed tomography (CT), magnetic resonance imaging (MR), single-photon emission tomography (SPET), positron emission tomography (PET), have become essential medical digital imaging means in the modern medical diagnosis. As soon as different imaging modalities are involved, which are divided into two categories of structural imaging and functional imaging, corresponding structures may be difficult to identify and match. Structural imaging can clearly show the anatomical structure of the organ, and its resolution is relatively high. While functional imaging can reflect the functional and metabolic information of human tissues, and locate the lesions because of the high metabolism of tumors, but generally the resolution is relatively low. In clinical diagnosis, doctors usually require images with different imaging modalities to make comprehensive analysis. Multi-modality image registration and fusion can take full advantage of the characteristics of the imaging modalities and achieve information complementary to improve medical diagnosis and treatment level.

Image fusion can take advantage of the respective information of different images, and express structural and functional information in one image. These images often have different imaging mechanisms, and acquired at different viewpoints, different times. So before image fusion and comprehensive analysis, we should solve the strict alignment problems of several images in the same spatial coordinates, which is the so-called medical image registration. Image registration is to find an optimal geometric transform that maps points from one image (moving image) to homologous points on a object in the second image (reference image).

Medical image registration development together with the general development of image registration techniques and is the application in the field of medical imaging. Medical image registration roughly experienced three stages: the first stage is based on the framework and the external characteristics of medical image; second stage is based on anatomical characteristics and organizational characteristics of medical image registration; third stage medical image registration is based on the invariants and information.

Medical image registration can be divided into applications between mono-modality images, multi-modal images, and an image with a model; medical image registration can be divided into intra-subject registration, inter-subject registration according to the source of images; medical image registration can be divided into rigid registration and non-rigid registration according to geometric transformation; medical image registration divided by the dimensions of the image registration, including between 2D/2D, 2D/3D, 3D/3D registration. Medical image registration experienced from single-mode to multi-modal registration, and multimodal medical image registration combined structural imaging and functional imaging information, gradually become the development trend of today's medical diagnosis. Medical image registration experienced a rigid registration to non-rigid registration from the points of geometric transformation.

After years of research, the image registration technology has made a lot of research. Multi-modality medical image registration becomes today's research focus and difficult in the field of registration. Collignon (1995) [1], Viola and Wells (1997) [2] first use the mutual information as a similarity measure for image registration. Subsequently, registration based on mutual information method wide spread in academy field. A large number of references have proved the validity of the registration based on mutual information similarity measure for multi-modality registration. However, mutual information measure considered only the statistical information of the image intensity value, ignoring the spatial information inherent in the image recent years. That is to say mutual information measure ignores dependencies to adjacent pixel gray values in the image, resulting in the presence of local extrema and lower robustness.

Studhulme (1999) [3] proposed a normalized mutual information measure method to reduce the dependence on the overlap region of the two images; Rueckert (2000) [4] proposed the concept of the second order mutual information taking into account the impact of each pixel's adjacent pixel; Lu Zhentai (2007) [5] proposed a similarity measure method based symbiotic mutual information taking account of the impact of the different directions of the neighborhood pixels in the two images at the same time on the basis of the second order mutual information, which effectively eliminated the local extrema problem of medical image registration based on mutual information when the image without significant deformation.

Mutual information registration algorithm was reviewed by (Pluim et al, 2003) [6], including preprocessing of images, gray value interpolation, optimization, adaptations to the mutual information measure, and different types of geometrical transformations, and cited the mutual information registration applications, on different modalities, on inter-patient registration and on different anatomical objects. The typical method of image registration was introduced by(Barbara Zitova et al,2003) [7], it reviewed approaches are classified according to their nature (area based and feature-based) and according to four basic steps of image registration procedure: feature detection, feature matching, mapping function design and image transformation and resampling.

Chen Weiqing(2005) [8] proposed a coarse-to-refine medical image registration which combined mutual information and the gradient image's shape information considering the problem of image registration based on mutual information which ignores the global spatial information inherent in the image and time-consuming.

Medical image registration technology is still a difficult issue mainly because of the diversity of data sources, the complex image distortion between the images. As the different requirements of the various applications of medical image registration, it still needs further development. Therefore, the study of the medical image registration techniques has important practical significance.

Most of the above literature is about brain image registration, lung image registration needs further study especially for PET-CT registration. Mutual information method has achieved good result in the registration of brain CT or MR images and PET images, and has been proved to reach the sub-pixel accuracy. Brain PET images have a large number of anatomical information and have larger the correlation with brain CT images, which can guarantee the realization of the alignment. But lungs PET images are very fuzzy which contains only functional information which makes lung PET-CT image registration more difficult. Rueckert (2006) [9] has effectively achieved brain image registration. While the lungs PET image is so fuzzy and noisy whose gradient image has much redundancy information. This paper uses the coarse-to-fine image registration method based on region information and mutual information. In the coarse rigid registration phrase, we align the PET image and CT image globally, which can guarantee the out chest region aligned with each other. In the refine elastic registration phrase, our purpose is aligning the lung nodule in the PET and CT images.

EXPERIMENTAL SECTION

Mutual information theory: Mutual information is a fundamental concept in information theory, which used to measure the correlation between two random variables. According to the theoretical knowledge of mutual information, the entropy of reference image IR and floating image IF indicates the uncertainty of the pixel gray values of images, and can be defined as:

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$$H(I_F) = -\sum_{b \in I_F} P(b)\log P(b)$$ **Error! Reference source not found.**

(2)

Where a and b respectively represent for a particular gray value in the reference image and the floating image. The joint information entropy of the reference image and the floating image can be defined as:

Error! Reference source not found. (3)

The mutual information between two images is

Error! Reference source not found. (4)

Although two images derived from different imaging devices in multimodality medical image registration, they are all based on the anatomy of the human body. So when the two images of the spatial position is entirely consistent, the information contained in the other image should be the maximum. The principle of image registration based on the mutual information can be said to find an optimal transformation, which makes the mutual information of corresponding pixel gray value in two images reaches maximum, which can be expressed as:

$$T_0 = {}^{\mathrm{argmax}}{}_{T} MI(I_R, T(I_F))$$ **Error! Reference source not found.**

(5)

This equation is objective function of the image registration based on mutual information, T on behalf of the space transformation model in the registration process.

Image registration based on the mutual information is a kind of automated method on the pixel gray, without pre-extraction of the relevant characteristics of the image, and don't need to assume that the value of the corresponding region of the two image have some relationships. It only concerned with the probability of the gray value, which is easily calculated, so the registration based on mutual information technology has been widely used.

In recent years, a considerable literature suggests that mutual information measure exist local extrema in the registration process, sensitive to the size of the overlap region, which is easy to cause mis-alignment. A normalized measure of mutual information was proposed by Rueckert [9], which is less sensitive to changes in overlap.

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B-spline elastic deformation model: B-spline function is a local control function, and the movement of a control point affects only its adjacent points, so spline interpolation is widely used in the field of non-rigid registration. The area of the image is represented as**Error! Reference source not found.**, **Error! Reference source not found.** represent the image grid make up of $n_x \times n_y$ **Error! Reference source not found.** control points whose spacing δ. elastic transform based on B-spline functions defined can be expressed as:

$$T(x, y) = \sum_{l=0}^{3}\sum_{m=0}^{3} B_{l,3}(u) B_{m,3}(v) \varphi_{i+l, j+m}$$ **Error! Reference source not found.**

(7)

Where $i = \frac{x}{\delta} - 1, j = \frac{y}{\delta} - 1, u = \frac{x}{\delta} - \frac{x}{\delta}, v = \frac{y}{\delta} - \frac{y}{\delta}$ **Error! Reference source not found.**, and $B_{l,3}(u)$ **Error! Reference source not found.** are the basis functions of cubic B-spline curve which defined as follows:

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$$\begin{cases} B_{0,3}(u) = \frac{1}{6}(1-u)^3 \\ B_{1,3}(u) = \frac{1}{6}(3u^3 - 6u^2 + 4) \\ B_{2,3}(u) = \frac{1}{6}(-3u^3 + 3u^2 + 3u + 1) \\ B_{3,3}(u) = \frac{1}{6}u^3 \end{cases}$$

(8)

Where $0 < u < 1$, represents contribution weight of each control point for a curve function which is based on the distance of the control grid vertices to the (x, y).

B-spline-based registration belongs to the regional registration method. It determines the grid control points by compute the corresponding similarity regions, and uniformity distributes these points to reflect the local deformation of images. Its precision can reach sub-pixel level. After the get the set of the corresponding points of the image in this method, I use the transformation model to get the deformation function between the two images. The free deformation idea is that the object is embedded into a space, and the object deforms along with this space.

B-spline-based Freedom Deformation Model (FFD) can solve the problem of deformation of soft tissue. FFD Using B-spline basis functions in is one of many Freedom Deformation Models. It creates a uniform grid space using of the idea of free deformation model on the image to contact the two images to be registered. By the movement of the grid space to drive the image deformation compensate for the differences that exist between the two images. Each of the control point of the grid space affects its adjacent region and the object deformation occurs when operates a group of grid control points. The density of the control grid determines the complexity of non-rigid deformation based on B-spline. The movement of the grid space restrains by calculating the local normalized mutual information of images. Then use the B-spline technique to reconstruct the coordinate's field after image deformation, and the gray information of corresponding position to get the image after registration.

Due to the lung is a typical locomotive organ and PET and CT image data acquired in different time, the lung nodules location in the two sequences of images is changed. We use a non-rigid registration to simulate the lung tissue deformation. In this paper, we use B-spline deformation function to achieve non-rigid registration.

Implement: Image registration method involves feature space, search space (spatial geometric transformation), optimization search algorithm, and similarity measure. Image registration based on mutual information calculates the gray value statistical correlation between the two images, without the need for feature selection and extraction. Similarity measure measures the statistical correlation between the gray values of reference image and transformed floating image. Transform parameters are constantly changing through optimization search algorithm, so that the similarity measure function reaches optimal. Eventually the problem becomes discrete multi-parameter optimization problem. Image registration flow chart as follows:

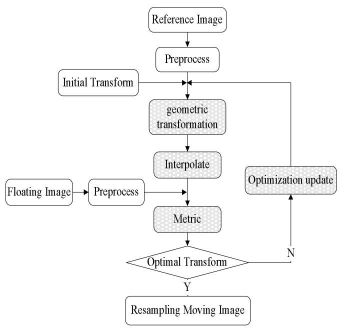


Fig 1 multi-modal image registration flow chart

We use the sequence of images collected from hospital as the experimental data, where the CT images resolution is 512 × 512, voxel size is 0.976562 0.976562; PET images resolution is 128 × 128, voxel size is 4.6875 × 4.6875. In the registration process, a CT image as a reference image, PET image as a reference image to be equipped. In this paper, we used normalized mutual information, LBFGSB optimization algorithm to reduce the impact of local extrema, and used B-spline-based freedom deformation model to achieve pulmonary PET-CT images non-rigid registration.

As the different imaging principle of modalities medical images and the resolution and signal-to-noise ratio (SNO) vary during the multi-modality image registration, we should first preprocess images. It can enhance the useful information that can be detected in the image by the preprocessing, which can eliminate the influence of these factors on the accuracy of the registration algorithm.

① PET images resolution is relatively low than CT images, it must be interpolated to the same resolution with CT images, to facilitate the subsequent coordinates mapping.

② With the presence of background noise PET images and CT images, it must be removed from the original PET and CT images.

③ Functional image usually introduces lots of noises when the acquisition, the region of interest (lung nodule area)should be enhanced to highlight.

Because image registration based on mutual information ignore global spatial information of the two images, and the lungs PET image is so fuzzy that has fewer correlations with the lungs CT image. We consider aligning the images with a coarse registration first. Multimodality medical images of the same organ usually have similar shapes, so they may be registered approximately by their shape parameters indicated in their shape information. In the coarse registration step, we segment the CT and PET images with marked chest region and lung nodule regions firstly. Then the mean squares metric was used to the rigid registration of the CT and PET marked region images. At last we got the final affine transform parameters. The flow chart of coarse registration as follows:

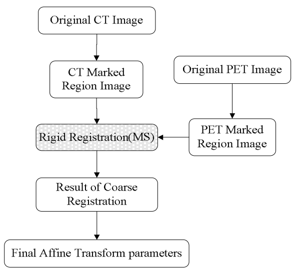


Fig2 the flow chart of coarse registration

We resample the interpolated PET image using the final affine transform parameters. In this method the PET lungs image can globally be mapped to the CT lungs image coarsely. In the refine registration step, the transformed PET image in the last step input to elastic registration as the moving image, and we use mutual information metric as the similarity method. The flow chart of refine registration as follows:

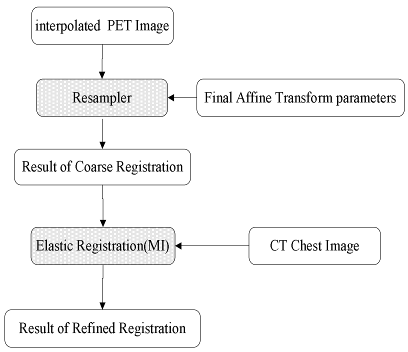
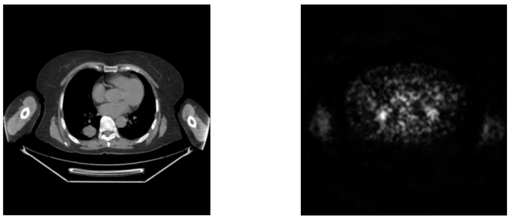


Fig3 the flow chart of refine registration

RESULTS



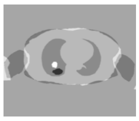
(a) (b)

Fig 4. (a) Original PET image with resolution of 512 × 512; (b) original PET image with resolution of 128 × 128;

The result of PET CT marked image registration using mean squares metric and affine transformation in coarse phrase shown show as follows:

(a) (b)

(c) （d）

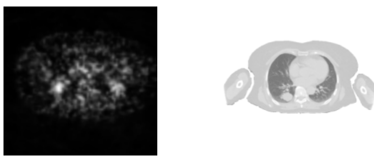


（e）

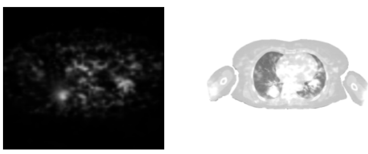
Fig 5. (a) the marked region CT image as the fixed image in the coarse registration, (b) the marked region PET image as the moving image in the coarse registration, (c) image combined a and b ,d) the registered moving image, (e) image combined a and d

Because the lungs PET image is so fuzzy that has fewer correlations with the lungs CT image which can be seen in Fig4. At the same time, mutual information ignores the global spatial information. We marked the CT image and PET image firstly before use mutual information image registration method. Note that the inside nodule area has a gray value of 0, the chest area has a gray value of 193, the background area has a gray value of 255, and the lungs area has a gray value of 128 in the CT image. From the Fig 5(e) we can see that the coarse image registration globally aligns the chest region in PET and CT images. The interpolated PET image transformed by the result affine transform parameters obtained in the coarse registration shown as follow:

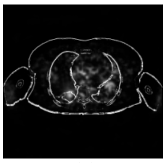
The result of transformed PET image and CT image registration using mutual information measure and free-form deformation model based on B-spline in the refine phrase as shown below:



(a) (b)



(b) (d)



(e)

Fig 6. (a) The PET image transformed by the result transform parameters, (b) the registered PET image (c) the registered PET image, combined with CT image, (d) the image of the registered PET image combined with CT edge image

In this phrase we use the CT chest image removed background noises as fixed image and the PET image transformed by the result transform parameters as moving image. From the Fig 6(b) and (c) we can see that the refine image registration achieved a good result which locally overlaps nodule lesion anatomical structure area in CT image and nodule highlighted functional area in PET image.

Table I The metric of coarse and refine registration

metric	Before Registration	After Registration
Coarse Registration(MS)	1519.06	694.291
Fine Registration(MI)	-0.2614	-0.3379

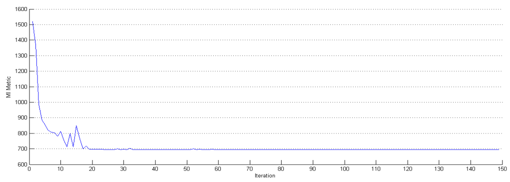


Fig 7 Metric Curve of Coarse Registration

From Fig 7 we can see that the metric curve of coarse image registration stabilized at last. This phrase globally aligns the chest region in PET and CT images.

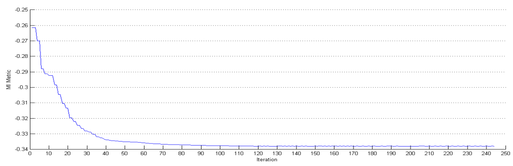


Fig 8 Metric Curve of Refine Registration

From Fig 8 we can see that the metric curve of refine image registration stabilized at last. This phrase locally aligns the lungs nodule region area in PET and CT images.

CONCLUSION

This paper detailed analyzes exist problem of mutual information method in the lungs PET-CT registration firstly. ① Mutual information ignores global spatial information of the two images②the lungs PET image is so fuzzy that has fewer correlations with the lungs CT image. Then propose a coarse-to-fine image registration method by combining mutual information and region-based information. In this method we have achieved good result in the PET and CT lungs images registration, and increased the mutual information robustness as well by improving it with region-based information. For the lungs three-dimensional image registration, as well as two-dimensional and three-dimensional image registration has yet to be further research.

Acknowledgements
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REFERENCES

[1] Collignon, F. Maes, D. Delaere, et al. *Automatedmulti-modality image* registration *based on information theory*. 1995, 3: 264-274.
[2] P. Viola, W. Wells. Alignment by Maximization of Mutual Information. 1997, 24(3): 137-154.
[3] Studholme, D. L. G. Hill, D. J. Hawkes. An overlap invariant entropy measure of 3D medical image alignment. 1999, 32(1): 71-86.
[4] Rueckert, M. J. Clarkson, D. L. G. Hill, et al. *Non-rigid registration using higher-order mutual information*. 2000, 3979: 438-447.
[5] Lu Zhentai, Chen Wufan. *Unsupervised Segmentation of Medical Image Based on Maximizing Mutual Information*. 2007, 30(6): 1022-1027.
[6] J. P. W. Pluim, J. B. A. Maintz, M. A. Viergever. *Mutual-information-based registration of medical images: a survey*. 2003, 22(8): 986-1004.
[7] Barbara Zitová, Jan Flusser. *Image registration methods: a survey*. 2003, 21(11): 977-1003.
[8] Chen Weiqing, QuZongying, Song Weiwei. *A Coarse-to-Refined Approach of Medical Image Registration Based on Combining Mutual Information and Shape Information*. 2005, 2: 816-820.
[9] Rueckert, P. AIjabar, R. Heckcmann, et al. *Medical Image Computing and Computer Assisted Intervention*. 2006, 9(2):702-709.