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Adam Grant Chandler, Thomas Netsch, Chris A. Cocosco, Julia A. Schnabel, David J. Hawkes, "Slice-to-volume registration using mutual information between probabilistic image classifications," Proc. SPIE 5370, Medical Imaging 2004: Image Processing, (12 May 2004); doi: 10.1117/12.534966

SPIE.

Event: Medical Imaging 2004, 2004, San Diego, California, United States

Cum Laude Poster Award

Slice-to-volume registration using mutual information between probabilistic image classifications

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ABSTRACT

Intensity based registration algorithms have proved to be accurate and robust for 3D-3D registration tasks. However, these methods utilise the information content within an image, and therefore their performance is hindered for image data that is sparse. This is the case for the registration of a single image slice to a 3D image volume. There are some important applications that could benefit from improved slice-to-volume registration, for example, the planning of magnetic resonance (MR) scans or cardiac MR imaging, where images are acquired as stacks of single slices. We have developed and validated an information based slice-to-volume registration algorithm that uses vector valued probabilistic images of tissue classification that have been derived from the original intensity images. We believe that using such methods inherently incorporates into the registration framework more information about the images, especially in images containing severe partial volume artifacts. Initial experimental results indicate that the suggested method can achieve a more robust registration compared to standard intensity based methods for the rigid registration of a single thick brain MR slice, containing severe partial volume artifacts in the through-plane direction, to a complete 3D MR brain volume.

Keywords: Slice-to-volume registration, fuzzy classification, c-means, normalised mutual information

1. INTRODUCTION

Image registration is commonly defined as the spatial alignment of two medical images via a transformation, which can consist of translations, rotations, scaling, shear and in some cases warping, so that spatial voxel correspondence is achieved. It is clinically beneficial to spatially align images for improved clinical diagnosis as well as planning, guiding and evaluating surgical and radiotherapeutic procedures. Any registration technique consists of three components: A transformation that relates the coordinate system of one image to that of an other image, a registration metric (similarity measure) which measures the similarity between the images after transformation, and an optimisation which iteratively improves the transformation with respect to an associated cost function to maximize the similarity between the images. The majority of medical image registrations are performed on 3D images, known as 3D-3D registration, although 2D-2D, 2D-3D and slice-to-volume studies have also been performed[1,2]. The term 2D-3D registration is specific to the situation where the 2D image is a projection image[3]. Therefore, for clarity, the term *slice-to-volume registration* will be used throughout this paper to refer to a 2D to 3D registration where one image is a thick slice or a small number (stack) of thick slices, and the other is a volumetric image.

Fully automatic, accurate, and robust slice-to-volume registration would be beneficial in a number of medical imaging applications. For example in cardiac MR perfusion were the images are acquired as 2D slices, it is desirable to position these slices in relation to an anatomical or morphological 3D scan. Other possible applications include the alignment of dynamic contrast enhanced images of, for example, the liver or the breast, and the alignment of ultrasound slices acquired intra-operatively to pre-operative volume MR[4,5,6] or Computer Tomography (CT) images in image guided interventions. To date, few papers have been published tackling the problem of slice-to-volume registration. These papers applied their methods to the brain for the applications of functional MR imaging[7] and postmortem pathology studies[8], and to abdominal organs, in particular the prostate[9] for interventional guidance. The particular application that we address in this paper is the accurate and robust rigid registration of a 2D MR brain scout (planning) scan to a complete 3D MR brain image volume. Such a procedure will automate the protocol for the subsequent acquisition of volume brain scans: the initial scout scan can be automatically matched to a previously acquired 3D image of that patient's anatomy, eliminating the need for manual planning.

Medical Imaging 2004: Image Processing, edited by
J. Michael Fitzpatrick, Milan Sonka, Proceedings of SPIE Vol. 5370
(SPIE, Bellingham, WA, 2004) · 1605-7422/04/$15 · doi: 10.1117/12.534966

In recent years, a number of fully automated intensity based registration techniques which use an *information-theoretic measure*, in particular normalised mutual information[10] (NMI), have been shown to be significantly more accurate and robust than other techniques for a variety of medical image registration problems. For this reason, NMI is the similarity measure used in this paper. However, these methods utilise the information content within an image, and therefore their performance deteriorates as the volume of corresponding data is reduced. This is the case for the registration of sparse images such as a single 2D image slice to a 3D image volume. In order to improve such registration tasks, we have used an information based registration technique previously suggested by Rohlfing *et al.*[11] and D'Agostino *et al.*[12]. This technique uses images containing voxels that have been assigned a vector of probabilities of class memberships derived from the original image intensities. We believe that such a method will be more robust as it incorporates additional information into the registration framework, especially when images contain severe partial volume effects.

In section 2, we will discuss the NMI similarity measure in more detail and introduce the information based registration method used for our slice-to-volume registration approach. In section 3, we will discuss the experimental setup and results obtained using our approach with a comparison to results obtained using standard intensity based methods. Finally we conclude our work in section 4.

2. METHODS

2.1 Information theoretic measures

Information theory was originally developed to describe the transmission of information between a sender and a receiver. A central concept is that of entropy, which provides a quantitive measure of information. The Shannon entropy[13], *H*, was proposed in 1948 as a measure of the information transmitted along a particular channel. For image processing, the Shannon entropy for an image *A* containing a set of voxel intensities *a, H(A)*:

$$H(A) = -\sum_{a} p(a) \log p(a).$$

where *p(a)* is the probability that *A* contains voxel intensity *a*. The entropy of an image can be estimated from its intensity histogram, which is an estimation of the intensity distribution within the image.

As well as an information measure, the entropy can also be thought of as a measure of uncertainty: the more uncertain the contents of the image, the higher the entropy. Thus, an image consisting of only a few different intensities would have low entropy, whereas the entropy of an image containing a wide variety of intensities would be higher.

An entropy based measure can also be applied to a pair of images *A* and *B* to enable one to measure their total information content, or 'joint entropy', *H(A,B)*:

$$H(A,B) = -\sum_{a}\sum_{b} p_{AB}(a,b) \log p_{AB}(a,b).$$

where *a* and *b* are the image intensities. $p_{AB}(a,b)$ is the probability of image *A* containing intensity *a* and image *B* containing intensity *b*.

To calculate the joint entropy, Hill *et al.*[14] suggested first constructing a joint histogram for the two images *A* and *B* containing $a \times b$ bins. After a transformation *T* is applied to image *B*, a joint histogram is produced by pairing the intensity value for a voxel location *x* in image *A* (target image), *A(x)* with the intensity at the corresponding voxel location *T(x)* in image *B* (source image), *B(T(x))* and the appropriate bin (*A(x)*, *B(T(x))*) is incremented with a value of 1. This is repeated for all voxel locations in the overlapping domain $\Omega_{A,B}$. When each entry in the joint probability histogram of two images is divided by the total number of contributing voxels *N*, in the overlapping domain $\Omega_{A,B}$, an estimate of the joint probability distribution of the intensities can be obtained. The histogram can then be regarded as the probability distribution function (PDF) p_{AB} of the images *A* and *B* for intensities *a* and *b*. To optimise the transformation, the distribution of the probabilities has to be minimized. Therefore, the joint histogram needs to be as sharp as it possibly can be.

In practice, there is a problem with using joint entropy as a measure of similarity for registration. When the joint entropy is minimised, one is trying to find the overlap that contains the least information, not necessarily the most corresponding information, which is what is actually needed for a successful registration. Any registration algorithm attempting to minimize joint entropy can therefore find incorrect solutions. An example of this can be seen if one considers two images that only have areas of background overlapping. This will produce a sharp joint histogram and therefore low joint entropy.

A measure suggested simultaneously by Collignon *et al*.[15] and Viola *et al*.[16] overcame this problem by relating the changes in the value of the joint entropy *H(A,B)* to the entropies of the individual images; their 'marginal entropies' *H(A)* and *H(B)*. This similarity measure is known as *mutual information* (MI)

$$I(A,B) = H(A) + H(B) - H(A,B).$$

To obtain optimal registration, MI needs to be maximized. MI does not entirely solve the overlapping problem mentioned above and is still sensitive to difference in the volume of overlap. Studholme *et al*.[10] devised a measure that normalizes the joint entropy to overcome this problem. This is the ratio of the sum of the marginal entropies and the joint entropy. The measure is known as *normalised mutual information* (NMI)

$$NMI = \frac{H(A) + H(B)}{H(A,B)}.$$

2.2 Information based registration

Intensity based similarity measures as described above typically assume that voxel intensities are representing the objects within the images to be registered. This is not entirely the case in practice due to image artifacts, such as noise, or partial volume effects.

We propose to consider intensity based registration methods as a two-step process in which the voxels of the target and source images are initially assigned a vector of probabilities of class memberships, and are then matched by a registration method, we can generalise the intensity based registration framework (figure 1): a registration algorithm which uses mutual information based on joint histogram binning is applied to match probabilistic classifications of the images instead of the original intensity images.

The most important aspect of this approach is that the actual registration no longer depends on a relationship between voxel intensities and image objects, but just on the information content within the images. This potentially leads to a more soundly based theoretical justification for registration within the context of information theory. The first step of our method is to define a number of classes for each image, and to compute for each voxel the probability of belonging to each of the classes. This results in probabilistic vector-valued images, which contain estimates of the class fractions within each voxel (i.e. an estimate of the partial volume effect). The information content within the images can therefore be tailored, by means of classification, to incorporate prior knowledge about anatomical and spatially varying information within the image whilst potentially allowing irrelevant image content such as noise and other imaging artifacts to be reduced. An appropriate name for a registration using such an approach would be an *information based registration.*

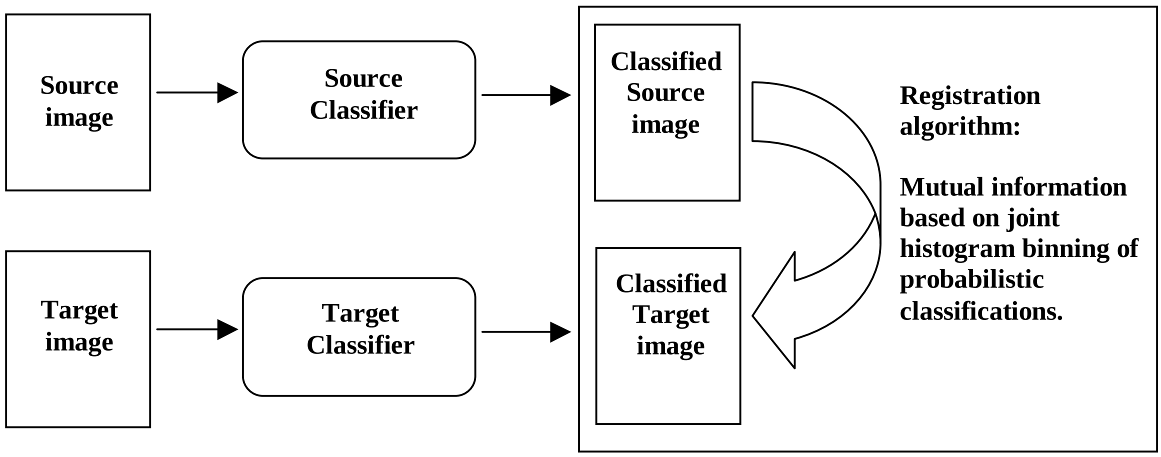

Figure 1: A generalized framework for intensity based image registration based on joint histogram binning.

Several authors have used probabilistic classified images to improve registration. Butz *et al.*[17] attempt the information-based registration of a 3D MR-scan to a 3D CT scan of another patient (inter-patient registration) by using images that were pre-classified to a single feature called *edgeness*. They pre-assign each voxel in the images the probability of it being an edge. The registration results were then compared to registrations using standard intensity based registration. For rigid cases, the quality of the results was comparable while for affine registrations the information-based registration produced much better results. The authors conclude that registering images representing edge information emphasises contours in the images while intensity based registration overemphasises the volumetric information in the images and therefore risks neglecting finer but important features in the images. Saha *et al.*[18] classified 2D MR images of the human brain by using a probabilistic labelling known as *tensor scale* before rigidly registering the images. The authors conclude that registration of tensor scale images inherently incorporates information about local structure size, orientation and anisotropy into the registration framework, which would be helpful in resolving the challenge posed by intensity homogeneity and noise. Penney *et al.*[6] present a method to register a preoperative liver MR volume to a sparse set of intraoperative liver ultrasound slices. The intensities of the MR and ultrasound images are pre-classified into vessel probability values before registration.

Each of these authors has made use of classified images for information based registration containing scalar voxel-values that represent the probability of only one particular class. This means that the traditional way of estimating the joint probability distribution from the joint histogram is still a valid method. If, on the other hand, one or both of the images to be registered contain vector valued voxels that represent the probability of more than one class (probabilistic vector-valued images), then a new method of joint histogram binning needs to be adopted to estimate the joint probability distribution.

2.2.1 Joint histogram binning of probabilistic vector-valued images

A method for joint histogram binning of probabilistic vector-valued data has been first suggested by Rohlfing *et al.*[11] and D'Agostino *et al.*[12]. If one of the images, say the target image, is classified into n classes and each voxel i in the target image is assigned a probability $C_{i,k}$ of belonging to the class k, where

$$\sum_{k=1}^{n} C_{i,k} = 1$$

and the source image contains a range of intensities or intensity bins b, the joint histogram can be represented as a $n \times b$ matrix. For each corresponding vector-valued voxel i in the target image and scalar-valued voxel j in the source image, the appropriate (k,b) bins will be increased with the probability $C_{i,k}$ for all classes k.

Rohlfing *et al.*[11] adopted such a method to improve 2D-3D registration. Traditionally, in order to register a 3D image to a 2D projection image one computes a Digital Reconstructed Radiograph (DRR) from the 3D image[19]. The DRR is then registered to the 2D projection image. However, the spatial information present in the 3D image is lost in the process of computing the DRR[11]. Therefore, the authors preserve the spatial information by producing a probabilistic vector-valued DRR (pDRR). Each pixel in the pDRR image corresponds to the probabilities of the distribution of values along the ray that resulted in the projection value at that pixel. The authors used this method to produce a pDRR from a 3D MR image. They then rigidly registered, using NMI, the pDRR of the MR image to a deterministic DRR image computed from a 3D CT image.

Alternatively, if the source image is classified, as well as the target image, into *m* classes and each voxel *j* is assigned a probability $C_{j,l}$ of belonging to the class *l*, where:

$$\sum_{l=1}^{m} C_{j,l} = 1$$

The joint histogram can be represented by the n $\times$ m matrix below

$$\sum_{(i,j)} \begin{vmatrix} C_{i,1} \cdot C_{j,1} & C_{i,1} \cdot C_{j,2} & \cdot\cdot & C_{i,1} \cdot C_{j,m} \\ C_{i,2} \cdot C_{j,1} & C_{i,2} \cdot C_{j,2} & \cdot\cdot & C_{i,2} \cdot C_{j,m} \\ : & : & & : \\ C_{i,n} \cdot C_{j,1} & C_{i,n} \cdot C_{j,2} & \cdot\cdot & C_{i,n} \cdot C_{j,m} \end{vmatrix}$$

Agostino *et al.*[12] used such a method for the improved multimodal non-rigid registration of brain images by minimising the Kullback-Leibler distance measure between the actual and ideal joint probability distributions of the voxel classes. By first classifying each image, the multimodal image registration problem can be reduced to a monomodal one that consists of aligning identically classified voxels rather than the multimodal intensities of the original intensity images. In order to avoid problems that may arise from using images with hard classified voxels[20], such as lack of information features in homogeneously labelled regions and interpolation artefacts at object boundaries, they adopt a fuzzy classification method in which probabilistic vector-valued images are used.

We adopt such a joint histogram binning method for our slice-to-volume registration algorithm. This allows us to iteratively optimise the rigid transformation between a classified 3D volume image and a classified slice image using a multi-scale registration technique, which maximises NMI. To our knowledge this is the first time such a method has been used for the problem of slice-to-volume medical image registration. We believe that by filling the joint histogram as described above and by using a fuzzy classification to produce probabilistic vector-valued images, we incorporate spatial information together with appropriate treatment of the partial volume effect which is severe in thick image slices.

3. EXPERIMENTS

Initial slice-to-volume rigid registration experiments using the information based method described above have been performed between a single thick transverse brain MR slice and a complete high-resolution T1 weighted 3D MR brain volume (256x256x160 voxels, 0.9x0.9x0.9mm^3 resolution, acquired on a Philips Gyroscan Intera 1.5T MR system) and compared to the results obtained using the standard intensity based methods using NMI.

3.1 Registration experiments using a simulated MR slice

For our simulation experiments (see figure 2), a thick transverse slice (256x256x1 voxels, 0.9x0.9x9.9mm^3 resolution) was simulated by extracting a stack of eleven 0.9mm slices from a real T1 weighted 3D volume at a position close to the centre of the brain. The intensities were then averaged through-plane to obtain a thick slice of 9.9mm thickness (thus containing partial volume effects in the through-plane direction). The volume and slice were classified into four fuzzy

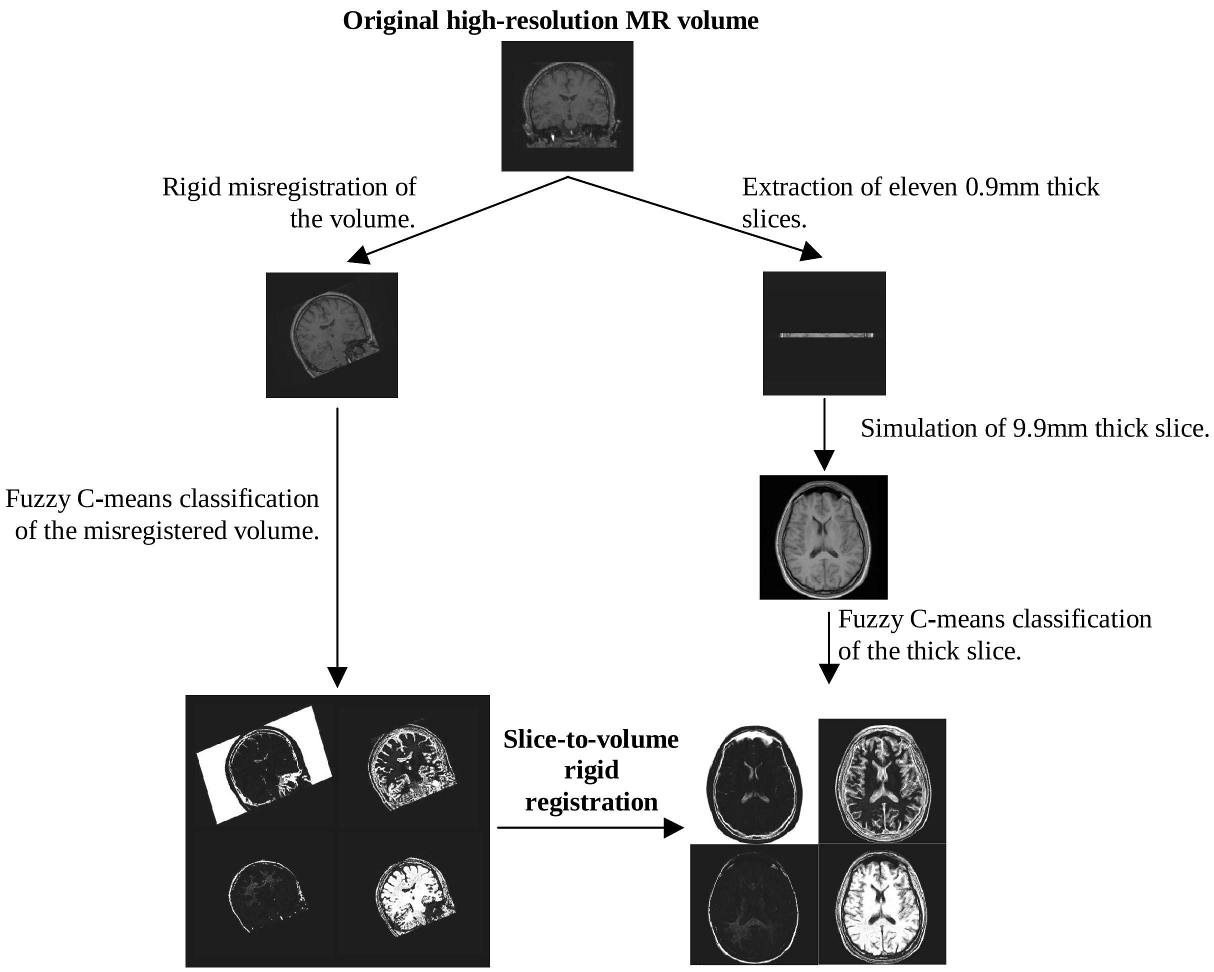

Figure 2: Experimental set-up for registrations using a simulated MR slice.

tissue classes (background, skull and skin, CSF, and grey and white matter) using the fuzzy c-means (FCM) classification algorithm[21].

Two experiments were performed on this data. In the first experiment, 75 random initial rigid misregistrations (ranging between –30mm and +30mm for translational parameters and -30 degrees and +30 degrees for rotational parameters) were applied to the classified volume, and the information based registration method, described above, was applied. The results were compared to the results obtained when standard intensity based registration methods using NMI were used.

In the second experiment, the capture range of our information based registration method was compared to the standard intensity based registration method. Twenty random initial rigid misregistrations were selected for every combination of total translation ranging from 0mm to 60 mm in increments of 5 mm and axis/angle representation ranging from 0 degrees to 40 degrees in increments of 5 degrees, totaling (13 x 9 x 20) = 2340 transformations. Each of the misregistrations was applied to the classified volume and both the information based registration method and the standard intensity based method were applied. The number of failed registrations for each set of 20 misregistrations was noted and plotted.

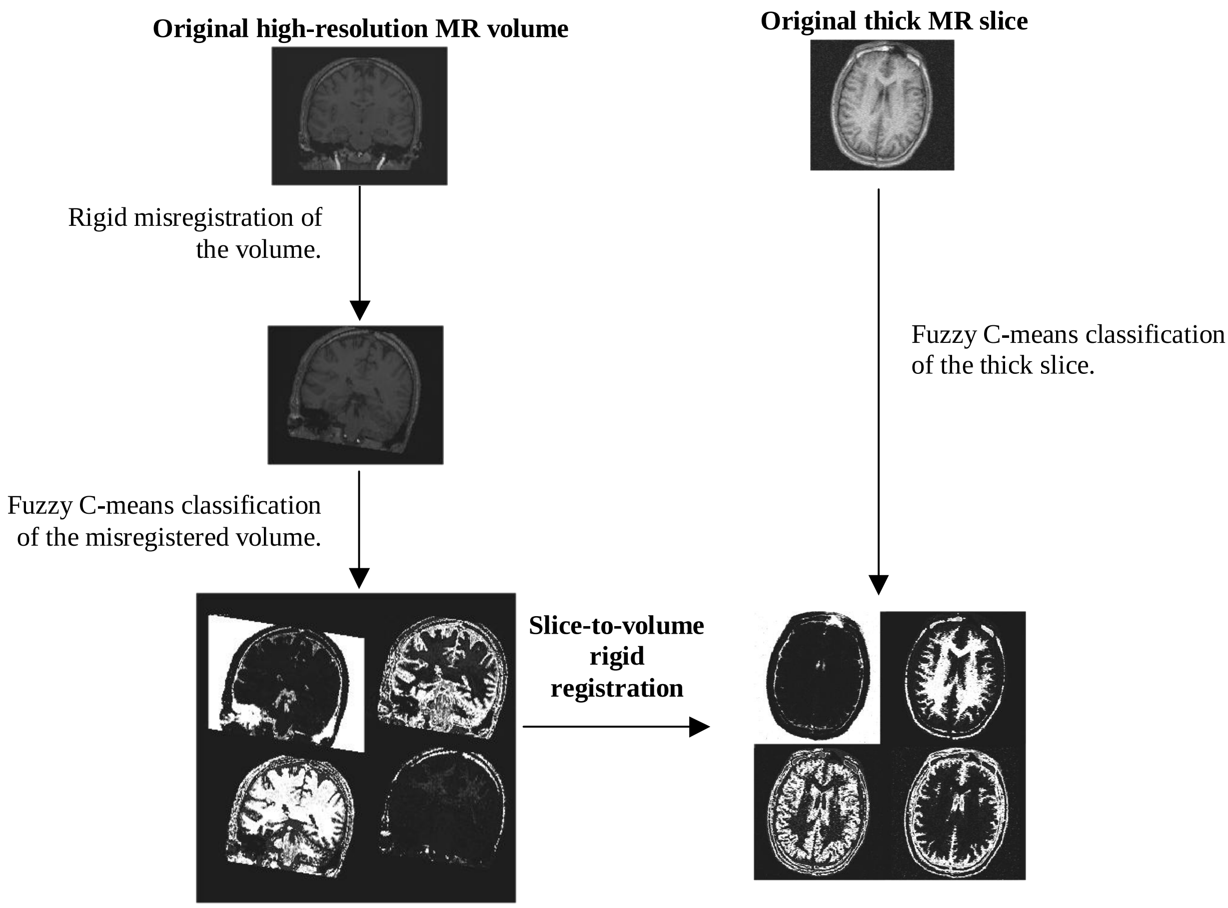

Figure 3: Experimental set-up for registrations using a real MR slice.

3.2 Registration experiments using a real scout scan MR slice

For our experiments using a real setup (see figure 3), the 3D MR volume and the thick MR slice (scout scan acquisition, 256x256x1 voxels, 0.9x0.9x10mm^3 resolution, acquired on a Philips Gyroscan Intera 1.5T MR system) were both acquired independently making sure that the patient did not move between the acquisitions. This data is more like the data that would be acquired in clinical practice. Once again the volume and slice were classified into four fuzzy classes using the FCM classification algorithm. The same two experiments described in section 3.1 were repeated on this data.

4. RESULTS

The *mean imaged patient voxel displacement*[22] (MIPVD), was used to determine if the misregistrations were or were not successfully recovered. The identity transform was used as a gold standard to validate the accuracy of the registration result. If the MIPVD for the set of voxels in the overlapping regions of the images was less than 1mm a successful recovery was postulated.

4.1 Results for registration experiments using a simulated MR slice

The results of the first experiment have shown a significant improvement in robustness for the slice-to-volume information based registration method compared to the standard intensity based slice-to-volume registration method. The results have shown that 95% of the misregistrations were successfully recovered using the slice-to-volume information based method compared to 88% for the standard intensity based slice-to-volume registration method.

The results of the second part of this experiment are illustrated in figure 4.The capture range graphs for the standard intensity based method and the information based method are shown in figure 4(a) and figure 4(b) respectively. If figures 4(a) and 4(b) are compared, it can be seen that both methods perform equally well at recovering misregistrations containing small translations, up to 20mm, and rotations, up to 10 degrees. For the larger misregistrations, the information based method has a lower number of failed registrations compared to the standard intensity based method. These graphs therefore show that the capture range for this information based method is larger than that for standard intensity based methods when registering a simulated scout MR slice to a high resolution 3D MR volume.

Standard Intensity Based Method **Information Based Method**

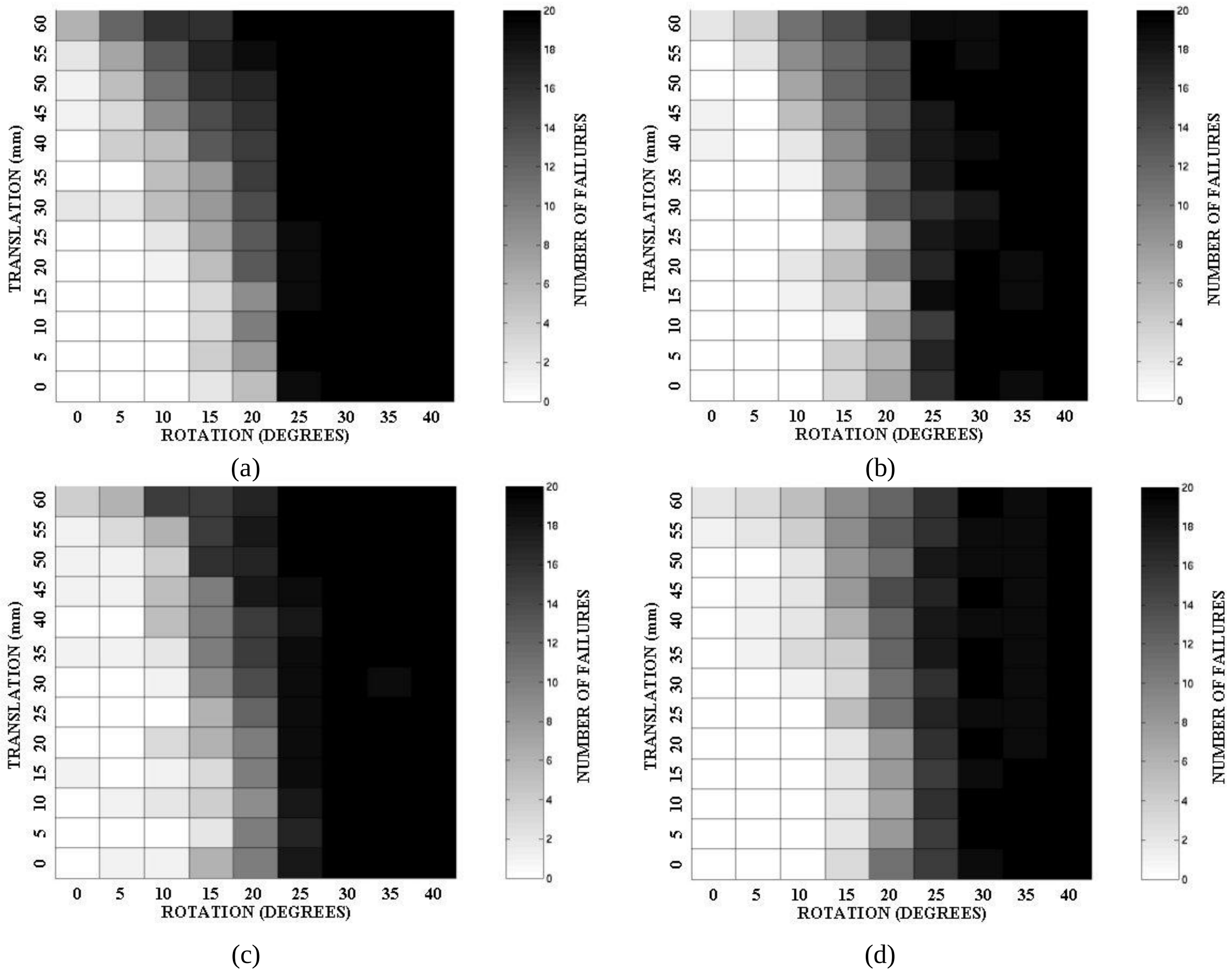

Figure 4: Results of the capture range experiments described in section 3.1 and 3.2. The capture range graphs for the rigid slice-to-volume registration of a simulated MR slice and a real scout MR slice using standard intensity based methods can be seen in (a) and (c) respectively. The capture range graphs for the rigid slice-to-volume registration of a simulated MR slice and a real scout MR slice using information based methods can be seen in (b) and (d) respectively. These graphs show that although both methods can recover misregistrations (MIPVD < 1mm) containing small translations and rotations robustly, the performance of the information based method is significantly better (less failures) than the standard intensity based method at recovering misregistrations containing larger translations and rotations for the registration of simulated and a real scout MR slices.

4.2 Results for registration experiments using a real scout scan MR slice

The results of the first experiment indicate that 91% of the misregistrations were successfully recovered using the slice-to-volume information based method compared to 87% for the intensity based slice-to-volume registration method.

The results of the second part of this experiment are shown in figure 4. The capture range graphs for the standard intensity based method and the information based method are illustrated in figure 4(c) and figure 4(d) respectively. A comparison of figure 4(c) and figure 4(d) shows that both methods perform equally well at recovering misregistrations containing small translations, up to 20mm, and rotations, up to 10 degrees. For the larger misregistrations, the information based method has a lower number of failed registrations compared to the standard intensity based method. These graphs therefore show that the capture range for this information based method is larger than that for standard intensity based methods when registering a real scout MR slice to a high resolution 3D MR volume.

5. CONCLUSIONS AND DISCUSSION

This paper has evaluated the use of information based registration based on vector valued probabilistic images derived from the original intensity images for slice-to-volume registration problems. We have shown a significant improvement in robustness and capture range compared to standard intensity based methods for the application of registering a thick brain MR slice, containing severe partial volume effects, to a high resolution MR brain volume. In future work we intend to make further refinements to the slice-to-volume information based method including an increase in the accuracy and the extension to non-rigid registration. Future experiments will be performed to try to improve slice-to-volume registration for some applications in which the existing methods fail, in particular cardiac MR applications. In order to tackle more challenging slice-to-volume registration tasks, such as MR/US, where the modalities are very different and imaging artifacts are more prominent, we are developing more sophisticated classification techniques.

ACKNOWLEDGMENTS

A.G. Chandler is funded by Philips Research Laboratories, Hamburg, Germany. J.A. Schnabel has received funding from Philips Medical Systems, Best, Netherlands.

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