Medical Image Registration using Voxel Similarity Measures

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1. Introduction

Patients frequently undergo multiple radiological imaging investigations that provide complementary information. It is becoming increasingly widely recognised that the use of image processing techniques to combine this information into a single representation of the patient can assist in the interpretation of the relevant radiological information [1]. The development of clinically useable automatic 3D medical image registration algorithms is therefore an important research area.

Medical images of the same region of a patient acquired with different imaging modalities are usually recognisably similar, even to a non-expert. For example, MR and CT images of many parts of the body contain broadly the same features, and observers who are new to these types of images will frequently recognise the part of the body that has been imaged, but mistake the modality. In these *visually-similar* images from different modalities, image features in the different modalities will appear with different intensity and texture, and some image features visible in one modality will be absent from another modality. There are important exceptions: projection angiograms (especially subtracted ones) are difficult to relate to cross-sectional images of the same part of a patient because they share almost no image features due to their different dimensionality; nuclear medicine images acquired using very specific functional tracers provide little anatomical information to relate to other modalities.

Where visually-similar images are being combined, image registration can be accomplished by manually, or perhaps automatically, identifying a small number of equivalent features such as points or surfaces in the images [2,3,4,5,6]. An alternative approach is to perform registration using all, or at least a large number of the voxels in the images rather than a small number of derived features. The basis of this approach is the assumption that some arithmetic combination of voxel values in two images, when applied to each image voxel in turn, provides a similarity measure that has an optimum value when the images are aligned. The best known algorithm of this type is cross correlation. This paper reviews algorithms using voxel similarity measures that have been applied to medical images, and presents new work on a methodology for devising improved similarity measures.

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Funded by the UK Science and Engineering Research Council.

1.1. Cross Correlation of Intensity Values

The *cross correlation* of two functions is frequently used in signal processing and image processing as a measure of how well two functions A and B *match up* when they are transformed with respect to each other. The transformation T that provides the best match between the functions has the highest correlation value.

For two 3D real valued images A and B with p x q x r voxels, the correlation value for a transformation T is given by equation 1.

$$[A \oplus B]_T = \sum_{i=0}^{p-1} \sum_{j=0}^{q-1} \sum_{k=0}^{r-1} A_{ijk} \cdot T(B_{ijk}) \qquad (1)$$

To determine the transformation that most closely matches the two functions, it is necessary to find the value of T that maximises the right hand side of this equation. The transformed value of B_{ijk} is unlikely to lie on a sample point in the data, so interpolation is normally used in the evaluation of $T(B_{ijk})$.

Published work in medical image registration using cross correlation of intensity values has been less successful than alternative approaches, such as landmark registration and surface matching. Two recently developed techniques, which are closely related to cross correlation, have been much more successful.

1.1.1 Cross Correlation of Image Gradients

Van den Elsen [7] proposed an algorithm for image registration by correlation of image intensity gradients. In her algorithm, the second derivative of the image in the direction normal to the local intensity gradient is used as a ridge detector. By choosing an appropriate scale at which to calculate the derivative, the bone ridge from MR and CT images can be automatically extracted from the images, and the resulting gradient images can be cross correlated to determine the correct registration transformation.

1.1.2 Minimising the Coefficient of Variation of Intensity Ratios

Roger Woods [8,9] has proposed an algorithm that is related to cross correlation, but incorporates an important modification. His algorithm is based on an idealised assumption that states: if two images are accurately aligned, then the value of any voxel in one image is related to the value of the corresponding voxel in the other image by a multiplicative factor R. In other words, for all voxels a_i and b_i in images A and B

espectively, $\frac{a_i}{b_i} = R$. When A and B are acquired from the

ame patient using the same modality at different times, here will be a single value of R for all intensity values. When A and B are acquired from the same patient using different modalities, there might be a different value of R for ach intensity value in either image. The Woods algorithm as been developed specifically for registration of multiple ET images from the same patient, and for registration of ET images to MRI images of the same patient. Clearly, the dealised assumption will not hold in either of these applications, but, if R is more uniform (has a lower variance σ^2) when the images are in registration than when the images are ot, and if σ^2 increases as the degree of misregistration ncreases, then image registration can be accomplished by inimising the coefficient of variation of the intensity ratios.

Ve have previously shown how this technique can be modied in order to automatically register MR and CT images of e head, provided there is sufficient axial sampling [10].

he success of these techniques for solving specific registraon problems encouraged us to devise a methodology for rther investigating voxel similarity measures.

. Method

Ve have accurately registered many dozens of medical nages using anatomical landmarks [1]. This provides us ith a large number of reference datasets with which to evalate alternative registration algorithms. We have devised two chniques for assessing possible voxel similarity measures: eature space sequences and similarity measure plots.

.1. Feature Space Sequences

. qualitative way of considering the effect of misregistration n voxel similarity measures, is to use feature spaces. For e work presented here, feature spaces are constructed from nage intensities. Extending this work by generating feature paces from image gradients or texture might prove useful.

. feature space sequence is a series of feature spaces calcuted from a pair of images transformed relative to each ther. One image in the sequence is calculated when the nages are correctly registered, the others are calculated ith known transformations in a chosen degree of freedom. . feature space sequence can be calculated for each degree f freedom of the rigid body transformation. It therefore proides a way of studying the change in the appearance of a eature space with misregistration. Alternative similarity easures can be calculated directly from the feature spaces.

2.2. Similarity measure plots

A quantitative indication of the performance of voxel based registration algorithms can be gained by studying the way in which the similarity measure changes with misregistration. Using registered reference images, the similarity measure is evaluated for the images at registration, and when misregistered by known transformations in each of the degrees of freedom of the desired registration transformation. For rigid body registration, this provides a series of six one dimensional curves, each of which is a plot of similarity measure value against misregistration for a single degree of freedom. We term the resulting graphs similarity measure plots. The similarity measures are formulated as cost functions, so an ideal similarity measure plot has a minimum value at registration, and is a monotonically increasing function of misregistration. It must be emphasised that these similarity measure plots do not sample all of the parameter space, and there are likely to be many local minima (or even the global minimum) that are not visible in the similarity measure plots.

2.3. Initial Evaluation of Similarity Measures

These techniques have been used to evaluate similarity measures on preregistered MR, CT and PET images.

3. Results

3.1. Feature Space Sequences

A feature space generated from two identical, perfectly registered images, is a line of unit gradient. The appearance of the feature space changes in a similar way with misregistration in each degree of freedom in turn. The distinctive diagonal line gradually blurs in the horizontal and vertical directions, Horizontal and vertical lines appear, intersecting at peaks in the original feature space, once the misregistration is sufficiently great that a given intensity value in one image can underlie any intensity value in the second image. Feature space sequences were also generated for other more relevant image combinations. A feature space sequence was generated from two similar but not identical MR images. One MR image was generated from the original by adding Gaussian noise with a standard deviation similar to the standard deviation of the air in this image, followed by adding an offset of 100 to each voxel value. The second MR image was generated from the same original by setting the left most third of the voxel values to 0. The resulting feature space sequence is shown in figure 1.

A similar feature space sequence generated from T_1 weighted MR and CT images of the skull base is shown in figure 2.

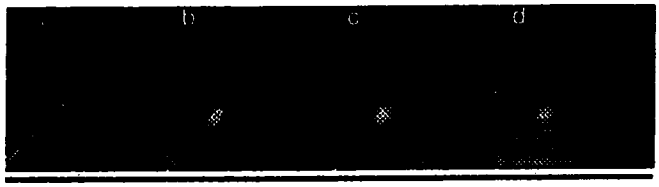

Figure 1. A feature space sequence generated from two similar MR images registered (a) and translated laterally by 3mm (b), 9mm (c) and 25mm (d).

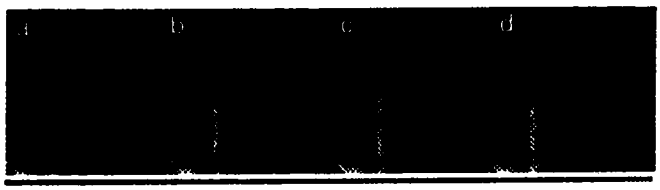

Figure 2. A feature space sequence generated from MR and CT images registered (a) and rotated by 2.5° (b), 7.5° (c) and 20° (d) about a cranio-caudal axis.

The feature space sequences shown in figures 1 and 2, and others generated from alternative image combinations, look quite different. However, there are common characteristics:

1. diagonal features in the images at registration disperse when the images are misregistered.
2. except at the origin, the highest intensity pixels get less bright with misregistration.
3. the number of low intensity pixels increases with misregistration
4. horizontal and vertical lines appear in the feature spaces when the images are significantly misregistered.

We devised a new similarity measure, designed to be sensitive to some of the changes in feature space appearance listed above: the third order moment of the intensity histogram of the feature space. The histogram of the feature space contains information about the distribution of feature space intensities. It is weighted towards high values if a small number of feature space pixels have high intensity, and is weighted towards low values if a large number of feature space pixels have low intensity. The higher order moments of this histogram quantify its distribution. We chose to use the third order moment of the feature space histogram, but the choice of this rather than any other moment of order 2 or above was arbitrary.

Figure 3 shows the similarity measure plots for pre and post Gadolinium MR images. These images were acquired in the normal clinical routine. The patient was removed from the MR scanner for injection of contrast between acquisitions, and the voxel dimensions were different in the two images.

These plots demonstrate that the cost increases almost monotonically with misregistration in each of the degrees of freedom. The equivalent plots obtained using cross correlation and the coeffecient of variation of intensity ratios contain local minima in each degree of freedom.

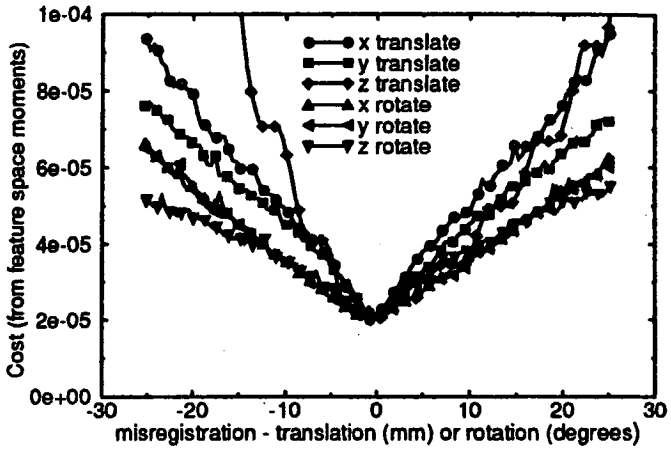

Figure 3. A similarity measure plot calculated using the 3rd order moment of the feature space histogram, for two T_1 weighted MR images (pre and post Gadolinium).

Pre and post Gadolinium MR images have been successfully registered automatically with this similarity measure using a genetic algorithm [11] with a population size of 100 and 30 generations, at two scales.

4. Discussion

In order to register images using equivalent or similar features it is first necessary to identify these features. Registration algorithms of this type require considerable interaction from a trained operator, because automatic segmentation and labelling of anatomical features in medical images remains a difficult problem. Registration algorithms that use voxel similarity measures potentially overcome this difficulty by using image voxels rather than derived geometric features for registration. Both Roger Woods at UCLA and Petra van den Elsen at Utrecht have implemented algorithms using voxel similarity measures and successfully registered MR and PET, and MR and CT images respectively. The former technique requires presegmentation of the brain from the MR images, and the latter has only been applied to images with considerably higher resolution than those that are routinely acquired clinically.

We have previously demonstrated that Roger Woods' algorithm can be extended to the registration of MR and CT images, by modifying the algorithm to use only voxel inten-

sities within certain ranges. However, the algorithm failed to register images with insufficient axial sampling.

We have devised a methodology for further evaluation of voxel similarity measures, in particular the generation of feature space sequences. All the feature space sequences produced shared common characteristics that might be used for registration. The coefficient of variation of intensity ratios algorithm makes one dimensional measurements in feature space: it calculates the coefficient of variation along the ordinate axis. One consequence of this is that in MR and CT registration, there is a high cost associated with soft tissue from MR overlying bone from CT, but there is not a corresponding high cost for soft tissue from CT overlying bone from MR. An algorithm that operates on both dimensions of the feature space might be more reliable.

We devised an alternative measure of the change in appearance of the feature space images. This measure, the third order moment of the feature space histogram, was successfully used for the automatic registration of MR images pre and post injection of Gadolinium. This is an important application of image registration, as subtraction of these images can provide useful clinical information [12], and patients normally move between the acquisition of these sequences. It is an example of a large class of image registration problems, in which a time series of images need to be related. Obvious examples include monitoring disease progression (eg: plaque volume in patients with multiple sclerosis), and correcting for movement artifacts in functional MR [13].

Searching parameter space for the minimum evaluation of a voxel similarity measure is difficult. There can be an enormous number of local minima. Even if the similarity measure plots suggest that the similarity measure increases monotonically with misregistration, there can be local minima, or even a global minimum in an unmeasured part of parameter space. One reason for this is that the similarity measures tend to assign a high cost to air overlying tissue. For axial images, misregistration caused by translations in the lateral and posterior-anterior directions, and rotations about all three axes lead to air overlying tissue. However, many incorrect transformations will also reduce the amount of air overlying tissue, leading to a local minimum.

More work is needed to devise and test appropriate similarity measures, but the approach shows great promise of producing an accurate, automated method for registration of voxel datasets in 3D medical imaging.

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