Local Similarity Measures for ROI-based Registration of DCE-MRI of the Breast

Sebastian Schäfer
schaefer@isg.cs.uni-magdeburg.de
Clemens M. Hentschke
cmh@isg.cs.uni-magdeburg.de
Klaus Tönnies
toennies@isg.cs.uni-magdeburg.de

Department of Simulation and Graphics
University of Magdeburg
Magdeburg, Germany

Abstract

Dynamic contrast-enhanced MRI (DCE-MRI) of the breast is widely used for detection and quantification purposes of breast cancer. In this paper, we present an evaluation of three similarity measures for local region of interest registration of small lesions in DCE-MRI. We evaluate the different registration results using a pharmacokinetic model function and compare measured perfusion data to the modelled function values. In addition, we use acquisitions from different time frames (pre- and post-contrast) as fixed image and observe the influence on the registration quality. The registered images lead to an improvement between 25.9% and 48.8% in terms of fitting quality to the pharmacokinetic model. Improvements could be achieved with all three similarity measures.

1 Introduction

Dynamic medical images like DCE-MRI are used to display active processes within the human body. Therefore, a series of images showing the exact same scene has to be acquired to reveal a signal change over time. The blood flow of specific body parts is visualised through an injected contrast agent (CA). DCE-MRI for breast cancer diagnosis highlights suspicious lesions inside the female breast, because tumours lead to formation of new vessels (angiogenesis) which accumulate contrast-enhanced blood. Moreover, the vessel permeability can be examined, giving relevant information for diagnosis. DCE-MRI is particularly sensitive for small lesions and spread tumour cells [3].

In dynamic imaging, identical conditions cannot be guaranteed to be achieved for each snapshot of a time series. Apart from camera system dependent influences like noise artefacts, motion of the patient poses a main problem in dynamic image acquisition. This motion evokes false inter-voxel correspondences between different time acquisitions. This leads to incorrect assumptions in diagnosis as physicians evaluate perfusion behaviour over time voxel-wise. DCE-MRI is very sensitive for detecting small enhancing lesions on which we will concentrate here. Motion influence has a particularly strong impact on enhancing structures consisting only of a small number (10–100) of voxels.

To compensate for this, registration algorithms try to find a transformation to align images by optimising a similarity measure indicating best matchings. In general, registration

approaches try to find the best solution minimising a global criterion on the whole image. If a region of interest (ROI) – representing a part of the whole dataset – is examined, it cannot be assumed that the best possible matching in terms of the local observation is obtained.

We employ a two-step registration procedure beginning with the first step registering the whole dataset with a global non-rigid approach [6]. In the second step only the ROI is addressed and registered using a rigid approach. For the second step we investigate the performance of three different similarity measures: Mutual Information (MI) [4], Sum of Mean-Squared Distances (MSD) and Normalized Cross Correlation (NCC).

The evaluation is performed by the use of a pharmacokinetic model [5] which simulates the concentration of CA at specific times after the injection. The measured MRI signal enhancement in tumourous regions before and after the second registration step is compared to the simulated signal in order to obtain a fitness quality value.

2 Related Work

For DCE-MRI data of the breast a non-rigid registration procedure is required, because the soft tissue leads to deformation that cannot be described by affine transformations. Guo et al. [2] give a survey about recent approaches of breast image registration techniques in DCE-MRI. Some of those techniques already use a two-step strategy by applying a global rigid and a local non-rigid approach sequentially (e.g. [6]). For two reasons this does not enable optimal results for ROI with small enhancing lesions. First, the criterion to find the local transformation must still be globally constrained to prevent arbitrary deformation. Second, the step finding local transformations aims for a compromise to suit best for all areas in the image. In contrast, we seek a registration for a ROI only.

Tofts et al. [7] have published the first perfusion model to quantitatively analyse DCE-MRI data of the breast. They calculate the CA concentration depending on physical properties, acquisition related parameters and the physiological character of tissue. In general, the latter is unknown and thus is determined by fitting the function to the concentration measured in the image data, leaving physiological values as free parameters. Radjenovic et al. [5] developed a modified model function and performed a practical clinical study to show the applicability of their model. We use it to evaluate our registration results.

3 Registration

The first step of our registration procedure uses the approach of [6] on the whole image. Subsequently, there still exist regions where motion is present. Therefore, the second step performs rigid registration on defined ROI assuming one image out of the series to be fixed and finding transformations for each of the remaining images to match the fixed image. We assume transformations in small ROI to be almost limited to translations with a maximum shift of three voxels and rotations with small angles (up to 10 degrees). ROI are manually defined such that they have approximately the double size of the lesion to be examined.

We want to investigate the performance of different similarity measures to determine the capability to compensate for motion in the presence of noise and signal variation due to CA enhancement in the ROI. We choose the commonly used approaches: MI (as described by Mattes et al. [4] is used), MSD (Eq. 1) and NCC (Eq. 2).

$$MSD(A,B) = \frac{1}{N}\sum_{i=1}^{N}\left(A_i - B_i\right)^2\right) \tag{1}$$

$$NCC(A,B) = \frac{\sum_{i=1}^{N}\left(A_i \cdot B_i\right)}{\sqrt{\sum_{i=1}^{N} A_i^2 \cdot \sum_{i=1}^{N} B_i^2}} \tag{2}$$

A_i and B_i are the i^{th} voxels of an image A and B resp. N is the total number of voxels. We aim to register a set of dynamic images that focus on regions showing perfusion dynamics. MI is used to register images acquired with different modalities as it takes into account the joint entropy of two images. In our case, the images are from the same modality, but are showing different image intensity levels. The MSD measure aligns voxels showing same intensities, which cannot be assumed in our case. However, there are parts of the images showing no dynamics and thus fulfilling the requirement. We expect these parts – the surroundings of enhancing structures – to be sufficiently dominating to guide the registration process. The NCC metric compensates for multiplicative intensity factors through normalization.

4 Evaluation

For evaluation, no ground truth is available because the true motion shift and the resulting deformation of tissue are unknown. Thus, we decided to use the properties of the perfusion and the CA distribution to measure the accuracy of the second registration step. Therefore, the pharmacokinetic model function from [5] is deployed to produce CA concentration over time from areas where perfusion is present (at least 60% on enhancement). The signal intensity SI can be calculated at time t with the two free physiologic parameters v_e and k_{ep} defining the leakage space and capillary permeability using Eq. 4.

$$C_t(t,v_e,k_{ep}) = v_e \frac{D\,(a_1+a_2)}{T}\left(\frac{k_{ep}}{k_{el}^W}\left(e^{k_{el}^W \tau}-1\right)e^{-k_{el}^W t} - \frac{1}{k_{ep}-k_{el}^W}\left(e^{k_{ep}\tau}-1\right)e^{-k_{ep}t}\right) \tag{3}$$

$$SI(t,v_e,k_{ep}) = \left(1+\left(\left(\frac{e^{\frac{-TR}{T1}}}{1-e^{-\frac{-TR}{T1}}}\right)TR\cdot R1\right)C_t(t,v_e,k_{ep})\right)SI_0 \tag{4}$$

The approach uses acquisition related parameters (D, T, $T1$ and τ) and physical constants (k_{el}^W, a_1, a_2) taken from [5] as well as the camera related parameter TR. SI_0 is the pre-injection signal at $t = 0$ and $R1 = 4,5\ mMols^{-1}$ is a relaxivity constant[1]. By varying the two physiologic parameters and least square fitting the resulting function values of $SI(t)$ to the signal enhancement of measured data, the best fitting parameters are determined. A fitness value f characterizing proximity to the model function can be derived by calculating the squared distances to the true MRI signal $M(t)$ with n time steps measured:

$$f = \sum_{t=0}^{n}\left(SI(t,v_e,k_{ep}) - M(t)\right)^2 \rightarrow min. \tag{5}$$

[1] see [5] for more details on parameters

Two different experiments are performed to determine the fitness value achieved by the second registration step. Each experiment is performed before and after the second registration step for each similarity measure. The first experiment calculates a voxel-based fitness value by applying Eq. 5. The second experiment takes into account that single voxels are strongly subject to noise. The region merging procedure from [1] grouping voxels with similar perfusion characteristics is used to average the time signal of several voxels to reduce influence from noise. Then the fitness value of each region is obtained.

In addition, these experiments are performed twice, using a pre-contrast (time step 0) and post-contrast (time step 2) image as fixed image for registration. In pre-contrast phase enhancing structures are not visible and cannot be used in registration. Similarity between different time step images is increased using a post-contrast image as fixed image. The hypothesis is that post-contrast images lead to better results than using the pre-contrast image.

5 Results and Discussion

We carried out the described procedure for 20 small lesions from 16 patient datasets. The datasets have been acquired with a 1.5 T MRI scanner (Philips Medical Systems) using a Spoiled Gradient Echo Sequence with TR $\approx$ 11 ms, TE $\approx$ 6 ms and a flip angle of 25°. For each patient 5–6 dynamic scans have been performed with varying temporal resolution between 62 ms and 110 ms. The first scan is performed without CA. At the end of the first scan CA is injected. The spatial resolution of the whole examination area is 512 $\times$ 512 voxels with 55 to 100 slices acquired. The pixel spacing is 0.6 mm, the slice spacing 1.5 mm.

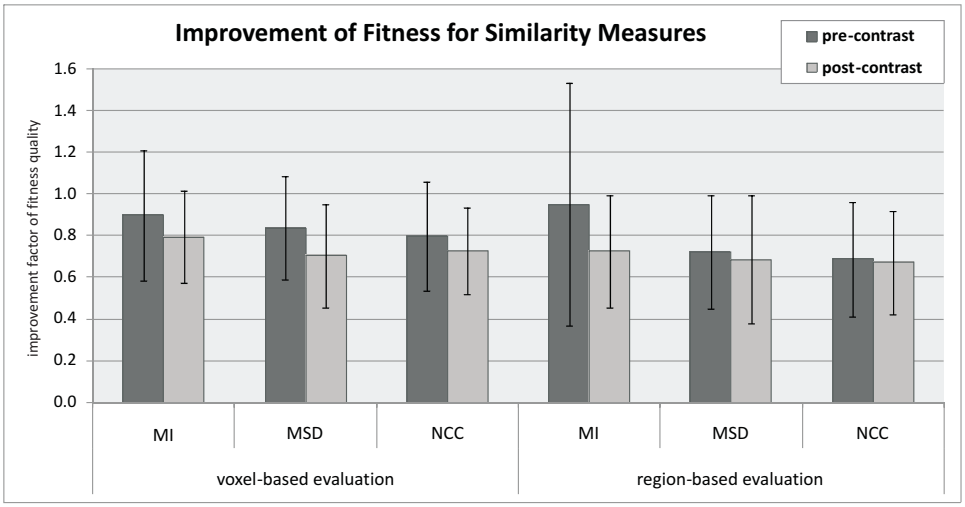

Figure 1: The average improvement of fitness and standard deviation of the experiment: values < 1 indicate improvement, values > 1 indicate deterioration.

We compared three different similarity measures for ROI-based registration of contrast-enhancing lesions in DCE-MRI of the breast. Consistent to our expectations, improvements could be achieved by using all similarity measures, independent of the fixed image used for registration (Fig. 1). In general, the post-contrast image used as fixed image achieves better results. This may be due to the point, that some enhancing structures are simply not visible yet in pre-contrast images. Concerning the similarity measures, NCC achieves the

best improvement overall with 39.4%, followed by MSD with 36,5% and MI with 20.1% (all values averaged over pre- and post-contrast results).

The MSD measure expects same intensities and is based on the surroundings of perfused areas in the first place. Other areas are confounding factors. NCC expects linear correlated scenes, i.e. includes areas which change their intensities in equal measure. On the other hand MI considers local similar areas taking into account that between time steps there may be unequal changes of intensity in different perfusion areas.

Hence, we conclude that the performance of each measure depends on the properties of the ROI, especially the proportion of perfused and non-perfused parts in the image and the dynamic behaviour of lesion surroundings. Through visual exploration we found out that MI performs better, when the whole ROI exhibits CA enhancement at various extent. A more detailed analysis on that is left for further investigation. A general improvement could be to mask out confounding parts of the image depending on the similarity measure used and not considering them in similarity calculation.

The evaluation using a pharmacokinetic model shows that the fit in relation to measured data improves through local registration. This improves the image information relevant for breast tumour diagnosis. In the future, we plan to use the model to describe the change of intensity between the images recorded at different time steps. We want to focus on a combination of the region-based evaluation (segmentation) and a registration process.

6 Acknowledgements

We thank Uta Preim for providing the medical data. This work has been funded by DFG (research grant no. TO166/13-1).

References

[1] S. Glaßer and et al. A visual analytics approach to diagnosis of breast DCE-MRI data. In *Proc. on Vision, Modeling, and Visualization (VMV)*, pages 351–362, 2009.

[2] Y. Guo and et al. Breast image registration techniques: a survey. *Medical and Biological Engineering and Computing*, 44(1):15–26, 2006.

[3] C. K. Kuhl. The current status of breast MR imaging, part I. *Radiol.*, 244(2):356–378, 2007.

[4] D. Mattes and et al. PET-CT image registration in the chest using free-form deformations. *IEEE Trans. on Medical Imaging*, 22(1):120–128, 2003.

[5] A. Radjenovic and et al. Measurement of pharmacokinetic parameters in histologically graded invasive breast tumours using dynamic contrast-enhanced MRI. *Br J Radiol*, 81 (962):120–128, 2008.

[6] D. Rueckert and et al. Nonrigid registration using free-form deformations: application to breast MR images. *IEEE Trans. on Medical Imaging*, 18(8):712–721, 1999.

[7] P. S. Tofts and et al. Quantitative analysis of dynamic Gd-DTPA enhancement in breast tumors using a permeability model. *Magnetic Resonance in Med.*, 33(4):564–568, 1995.