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A Framework for Automated Registration of DCE-MRI Breast Image

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ABSTRACT

Dynamic contrast-enhanced magnetic resonance imaging (DCE-MRI) is a novel imaging technique that is in many aspects superior to mammography USG and regular MRI, for breast cancer diagnostics. Unintentional patient's movement during imaging session greatly reduces value of the acquired data. It can be successfully restored by application of the presented image registration framework.

Keywords : Breast Cancer, Image Registration, DCE-MRI

1. INTRODUCTION

Breast cancer mortality has been greatly reduced in the recent years, thanks to mammography and ultrasonography (USG). However, the World Health Organization reports that still *breast cancer is the leading cancer killer among women aged 20-59 years in high-income countries* 1.

Dynamic contrast-enhanced magnetic resonance imaging (DCE-MRI) is a novel imaging technique that is in many aspects superior to mammography, USG and regular MRI (magnetic resonance imaging) 20. During a DCE-MRI session, a few series of images of the same body region are rapidly acquired before, during and after injection of paramagnetic contrast agent (Gd-DTPA). Propagation of the contrast agent causes modification of MR signal over time. Its analysis provides information on tissue, including tumour characteristics, unavailable with the regular MRI.

A special patient positioning system usually provides stable patient's position during the whole session. For some patients, it may be hard to remain in the same, uncomfortable position for quite a long time. Unintentional movements result with breast deformation and misalignments between consecutive sequences of images. Their analysis is then difficult, inaccurate or even impossible. Repetition of the whole session is problematic due to various factors, including costs. Besides, it does not guarantee a success. The best solution is to restore the proper alignment of the images, by application of image registration techniques.

A great variety of image registration techniques is available 00008. It is relatively easy to choose an optimal algorithm for registration of carefully selected test images. However, it is still a challenge to create a system that could be used in a hospital, in a routine manner. The following problems have to be addressed:

- full automatisation, no need for a specially trained operator,
- no need for special image preprocessing,
- working with not always perfect data, obtained in a hospital, in a routine manner,
- reliability and accuracy adequate to the application,
- acceptable processing time,
- no need for special hardware, working on a standard PC.

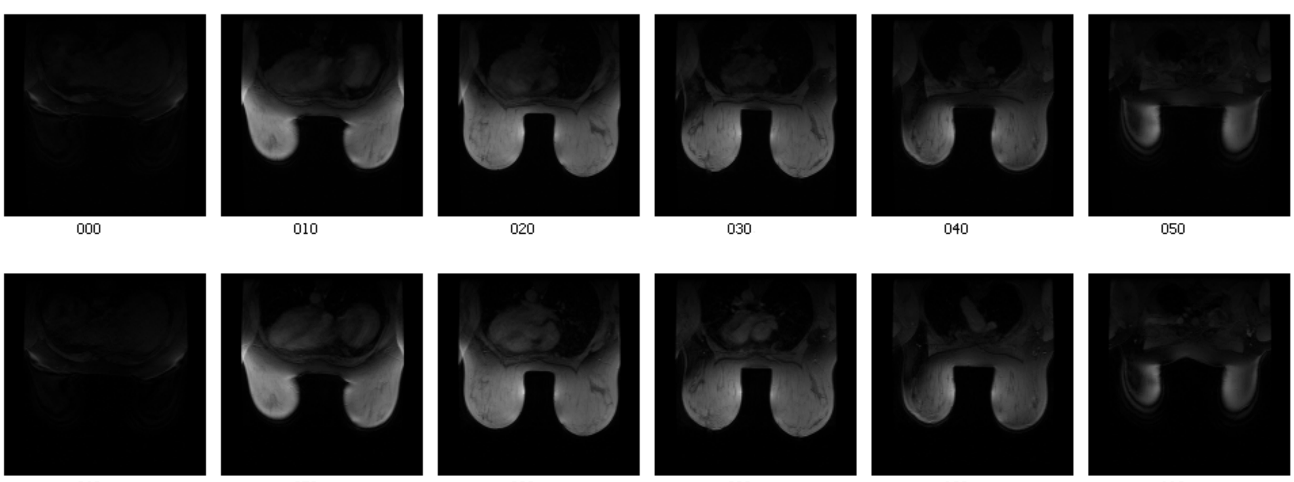

Figure 1: Fragments of the 1st and the 2nd sequence out of 6 image sequences in a single session

2. MATERIALS AND METHODS

2.1 Image data

The main (dynamic) part of every DCE-MRI session consists of six consecutive image sequences showing the same body fragment (Fig. 1.). Each sequence includes around 60 T1 FATSAT axial slices. Their size is 512 by 512 pixels. Every slice is time stamped.

The first sequence is treated as a fixed image. The remaining five sequences are registered to the first one. The whole procedure consists thus of five independent registration subtasks. The registered images are then combined into a new DICOM dataset, preserving all study details.

2.2 Algorithms

In the presented problem, subtle local deformations are expected, rather than large rotations, translations, scaling or shearing distortions. It has been shown that deformable transform, using a B-spline representation is appropriate for breast image registration 00000.

A coarse grid of nodes is associated with an image. Knowing deformations of the node points, a deformation vector for any image point can be then calculated, using B-spline interpolation. Actually, additional 3 nodes are required as a finite support region for the B-spline computation. For example, in order to create a 3D 5×5×5 grid of nodes within an image, 8×8×8 grid needs to be created. The transformation is then described by 1536 parameters (3 parameters per node in a 3D grid) that are to be found.

Then it is necessary to implement a metric, to measure how well images are matched, according to current transformation parameters. Due to tissue properties and type of deformation, registration based on localization of common points (natural structures or artificial markers) in the fixed and the floating image is problematic. It is recommended to use similarity measure that operates directly on image data. In case of multi-modality registration (where correspondence between grey levels in both images is not evident), mutual information is commonly employed:

$$I(X,Y)=H(X)-H(X\,|\,Y) \tag{1}$$

H denotes entropy and X, Y are images that are treated as random variables 0. This option has to be considered, because pixel intensities change during the session, according to concentration of the contrast agent. In the presented solution, implementation proposed by Mates has been tested 0. If intensity changes are negligible, then simple mean squares metric may be adequate 0:

$$MS(X,Y)=\frac{1}{N}\sum_{i=1}^{N}(X_i-Y_i)^2 \tag{2}$$

where X_i and Y_i are pixel intensities on i-th position in images, composed of N pixels.

Evaluation of pixel intensities in non-grid position is performed using a linear interpolator. The optimization process is done with the well known LBFGSB algorithm 0.

The software has been implemented in C++ language (GCC compiler), using ITK library 0 for image processing.

Choice of the above elements of the registration system is rather straightforward. Additional elements are intended to meet the requirements mentioned in the Introduction, related to performance, accuracy and reliability.

The major part of ITK 0 image registration procedures is executed in a single thread, while most of modern PCs have more than two CPU cores. A single registration task consists of five independent image pairs registrations, so it is reasonable to run them in parallel, in five threads. The multithreading features, are based on Boost library (http://www.boost.org/).

The amount of data to be processed can be greatly reduced by performing registration of a region of interest, instead of the whole dataset. However, it needs to be manually selected.

Multi-resolution is a widely used technique to improve both speed and quality of a registration process. Registration is at first performed with smaller (scaled down) images. When the registration criterion is reached, the calculated transformation parameters are used as a starting point for the next step, with larger images. This procedure is usually repeated until the final registration performed with full-scale images.

In the presented framework with B-spline transformation, there are at least two possible ways of multi-resolution implementation. Either several resolutions of the image itself or several resolutions of B-spline grid can be used. Both approaches have been tested. The other possibility is a combination of the two methods mentioned.

3. RESULTS

Figure 1 presents a fragment of a typical dataset. Region of interested (190×180×60 pixels in this case) was selected, to be registered. Figure 2 presents fragments of corresponding slices from the 1st and the 3rd sequence of one of the most problematic datasets. Some misalignments are possible to discover by careful visual inspection. They become evident, when visualized using a pixel-wise squared difference between corresponding pixels (Figure 3) or a checkerboard test (Figure 5).

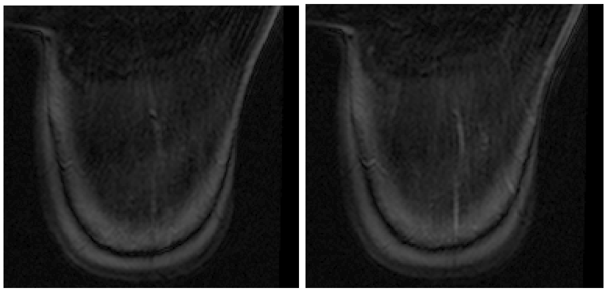

Figure 2: Selected, corresponding slices from the 1st and the 3rd sequence of a problematic dataset.

Figure 4 and Figure 6 present the registration result. The following registration parameters were used: 10 grid nodes on image in every dimension, mean squares metric, gradient tolerance 0.05 (the optimizer's stop criterion). Figure 7 illustrates the registration time, using a simple quad-core PC. Parallelization of the procedure (running each out five registration tasks in a separate thread) resulted with more than 50% time reduction.

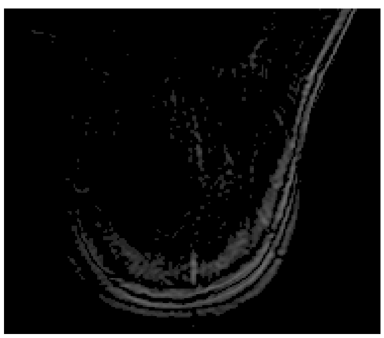

Figure. 3: Pixel-wise squared difference between corresponding slices, before the registration

Figure. 4: Pixel-wise squared difference between corresponding slices of the registered images

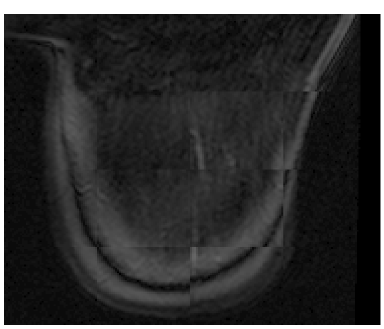

Figure. 5: A checkerboard test for corresponding slices in the 1st and the 3rd sequence, for original slices

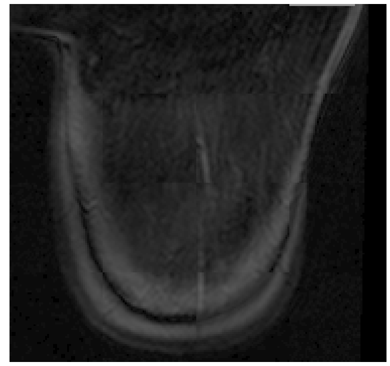

Figure 6: A checkerboard test for corresponding slices in the 1st and the 3rd sequence, and after the registration

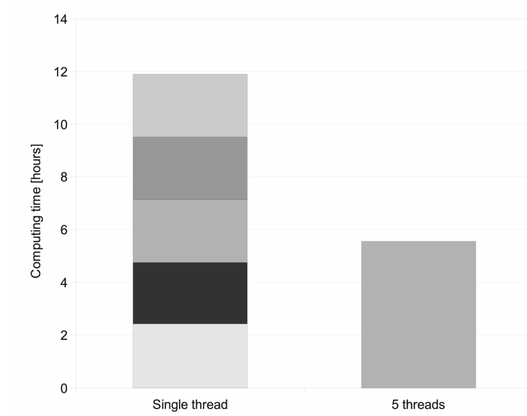

Figure 7: Computation time of five registration subtasks performed sequentially in a single thread or in parallel, using multiple threads on a quad-core processor (Intel™ Core® i5 M520, 2.4 GHz) computer

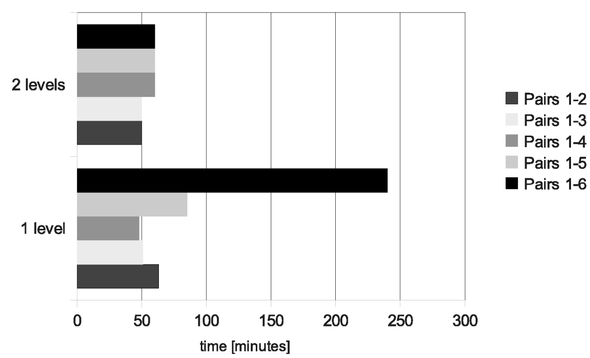

Figure 8: Optimization time, with multi-resolution approach (2 levels) and without it (1 level), Intel R CoreTM i7, 3.2 GHz computer; all image pairs registered in parallel

Figure 8 presents real processing time on a modern computer (with 6 physical processor cores), with and without multiresolution approach (in both cases, all subtasks were performed in parallel). In the multiresolution approach, 7 grid nodes were used in the first level and 10 grid nodes in the second one. Without the multiresolution, one of the image pairs was problematic, due to local extrema problem, extending the whole processing time. In many cases, influence of the multiresolution technique on registration procedure is not evident, but generally, it strongly reduces risk of falling into local minimum (as presented in Fig. 8.).

4. DISCUSSION

Experiments similar to those presented in the above section have been performed on most images from the authors' collection. Registration progress and time vary from image to image and cannot be accurately predicted. However, usually image displacements are much smaller and less complex (thus easier to correct) than the presented ones.

The registration process was successful using both mutual information and mean squares metric, despite the fact that some pixel intensities change during the session. Mutual information estimation is much more computationally and memory intensive, but did not provide superior results in the examined datasets.

The next problem is to set the optimal grid size for B-spline transformations. Adding more nodes results with better accuracy but costs more processing time. It is necessary to find a trade-off between required accuracy and acceptable computing time. Processing time can be greatly reduced by limiting registration process to the region of interest only, but it has to be manually selected by a doctor. Having selected the region of interest, the grid size of 10 - 15 nodes seems to be optimal.

Among other aspects, the optimizer's stop criterion (gradient tolerance) should be considered. Registration accuracy is also limited by the fact that usually voxel size along *z* axis is considerably larger than in *xy* plane, and intensity approximation is needed.

Multithreading usage on a quad-core processor has reduced the computing time by more than 50%. It makes both the accuracy and the computing time acceptable for the hospital the example data comes from.

Multi-resolution application is expected to reduce computing time and to improve accuracy. In most cases, the results were compliant with the expectations (the time was reduced by a few percent, a slightly deeper minimum of the registration criterion was found). For a few percent of the datasets, no positive influence has been observed. For some cases, proper results were very hard to obtain without multi resolution. Generally, multi-resolution approach makes the registration process more stable and predictable, and reduces risk of falling into local minimum. Two multi resolution levels were used. Because of subtle nature of the deformations, application of more levels was pointless. Very similar results were obtained by changing number of grid nodes and by changing image resolution.

To sum up, the accuracy in the region of interest of most of the tested images was satisfactory and made performing of the desired DCE-MRI analyses possible.

Selection of datasets that do need to be registered is also a problematic task. Except for evident cases, it is not trivial to distinguish between misalignments that are acceptable and those that should be corrected. In authors' opinion, it is reasonable to perform a registration process on all datasets. If images are initially properly registered, then the optimisation procedure relatively quickly converges to the identity transform.

5. CONCLUSION

Elastic registration of complex image data, like DCE-MRI breast images, is still a demanding task. However, it has been shown that it is possible to obtain satisfactory and useful results within reasonable time, using a commonly available hardware. The result of multithreading feature is the most spectacular – computing time can be reduced by more than 50%. The effect of multi-resolution technique is more subtle and varies from image to image, but it is assumed to reduce the risk of problems related to local minima.

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