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Dynamic breast MRI: Image registration and its impact on enhancement curve estimation

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Abstract—**A novel algorithm for performing registration of dynamic contrast-enhanced (DCE) MRI data of the breast is presented. It is based on an algorithm known as iterated dynamic programming originally devised to solve the stereo matching problem. Using artificially distorted DCE-MRI breast images it is shown that the proposed algorithm is able to correct for movement and distortions over a larger range than is likely to occur during routine clinical examination. In addition, using a clinical DCE-MRI data set with an expertly labeled suspicious region, it is shown that the proposed algorithm significantly reduces the variability of the enhancement curves at the pixel level yielding more pronounced uptake and washout phases.**

I. Introduction

Dynamic contrast-enhanced (DCE) magnetic resonance imaging (MRI) of the breast is becoming more widely used in the clinical setting as a supplemental imaging modality [1-6] to conventional x-ray mammography and ultrasound. In particular it is being used to rule out cancer in the case of suspicious lesions found using conventional x-ray mammography, and to evaluate the extent of disease within a breast affected by cancer [7]. During a DCE-MRI examination the breast volume is imaged as a set of two-dimensional slices, before and at several times after the injection of a contrast agent, to yield a four-dimensional data set (see Fig. 1). The pattern of contrast enhancement, i.e. the change in signal intensity over time, is an important criterion for the differentiation of malignant from benign lesions. The patterns for most cancers show an early steep rise within five minutes of contrast-agent injection, followed by a plateau, and then washout, whilst those for benign lesions either do not enhance, or exhibit slowed continued enhancement with delayed washout [3]. These enhancement patterns reflect the underlying microvascularity differences between malignant tissue exhibiting neovascularisation and benign lesions with more normal microvascularity [8].

Typically, a DCE-MRI examination takes about 10-15 minutes during which time the patient is expected to lie perfectly still. In the routine clinical setting, subtraction data (post-contrast minus pre-contrast) are visually assessed to determine whether or not there has been any significant movement during image acquisition. In the absence of any obvious movement, it is generally assumed that the patient has not moved and that each voxel (three-dimensional pixel) of the acquired data corresponds to a single spatial location in the breast. In reality any movement during acquisition, including subtle long-term movements such as relaxation of the pectoral muscles, invalidates this assumption. The time-course data for a single voxel may then in fact be a combination of enhancement curves for different tissue types. This can lead to misinterpretation of the significance of enhancing lesions. This is especially true for small lesions. To improve the accuracy of enhancement curve estimation it is necessary to perform volume registration; i.e. to spatially align the pre- and post-contrast volumes.

Rigid registration methods (i.e. methods that compensate for global motion) are in general not well suited to spatial registration of DCE-MRI breast data. This is because breast tissue is heterogeneous and elastic and patient movement is likely to cause local non-linear deformation. Consequently, non-rigid registration is preferable [9-14]. An additional complication peculiar to the registration of DCE-MRI breast data is that the injection of contrast agent leads to localized changes in intensity over time. As a result intensity-based non-rigid registration algorithms tend to increase or decrease the volume of enhancing structures [15]. In this paper we present a novel non-rigid registration algorithm based on iterated dynamic programming [16]. We demonstrate the efficacy of the algorithm using synthetic data. In addition we demonstrate that the method can significantly improve the quality of enhancement curve estimation in real data.

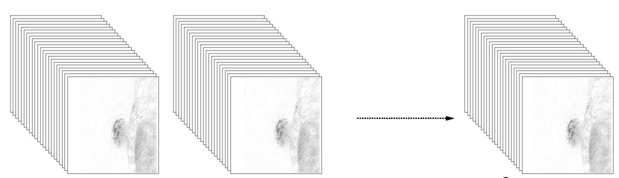

Fig. 1: Four-dimensional DCE-MRI data set (sagittal slices)

II. Iterated Dynamic Programming

A. Overview

Iterated dynamic programming (IDP) is an optimization algorithm that can be used to determine a registration

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solution by finding the optimal solutions to a set of one-dimensional problems using dynamic programming (DP [17]). In any given iteration the solution for a given pixel takes into account the solutions of its neighbors. The algorithm limits the search space of possible solutions by considering only integer pixel shifts. This opens the possibility for performing registration faster than other algorithms published in the literature.

Iterated dynamic programming was originally devised to solve the stereo matching problem. The stereo matching problem is concerned with estimating a three-dimensional scene from a combination of right eye and left eye two-dimensional images of the scene. This involves finding the location of each object in both the right and left eye views. The apparent displacement, called parallax, of an object between the two images is used to infer the distance the object is from the viewer. This is very similar to the motion correction problem in the sense that one image is distorted such that the same physical location ends up in the same image location across the set of images under study.

DP is of interest in image registration because the optimal solution to a one-dimensional registration problem can be expressed as a *shortest path* problem which can be solved via DP. Attempting to find a solution to a multidimensional problem by decomposing it into a set of one-dimensional problems and solving these independently is unsatisfactory. In the two-dimensional case a solution obtained by solving row-wise with DP is unsatisfactory because the rows are treated independently and solutions for adjacent rows can be significantly different. IDP overcomes this problem by adding a weighting factor to the row solution that forces each row to take into account the solutions for the rows above and below. Given that these solutions are not initially known an initial estimate is required. This is usually obtained by solving each row independently using DP[1]. The IDP algorithm iterates through the rows solving each single row with DP to obtain its current optimal solution with respect to those already obtained. After several passes through the data the algorithm converges and a minimum is reached. The algorithm does not guarantee that this is the global minimum but only a *strong* local minimum.

IDP was originally devised for the stereo matching problem and as such the parameters and error functions used within the optimization are designed to be discontinuity preserving; i.e. designed not to smooth the discontinuities that occur along the edges of objects. In the case of the DCE-MRI breast registration problem, however, there are no discontinuities. For this reason we devised two major changes to the IDP algorithm as originally described: (i) a new edge function; and (ii) a larger window size.

B. Proposed modifications for breast MRI registration

In the case of stereo matching discontinuities in the shift between adjacent pixels are expected at object boundaries as a sudden change in depth is observed. If the smoothness of the solution between adjacent pixels is enforced across this boundary then the edges of the object will not be correctly assigned. In relation to the breast registration problem, there are no discontinuities within the solution space because the breast tissue is continuous, and as such any solution in which discontinuities are present should be avoided.

The major factor in the original IDP algorithm that determines the likelihood of discontinuities within the solution is the edge function. This function defines how differences in movement between adjacent pixels are penalized with distance. The original error function is a piece-wise linear function (see Fig. 2) with a constant error or penalty if the difference in movement between adjacent pixels (i.e. *shear* in the image) is more than one pixel. When applied to the breast registration problem this can yield large-scale image shear. This is because the error function equally penalizes both small and large shifts either side of the V shape. This motivated the definition of the new error function shown in Fig. 2. The new function does not significantly penalize small differences, allowing the solution to include fine adjustments for local non-linearities. However, any solution that has a shear between adjacent pixels of more than one is deemed to be worse than one with a smooth solution. In contrast to the original error function the new function results in larger discontinuities being penalized more strongly than smaller ones, allowing the algorithm to converge to a solution with the least number of discontinuities. The largest shear permitted by the new error function is a single pixel shift per pixel. This ensures that areas which previously had a large shear attain a solution similar to their neighbors. The exception to this is if the statistical match at the current location is much stronger than any other alternative within the search region.

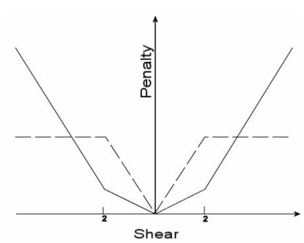

Fig. 2: The original (dashed line) and proposed (solid line) error functions. Note that shear is an absolute value, and as such the graph is symmetric.

The second modification to the IDP algorithm is the window size defining the neighborhood in which the match is performed. This was increased from 4, optimized for stereo matching, to 11 to compensate for noise and the lack of small-scale geometric features in the breast MRI images. This permits a better statistical match to occur at each individual location and thus leads to an overall improvement

[1] IDP converges to a similar solution when an initial guess of no movement is chosen.

in the solution[2]. The larger window size permits neighboring pixels to attain a strong match for the same area and thus achieve similar solutions. This helps to preserve the desired spatial continuity.

C. Evaluation on artificially distorted image data

To evaluate the suitability of IDP for the registration of DCE-MRI breast data, several artificial distortions of a real DCE-MRI breast image (sagittal slice, 512×512 pixels, 16-bit gray-scale) were created using a custom control-point-based non-linear distortion algorithm. Fig. 3 shows one such example where a grid of 5×5 control points was used and each control point allowed to move independently within 25 pixels (x and y) of its original location. New x and y coordinates for each pixel were interpolated and the distorted image generated by resampling the original image at these locations. The modified IDP algorithm was then used to register the distorted image to the undistorted image (requiring a 51×51 pixel search region for the correct solution). Apart from some (minor) discontinuities in areas where the apparent volume of the features significantly changed as a result of the artificial distortion, the modified IDP algorithm performs very well. This is especially remarkable given the large distortion artificially generated.

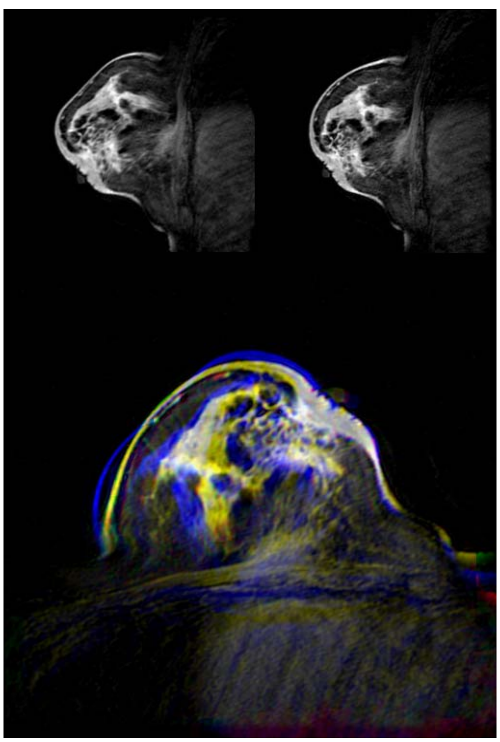

Fig. 3 Top left: Distorted image (source); Top right: Original undistorted image (target). Bottom: RGB composite image showing the registration of the source to the target (blue is the source, green is the target, and red is the registration result). Ideally no red or green should be visible.

[2] In the case of the stereo matching problem, a large window is a big disadvantage because it tends to smooth boundaries. Rather, a smaller window is advantageous because it produces a weaker edge effect at the discontinuities at the edges of objects.

III. The Impact of Registration on the Estimation of Enhancement Curves

Although a variety of methods for analyzing enhancement curves in DCE-MRI data of the breast have been proposed (see [18]), the most commonly adopted approach in routine clinical practice is the qualitative approach [4]. This involves the manual review of the raw four-dimensional data and derived subtraction images to identify areas of suspicious enhancement, and a qualitative evaluation of the shape of the associated enhancement curves. Tissue of a malignant nature usually exhibits characteristic rapid uptake, plateau, and washout kinetics. Benign tissue displays either no enhancement, or slowed continued enhancement with delayed washout [3]. Any movement by the patient can potentially change the shape of the enhancement curves. Intuitively one would expect the probability and severity of movement to increase the longer the patient has been lying in the MRI scanner. Registration should therefore improve the accuracy of the intermediate to late portions of the enhancement curve. To test this hypothesis we obtained a DCE-MRI data set from a routine clinical breast examination which exhibited significant movement (apparent in the subtraction images). Fig. 4(a) shows a subtraction image (last-post-contrast minus pre-contrast) for one of the spatial slices. The movement is particularly evident in areas where there is dark blue shadowing of several features. The arrow superimposed on the image shows the location of a small region-of-interest (ROI) selected by the interpreting radiologist. Fig. 4(b) shows the enhancement curve for each individual pixel in the ROI and also the mean curve (dashed black line) for the ROI. Fig. 4(c) shows the subtraction image for the same slice after registration of each post-contrast volume to the pre-contrast volume using the modified IDP algorithm. Fig. 4(d) shows the pixel enhancement curves for the ROI derived from the registered data. What is particularly striking about the enhancement curves after registration is that the intermediate to late portions of the curves have much less variation. A comparison of the two sets of curves suggests that significant movement occurred at the fourth time point. The dashed black curve, without registration, is the one used by the radiologist to evaluate the nature of the enhancing lesion. Interestingly this curve shows a small increase after seven minutes despite the fact that biologically the concentration of the contrast agent must be falling. After registration this anomaly is no longer present. Moreover it can be clearly seen that the curve has a more pronounced uptake and washout.

IV. Conclusion

In this paper a novel non-rigid registration algorithm for spatial registration of DCE-MRI data of the breast was presented. The algorithm is based on iterated dynamic programming and several modifications to improve its suitability for the breast MRI registration problem. The suitability of the proposed algorithm was demonstrated using artificially distorted real-world data. In addition the proposed algorithm was applied to DCE-MRI data from a routine breast MRI examination containing movement artifact of up to four pixels. It was shown that even with this small degree of movement, registration can significantly impact on the accuracy and quality of the estimated enhancement curves. In particular, correction for movement in the intermediate to late post-contrast phases of enhancement significantly influences the shape of the curve. Accurate registration should lead to a more accurate assessment of suspicious lesions. The proposed modified IDP algorithm shows promise as a method for accurate and fast spatial registration of DCE-MRI data of the breast.

V. ACKNOWLEDGMENT

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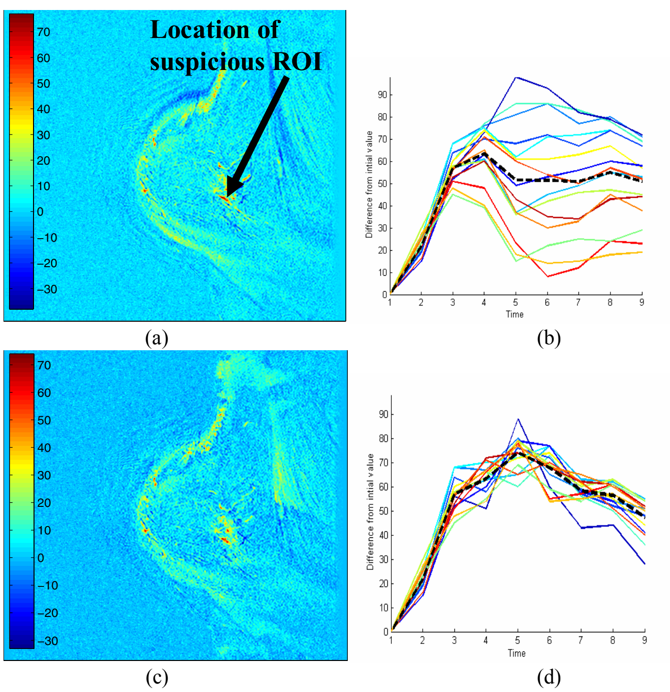

Fig. 4: (a) Subtraction image (last post-contrast minus pre-contrast) of a slice from a DCE-MRI data set containing significant movement artifact of up to four pixels (~2 mm). (b) Enhancement curves for the individual pixels of a suspicious 15 pixel ROI, indicated in *(a)*, selected by a radiologist. The dashed black curve is the mean. (c) Subtraction image corresponding to *(a)* after registration of each post-contrast volume to the pre-contrast volume using the proposed algorithm. (d) Enhancement curves for the ROI indicated in *(a)* after registration.

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