A practical method to compute coefficients for regularization term in nonrigid registration of DCE-MRI

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Introduction: Dynamic contrast-enhanced magnetic resonance imaging (DCE-MRI) allows an analysis of the variations of magnetic resonance (MR) signals by using contrast agents. The time-intensity curves can be used in the detection of tumors. However, the motion in between the image acquisitions can complicate the analysis. Nonrigid registration is extensively used in DCE-MR image analysis to achieve alignment between images. It can be formulated as an optimization problem to minimize the image dissimilarity [1]. However it not only reduces the occurred motion but also may change the volume of enhanced regions, e.g. cancer tissue in post-contrast images [2]. A spatial-variant rigidity regularization term was proposed to preserve the rigidity of tissues [3]. When applying the term in nonrigid registrations of DCE-MRI, it requires a coefficient on each voxel in a moving image to determine the penalty weight based on the tissue types. This study proposes a framework to compute the coefficients of rigidity terms, such that the terms can be applied practically without explicit tissue segmentation.

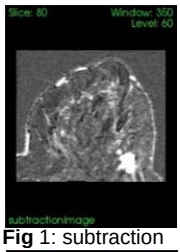

Fig 1: subtraction

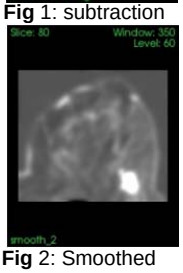

Fig 2: Smoothed

Method: The assumption of the method is more enhanced tissues are more rigid in DCE-MRI. A pre-registration is performed to register the pre-contrast image to each post-contrast image. A subtraction image (Fig 1) is obtained, identifying the corresponding tissue enhancement information. A sigmoid function is applied to map the voxel intensity in the smoothed subtraction image (Fig 2) to form the regularization coefficients (Fig 3). All parameters of the sigmoid function are determined by a k-means method. Let $I(x)$ be the intensity value at voxel x in a subtraction image, the sigmoid function $\gamma(x)$ is written as equation below. It transforms $I(x)$ to a new range with a center α and scale β.

$$\gamma(x) = \frac{max - min}{\left(1 + e^{-\left(\frac{I(x)-\beta}{\alpha}\right)}\right)} + min$$

$\max$ and $\min$ are maximum and minimum intensity of the smoothed subtraction image, α and β are determined by performing a k-means method on the smoothed subtraction image, by partitioning it into k groups with various intensity means. The highest intensity mean is assigned to β and the standard deviation is assigned to α.

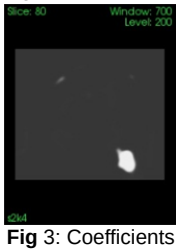

Fig 3: Coefficients

Evaluation: We use both clinical and synthetic DCE-MRI data in the evaluation. **1**.Synthetic data: We select 3 clinical DCE-MR breast images without obvious motions to generate 30 synthetic images with simulated deformations. A pre-contrast image f_0 and second post-contrast image g_0 are used to form an image pair. Enhanced tumors s_0 are manually segmented from g_0. In each deformation simulation, we randomly generate two rigid transformations (T_{r1}, T_{r2}) and two B-spline transformations with a control point space of 10 and 20mm. We later update these B-spline parameters to (T_{b1}, T_{b2}) such that the tumors are rigidly deformed by enforcing the related control points to be 0. The final transformation $T_{truth}(x) = T_{b1} \circ T_{r1} \circ T_{b2} \circ T_{r2}$ are used to construct synthetic pre- and post-contrast images (f_1, g_1) and tumor mask s_1 where $f_1 = f_0, g_1 = T_{truth}(g_0), s_1 = T_{truth}(s_0)$. **2**.Registration schemes: We perform registrations using two methods to compute regularization coefficients: $\gamma(x) = 1$ for volume-preserving constraint (VPC) [2]; and a binary function based on manual segmentation of tumors (MRC) and our proposed automatic method $\mathrm{ARC}(k = 2,3,4,5)$ for rigidity constraint [3]. Initial rigid registrations are employed in all tests. A multi-resolution scheme (grid space of $8,16,32,64$ mm) is employed in all bspline-based nonrigid registrations [1]. **3**.Metrics: Target registration error (TRE) is used to measure the alignment between two voxels in terms of deformations. Normalized correlation (NC) and mean square error (MSE) are used to measure the image recovery in terms of intensity. Tumor volume change is measured by applying the estimated transformation T_{est} on the tumor mask s_1.

Result: The results on synthetic images are shown on the left of Table 1. Rigidity constrained schemes of $\mathrm{ARC}(k = 3,4,5)$ and MRC perform better than volume-preserving constrained (VPC) schemes in terms of smaller mean TRE and RMS, higher NC over the whole breast and tumor regions and less tumor volume loss. As $\mathrm{ARC}(k)$ increases from 2 to 4, the registration performance improves, except for the TRE is larger over the breast regions. The reason could be $\mathrm{ARC}(2)$ apply penalty on larger enhanced regions, and preserve the deformation of these enhanced regions in addition to enhanced tumors. The registration results on 5 clinical images are shown on the right of Table 1. Only NC is used to compute the image similarity between the registered post- and pre-contrast images due to their different intensity levels. All registration schemes show similar NC value. ARC and MRC better preserve tumor volumes than VPC.

Conclusion: We proposed a framework to compute regularization coefficients in nonrigid registration in application to DCE-MRI of breast using a sigmoid mapping method on a smoothed subtraction image obtained from a pre-registration. The proposed method can replace the manual segmentation method to compute the rigidity term coefficients and the method is robust to the choice of k value.

Reference:[1] Rueckert et.al. IEEE TMI,1999. [2] Rohlfing et.al. IEEE TMI 2003. [3] Staring et.al. Medical Physics, 2007

Table 1. Evaluation results on synthetic and clinical data

	Synthetic data							**Clinical data**	
	Breast regions			Tumor regions				Breast regions	Tumor regions
	TRE	RMS	NC	Vol change	RMS	NC	Vol change	NC	Vol change
VPC	2.40±1.36	37.30±4.50	0.81±0.04	0.02±0.02	49.32±3.36	0.82±0.03	0.04±0.02	0.81±0.04	0.02±0.02
ARC(2)	1.32±1.04	35.61±4.67	0.81±0.04	0.00±0.00	45.35±6.22	0.85±0.04	0.04±0.04	0.81±0.04	0.00±0.00
ARC(3)	1.55±0.95	34.91±3.56	0.81±0.05	0.00±0.00	45.22±5.97	0.85±0.03	0.03±0.02	0.81±0.05	0.00±0.00
ARC(4)	1.60±0.97	34.62±3.87	0.81±0.04	0.00±0.00	44.59±5.41	0.85±0.03	0.01±0.01	0.81±0.04	0.00±0.00
ARC(5)	1.60±0.71	34.75±3.94	0.81±0.04	0.00±0.00	44.72±5.07	0.85±0.02	0.01±0.01	0.81±0.04	0.00±0.00
MRC	1.50±0.86	34.40±3.87	0.81±0.04	0.00±0.00	44.76±4.88	0.85±0.02	0.01±0.01	0.81±0.04	0.00±0.00