Intensity based image registration by minimizing exponential function weighted residual complexity

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ABSTRACT

In this paper, we propose a novel intensity-based similarity measure for medical image registration. Traditional intensity-based methods are sensitive to intensity distortions, contrast agent and noise. Although residual complexity can solve this problem in certain situations, relative modification of the parameter can generate dramatically different results. By introducing a specifically designed exponential weighting function to the residual term in residual complexity, the proposed similarity measure performed well due to automatically weighting the residual image between the reference image and the warped floating image. We utilized local variance of the reference image to model the exponential weighting function. The proposed technique was applied to brain magnetic resonance images, dynamic contrast enhanced magnetic resonance images (DCE-MRI) of breasts and contrast enhanced 3D CT liver images. The experimental results clearly indicated that the proposed approach has achieved more accurate and robust performance than mutual information, residual complexity and Jensen–Tsallis.

1. Introduction

Medical image registration is an essential and fundamental task to clinical diagnosis. On the aid of the image registration and fusion technology, physicians use computed tomography (CT) images to compute the radiation dose, and magnetic resonance (MR) images to describe tumors in radio-therapeutic treatment planning [1]. In operation navigation, surgeons can precisely locate a region of interesting in order to design a careful operation plan for surgery tracking according to the registration results of CT/MR/DSA [2]. In addition, medical image registration has a wide variety of applications in creation of population averages, cardiac motion estimation [3], the estimation of tumor parameters [4], and so on.

Similarity measure is a crucial component in image registration. For the sake of simplicity, it can be common to use intensity-based similarity measure rather than feature-based similarity measure. The frequently used intensity-based similarity measures are defined by corresponding pixel intensities between images to be aligned. The state of the art intensity-based similarity measures include sum of squared differences (SSD) [5], sum of absolute differences (SAD) [6], correlation coefficient (CC) [7] and mutual information (MI) [8,9]. The aforementioned methods are restricted to the assumption that the intensity relationship of the corresponding pixels is independent and stationary. However, images with intensity distortion or intensity bias field do not satisfy the assumption. The intensity distortion is mainly caused by intensity bias field in MRI. In addition, compared to pre-contrast enhanced image, post-contrast enhanced image of the same patient could be supposed to possess the property of intensity non-uniformity [10]. Non-uniformity image registration is a challenging task because of its violation on the assumption of the pixel-wise independence or stationarity.

To deal with this problem, a number of methods have been proposed over the years, which can be summarized into three categories. The first and the largest kind of category utilize local measures defined only on a small pixel neighborhood [11–13]. The intuitive idea of such approaches is that a spatially varying intensity distortion is constant within a small pixel neighborhood. In general, methods based on local similarity measures performed better than those using global similarity measures. However, such local approaches are much more sensitive to noise and outliers than global measures. Moreover, it is also an expensive computation. As an alternative approach, more probabilistic models are adopted to construct higher order pixel interdependence. Such technique heavily relies on the definition of local intensity interactions [14–16]. The third kind of methods correct for intensity distortions simultaneously with image registration. Friston et al. [17] proposed to align images with SSD. They corrected the intensity distortions with a convolution filter and nonlinear intensity transformation defined with linear combination of several basis functions. Moderstizki and Wirtz [18] used a similar approach and defined the multiplicative intensity correction function with a total variation regularizer. Such hybrid methods require intensity correction function to be defined accurately.
Moreover, such methods can be more time consuming. In more recent work, Khader and Hamza [19] proposed a generalized information-theoretic similarity measure for non-rigid image registration. This method optimized the Jensen–Tsallis (JT) entropic similarity measure using the Quasi-Newton as optimization scheme. Cubic B-splines was used to model the non-rigid deformation field. Then, the analytical gradient of JT measure was derived so that an efficient and accurate image registration can be achieved. However, it must use a similarity measure with suitable optimization technique to improve the image registration. Also, it requires fewer iterations but more computations. Andriy et al. [20] performed residual complexity measure to solve the intensity correction field. The problem of such approach is that it is sensitive to parameter. Relatively minor modification of the parameter can generate dramatically different results. In addition, it is sensitive to noise and outliers.

Inspired by the robust estimation [21], we present a robust similarity measure, Exponential function Weighted Residual Complexity (EWRC), to deal with this problem, which is an extension to the residual complexity. In this paper, residual complexity is modified by taking local variance of the reference image into account. To be more specific, we constructed an efficient weighting function using local variance [22] of the reference image in exponential form. The weighting function could automatically constrain the residual term in residual complexity. The residual term refers to residual image, which is defined as the difference image between reference image and warped floating image. Generally, local variance of noise or outliers is usually large in the medical image. Hence, if the local variance of the pixel is large in reference image, the corresponding pixel in residual image will be weighted with smaller weight to weaken the influence of outliers or noise, and vice versa. In other words, the new similarity measure weights residual image automatically, which ensures the accuracy and robustness of the registration.

The rest of the paper is organized as follows. In Section 2, we elaborate on the proposed EWRC in progressive manner, including residual complexity, local variance, EWRC, transformation and optimization. In Section 3, we test our method on artificial and real patient data. In addition, comparisons are made between the proposed approach and MI, RC, JT. Finally, the conclusion and future work orientation is presented in Section 4.

2. Method

2.1. Residual complexity

A widely used model to express the intensity relationship between the reference image \( I \) and the floating image \( J \) is as follows:

\[
I = f(x) + S + \eta \tag{1}
\]

\( S \) is an intensity correction field, \( \eta \) denotes zero mean Gaussian noise. \( \tau \) is the spatial transformation that aligns \( I \) and \( J \). We can estimate \( \tau \) and \( S \) by maximizing the posteriori probability:

\[
P(\tau,S|I,J) \propto P(I|\tau,S)P(\tau)P(S) \tag{2}
\]

where we assume that \( S \) and \( \tau \) are independent. The term \( P(I|\tau,S)\) and \( P(\tau)\) denote a joint likelihood of the images and the prior of transformation, respectively. \( P(S) \) is the prior of correct field that reflects the spatial intensity interaction. Generally, \( P(S) \) can be formulated as \( P(S) \propto e^{-\beta|PS|^2} \) (we have not yet specified the form of \( P \)). Maximization of the posteriori probability is equivalent to minimization of the following objective function:

\[
E(S,\tau) = ||J-I(\tau)||^2 + \beta ||PS||^2 \tag{3}
\]

where \( I, J \) and \( S \) are in column-vector form of reference image, floating image and intensity correction field, respectively. Compute the correct field \( S \) analytically by means of solving the derivation in (3) to zero:

\[
S = (Id + \beta PP^T)^{-1}r \tag{4}
\]

Then, substitute \( S \) back to the objective function (3):

\[
E(\tau) = r^T(\text{id} - \beta PP^T)^{-1} \tau \tag{5}
\]

where \( \text{id} \) is the identity matrix, and \( r = I-J(r) \) is the residual vector (residual image). For simplicity, the square matrix \( PP^T \) is symmetric and positive semi-definite. So it permits spectral decomposition \( PP^T = Q \Lambda Q^T \), \( \Lambda = \text{diag}(\lambda_1, ... , \lambda_n) \), \( \lambda_i \geq 0 \). Then

\[
E(\tau) = r^T Q \Lambda(\beta/1 + \beta \lambda_i) Q^T r = r^T Q \Lambda Q^T r = r^T \text{Ar} \tag{6}
\]

\( d() \) denotes the diagonal matrix, and \( A = Q \Lambda Q^T \). \( L = d(l_1, ... , l_n) = d(\lambda_i/(1 + \beta \lambda_i)), l_i \geq 0 \). Operator \( PP^T \) has the same eigenvector basis \( Q \) and different eigenvalues. We select discrete cosine transformation (DCT) [20] for the basis of eigenvectors. Now, if we choose a proper \( L \), then \( A \) is known. Therefore

\[
E(\tau, l) = r^T Ar = (Q^T r^T L Q^T r) \geq 0 \tag{7}
\]

It is obvious that if \( L \) is an identity matrix, then \( E(\tau, l) = ||r||^2 \), i.e. SSD. That is equivalent to no intensity correction. If \( L \) is a zero matrix, \( E \) achieves the minimum with no interesting. So we define a regularization term on \( L \):

\[
E(\tau, l) = (Q^T r^T L Q^T r) + \alpha RL(l); \quad l_i \geq 0 \tag{8}
\]

here, \( R(L) = \sum p_i \log(p_i/l_i) + l_i - p_i \). \( \alpha \) is a trade-off parameter. \( Q = [q_1, ... , q_n] \). \( q_i \) are eigenvectors in \( Q \). Differentiate Eq. (8) with respect to \( l_i \) and set the derivative to zero, after which, substitute the result back into Eq. (7), ignoring the terms independent of \( l_i \), we get the similarity measure:

\[
E(\tau) = \sum_{n=1}^N \log \left( \frac{(Q^T r^T)^2}{\alpha} + 1 \right); \quad r = I - J(\tau) \tag{9}
\]

2.2. Local variance image

Local variance [22] indicates the intensity relationship from pixel to pixel in a local region. We can achieve image details by analyzing the distribution of local variance. The local variance about the reference image \( I \) in position \((x,y,z)\) is as follows:

\[
V(x,y,z) = \frac{1}{(2R+1)^2} \sum_{k=-R}^{R} \sum_{l=-R}^{R} \sum_{w=-R}^{R} \sum_{s=-R}^{R} \left( h(k,l,p) \right) \left( \frac{1}{(2R+1)^2} \sum_{w=-R}^{R} \sum_{s=-R}^{R} \left( h(k,l,p) \right) w s w s \right) \tag{10}
\]

\( V(x,y,z) \geq 0 \), and \( N = (2R+1) \times (2R+1) \times (2R+1) \) is the window size of local variance. \( R \) is window radius. For ease of presentation, we used a brain MR in 2D. Fig. 1 demonstrates local variance images with different window sizes: \( N = 3 \times 3 \), \( N = 5 \times 5 \) and \( N = 7 \times 7 \).

For a fixed window size \( N \), local variance is small in the homogeneous region, and it is relative larger in the nonhomogeneous region as shown in Fig. 1. Furthermore, the local variance image with small window size expresses abundant and clear information. Conversely, the relative fuzzy information is described with large window size. In other words, window size influences the smoothness of the local variance images.

2.3. Exponential function weighted residual complexity

In statistics, an outlier is an observation that is numerically distant from the rest data. Huber [21] proposed the robust estimation theory to decrease the statistical error caused by outliers.
In theory, rule function is designed to meet the following condition: it can tolerate big data error so as to decrease the influence of outliers to solution. In other words, rule function assigns lower value to big data error, and higher value to small data error. Hence, this approach will not be pursued and is reasonable since the weighted values $\omega$ is required to avoid division by zero. However, if $V(x,y,z) \to 0$, then $\omega(x,y,z) \to 1/\epsilon$.

$\omega(x,y,z)$ acts as the weighting function constructed by the reciprocal of local variance of the reference image. A small value $\epsilon$ is required to avoid division by zero. However, if $V(x,y,z) \to 0$, then $\omega(x,y,z) \to \infty$. Hence, this approach will not be pursued and is presented here for completeness. Another efficient way of achieving this is to construct a new weighting function in the form of exponential function:

$$\omega(x,y,z) = e^{-\frac{V(x,y,z)}{\sum_{x=1}^{N}V(x,y,z)/h}}; \quad V(x,y,z) \geq 0$$

where $0 < \omega(x,y,z) \leq 1, m \times n \times s$ is the number of voxels, and $h$ is a constant to adjust the range of $\omega$. Too gathered value in $\omega$ is unreasonable since the weighted values $\omega$ are approximate for different intensities in residual image. To avoid this pitfall, we chose $h=0.01$ empirically in this paper.

Then, we substituted the weighting function to residual complexity in (9). Thus, the new similarity measure EWRC:

$$E(r) = \frac{1}{N} \sum_{n=1}^{N} \log ((\omega_0(r,0))^{2} / \alpha + 1)$$

where $\omega_0$ denotes the weight matrix. $\omega(x,y,z)$ is the element of weight matrix $\omega$. Note that there is no weighted term $\omega$ for residual image in residual complexity. In other words, all voxels in residual image are weighted equally, i.e. $\omega = 1$. If outliers and noisy points are weighted equally as other points in residual image, it will cause considerable bias and deterioration in the quality of the estimation. So we introduced weighting function to constrain the residual image automatically. The influence of weighting function to the voxel value in residual image is decreased when local variance is large, and increased when it is small.

As mentioned previously, it is a challenge task for non-uniformity image registration. We used two gray stripe images to illustrate it, and cropped down Fig. 3(a) symmetrically. Then, Fig. 3 (b) is obtained by corrupting it with spatially varying intensity field.

We shifted Fig. 3(b) from −50 to 50 (pixels) in horizontal axis and calculated the similarity measures between the reference image and the shifted floating image. The two images will be matched absolutely if the floating image translates zero pixels. The registration functions of SAD, MI, RC, JT and the proposed EWRC with respect to different translation parameters are shown in Fig. 4. If the two images are aligned successfully, the function of MI achieves the maximum. SAD, RC, JT and EWRC all come to the minimum.

We can observe that the registration functions of SAD and MI cannot get the optimum at the correct image alignment (zero translation). While, the registration functions of RC, JT and EWRC achieve the global minimum at zero translation. However, there are a lot of local minima in the registration functions of RC and JT.
\[ \tau \] from the position of the Free Form Deformation (FFD) transformation model \[23\]. The FFD transform based on cubic B-spline is chosen because of local control characteristic for the position \( x=(x, y, z) \) in each voxel the deformation is calculated from the position of the 4 × 4 × 4 neighborhood control points:

\[
\begin{align*}
\phi(x) &= \frac{3}{2} \sum_{i=0}^{3} \sum_{j=0}^{3} \sum_{k=0}^{3} B_i(u) B_j(v) B_k(w) \varphi_{ij,k} \delta_{m-i,n-j,k-n}, \\
\delta_{m-i,n-j,k-n} &= \begin{cases} 
1 & \text{if } m-i=n-j=k-n \\
0 & \text{otherwise}
\end{cases}
\end{align*}
\] (14)

where \( \varphi \) denotes a \( n_x \times n_y \times n_z \) mesh of control points \( \varphi_{ij,k} \) with uniform spacing \( \delta, i=[x/n_x], j=[y/n_y], k=[z/n_z], u=x-[x/n_x], v=y-[y/n_y], w=z-[z/n_z] \). \( B_i \) represents the \( i \)th basis function of the B-spline:

\[
\begin{align*}
B_0(u) &= (1-u)^3/6 \\
B_1(u) &= (3u^3-6u^2+4)/6 \\
B_2(u) &= (-3u^3+3u^2+3u+1)/6 \\
B_3(u) &= u^3/6
\end{align*}
\] (15)

B-spline is locally controlled, i.e. limited support, such that changing one control point only affects the transformation in local neighborhood of the manipulated control points. It makes the computation efficiently, even for a large number of control points.

### 2.4. Transformation

We model the transformation \( \tau \) using the Free Form Deformation (FFD) transformation model \[23\]. The FFD transform based on cubic B-spline is chosen because of local control characteristic for the position \( x=(x, y, z) \) in each voxel the deformation is calculated from the position of the 4 × 4 × 4 neighborhood control points:

\[
\begin{align*}
\tau(x) &= \frac{3}{2} \sum_{i=0}^{3} \sum_{j=0}^{3} \sum_{k=0}^{3} B_i(u) B_j(v) B_k(w) \varphi_{ij,k} \delta_{m-i,n-j,k-n}, \\
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resolution, the local variance image of the reference image is computed only one time since the reference is fixed.

3. Experiments and results

We have applied the proposed EWRC measure to brain MRI, DCE-MRI of breast and contrast enhancement liver images. Compared to MI, RC and JT measures, five sets of experiments were designed to validate the proposed technique. There is not only an initial affine transformation in image registration, but only FFD transformation model based on cubic B-spline was used. We normalized image intensity to interval [0, 1] before registration.

All the experiments were conducted on the Matlab R2011a environment on Widows Operatory System with Intel 2.33 GHz and 8 G of RAM. To assess the quality of registration, we have calculated the mean, variance of absolute residual image (ARI) as well as the similarity. For notation, we use μ and σ to denote mean and variance, respectively. Here, absolute residual image is defined as the absolute difference between the reference image and final warped floating image. We exploited mutual information to describe the similarity between the reference image and final warped floating image. To avoid the confusion, we denoted similarity by Msim:

$$A Ri(x, y, z) = |I(x, y, z) - J(τ(x, y, z))|$$

$$Msim = H(I) + H(J(τ)) - H(I, J(τ))$$

Here, $A Ri(x,y,z)$ is the absolute residual value in the position $(x,y,z)$. $H(I)$ and $H(J(τ))$ denote the marginal entropy of reference image $I$ and warped floating image $J(τ)$ respectively. $H(I, J(τ))$ is the joint entropy. In particularly, if the similarity $Msim$ is higher, the image registration method is more efficient, and vice versa. The lower $μ$ and $σ$ are, the smaller registration error is, otherwise, the higher $μ$ and $σ$ are, the bigger registration error is.

3.1. The registration of non-uniformity image with Gaussian noise

To validate the proposed methodology, we tested it using the MNI BrainWeb phantom (http://mouldy.bic.mni.mcgill.ca/brainweb) [24]. A cross slice (256 × 256 pixels) of the isometric T1-weighted MRI volume was used. We generated synthetic example by both geometric and intensity distortions. Thin-plate spline (TPS) transformation was adopted to perform geometric distortions. To simulate the spatially varying intensity distortion, images were corrupted according to the formula proposed by Andriy [20]. Moreover, various levels of Gaussian noise were considered. In order to avoid confusion, we used $μ_α$ and $σ_α$ to denote the mean and variance of the added noise respectively. In this section, we utilized these synthetic images to perform two groups of experiments. As shown in Fig. 6, the blank spaces between the columns separate the two groups of images.

In this experiment, the proposed EWRC measure was compared with other three widely used similarity measures, including MI, RC and JT. These four compared similarity measures were run with the same parameter in each group. In the two groups of experiments, $α = 0.8, δ = 8$ and $α = 0.6, δ = 7$ were used respectively. Fig. 5 shows the results obtained from this experiment, including the final warped image and the deformed mesh. The blank spaces between columns separate the four similarity measures. Columns from left to right: (a) MI, (b) RC, (c) JT, and (d) EWRC. The four rows correspond to the two groups of experimental results respectively. As is shown in the first two rows, if we used the algorithm based on the MI measure, multiple mis-registration regions appeared in final warped floating image, and serious folding effect displayed in deformed mesh. Then, mis-registration region appeared only in the pons part of brain, and relative less folding effect displayed.
in deformed mesh when exploiting image registration based on RC measure. The red arrows indicate the locations of mis-registration in Fig. 7. We observed that the mis-registration region still appeared only in the pons part of brain when performing image registration using JT measure. But there was less folding effect in deformed mesh than the one of RC measure. However, the two brain images were aligned successfully with the proposed EWRC measure, and there was no folding effect in the deformed mesh. In addition, we could observe the similar results in another group of experiment shown on the last two rows. As previously mentioned, MI measure showed poor performance with significant misalignment since MI is sensitive to noise and intensity distortion, while RC regularizes the intensity correction field automatically so as to generate the improved performance. Nevertheless, the poor robustness of RC results in undesirable registration results. JT measure is a generalized information-theoretic similarity measure. It is a combination of JT divergence and Tsallis entropy, a generalization of Shannon entropy. The analytical gradient of JT measure makes the registration efficient and accurate. Even though the results obtained by JT measure outperformed those obtained by RC measure, experimental results were provided to demonstrate that the results obtained by JT measure.
measure gave poor registration accuracy than those of EWRC measure. In this paper, the residual image was weighted by exponential weighting function constructed by local variance of the reference image. Therefore, the proposed EWRC achieved the satisfactory registration results, including the final warped floating image and final deformed mesh.

3.2. The sensitivity of registration to window size \( N \)

It is interesting to investigate whether the choice of window size \( N \) of local variance will influence the registration performance. To complete this, we introduced two groups of DCE-MRI of the breast from different patients. The dataset used in the experiments were obtained from Tianjin General Hospital, China. The images have a size of 384 × 384 pixels and a spatial resolution of 0.52 × 0.52 mm. Fig. 8(a) and (b) demonstrates two DCE-MRI images after contrast enhancement at different times for patient 1. Similarly, Fig. 8(c) and (d) shows two images at different times after contrast enhancement for patient 2. We defined both Fig. 8(a) and (c) as reference images, Fig. 8(b) and (d) as floating images. For all experiments in this section, EWRC measure was used with \( \alpha = 0.05, \delta = 8 \).

Fig. 9 demonstrates the residual color maps between reference image and warped floating image. Fig. 9(a) shows the performance before registration. Fig. 9(c) and (d) illustrates the results after registration with window sizes \( N=3 \times 3, N=5 \times 5 \) and \( N=7 \times 7 \) respectively. According to the color bar in Fig. 9, blue color denoted by ‘0’ indicates perfect registration, while red color denoted by ‘250’ presents poor registration. Visually, all registration results performed better than the ones before registration. Moreover, all results after registration provided a very similar improvement.

Further, we evaluated the performance quantitatively to validate there is no obvious discrepancy in registration results with different window sizes \( N \). This is reflected by Msim and \( \mu \) in Fig. 10. The labels ‘patient 1’, ‘patient 2’ in the horizontal axis correspond to the two groups of experiments in Fig. 10. The blue color denotes the experimental results before registration. The green, yellow and red color denote the registration results after registration with \( N=3 \times 3, N=5 \times 5 \) and \( N=7 \times 7 \) respectively. Obviously, the histograms were approximate for \( \mu \) and Msim with different window sizes. From this experiments, we found that the window size \( N \) of local variance had little influence to the performance of the proposed method. Therefore, we utilized \( N=3 \times 3 \) for all of the following experiments so as to improve computational efficiency, unless otherwise specified.

3.3. The sensitivity of registration to spacing \( \delta \)

We also tested the sensitivity of similarity measures to the mesh spacing \( \delta \) (defined in Section 2.4). The dataset used in the

![Fig. 8. DCE-MRI of breast for two patients. (a) and (b) Images after contrast enhancement at different times of patient 1. (c) and (d) Images after contrast enhancement at different times of patient 2.](image)

![Fig. 9. The residual color maps with different window sizes. The blank space between rows separates the patients. Columns from left to right: (a) The residual color maps before registration. (b)–(d) The residual color maps generated by the proposed EWRC measure with different window sizes: (b) \( N=3 \times 3 \), (c) \( N=5 \times 5 \), (d) \( N=7 \times 7 \). (For interpretation of the references to color in this figure caption, the reader is referred to the web version of this article.)](image)
experiments were obtained from Tianjin General Hospital, China. We selected DCE-MRI images at different times. The images have a size of 384 × 384 pixels and a spatial resolution of 0.52 × 0.52 mm. We defined one image as reference image in this test (Fig. 11(a)), and another image deformed artificially was defined as floating image in Fig. 11(b). Then, our similarity measure was compared with RC and JT measures using \( \delta = 6 \) and \( \delta = 10 \) in sequence respectively. In addition, the three compared similarity measures were executed with the same parameters.

In this experiment, we set the parameter \( \alpha = 0.05 \). Fig. 12 shows the results obtained from this experiment including the warped floating image and deformed mesh. The first two columns demonstrate the registration results using \( \delta = 6 \), and the last two columns demonstrate the registration results using \( \delta = 10 \). Rows from top to bottom: warped floating image and deformed mesh based on the RC measure, warped floating image and deformed mesh based on the JT measure, warped floating image and deformed mesh using EWRC measure. It was obvious that there were some mis-registration regions in warped floating image, and serious folding effect in deformed mesh when using RC measure with \( \delta = 6 \), as shown the first two figures on the top row, especially in the red arrows in Fig. 12. The red arrows indicate the locations of mis-registration. Similarly, the final warped floating image was completely wrong, and the serious folding effect also appeared when adopting RC measure with \( \delta = 10 \), as shown the last two figures on the top row in Fig. 12. If JT measure, a combination of JT divergence and Tsallis entropy (a generalization of Shannon entropy), was applied in this experiment, we can observe that both the warped floating image and deformed mesh outperformed those obtained by RC measure, as shown on the middle row in Fig. 12. In this paper, we incorporated local variance in the form of exponential function to constrain the residual image. No matter \( \delta = 6 \) or \( \delta = 10 \), the two images were matched successfully, seen in the last rows of Fig. 12. Note that the warped floating images obtained by JT and EWRC measures were visually similar. However, the deformed mesh resulted from EWRC measure was smoother than the one obtained by JT measure. Also, no folding effect appeared in the deformed mesh using proposed EWRC measure. These experimental results validated that the proposed approach is robust to mesh spacing \( \delta \).

Table 1 lists the statistical results using different mesh spacings for the three similar measures after image registration. For a fixed mesh spacing, the value of \( \mu \) or \( \sigma \) resulting from EWRC measure was smaller than the one of JT measure. Meanwhile, the values of \( \mu \) and \( \sigma \) obtained by RC measure achieved the highest among the three measures, and vice versa in Msim. This illustrated that the EWRC measure had the smallest registration error among the three similarity measures, and JT measure had a smaller registration error than RC measure. Moreover, it was obvious that there was large discrepancy for different mesh spacing in \( \mu, \sigma \) or Msim when using RC measure followed by JT measure. However, no obvious discrepancy was presented with the proposed EWRC measure. In this experiment, we found that the similarity measure, EWRC, was robust to mesh spacing than RC and JT measures.

3.4. Artificial deformation examples

In this section, we employed 4 groups of DCE-MRI of breast from different patients. The dataset used in the experiments were obtained from Tianjin General Hospital, China. The images have a size of 384 × 384 pixels and a spatial resolution of 0.52 × 0.52 mm. We defined four images at one time from four patients as reference images as shown on the top row in Fig. 13. The floating images could be obtained by artificially deforming the other four images at another time as shown on the bottom row in Fig. 13. For comparison, these four groups of DCE-MRI of breast were registered using MI, RC, JT, and EWRC, respectively. Then, we did qualitative and quantitative analyses.

We set parameters \( \alpha = 0.05 \). \( \delta = 6 \) for the first two groups of images in Fig. 13(a) and (b). Parameters \( \alpha = 0.9 \). \( \delta = 6 \) were used for the last two groups of images respectively, seen in Fig. 13(c) and (d). The residual maps between the reference image and final warped floating image are shown in Fig. 14. The blank spaces between rows separate the similarity measures. The rows from top to bottom: MI, RC, JT, EWRC. Each column represents the residual maps for a patient. According to the gray bar in Fig. 14, too dark or too bright color indicates poor registration. We observed that there were many dark and bright pixels in residual map when using MI measure as seen on the top row in Fig. 14. Some pixels were dark and bright in residual maps when using RC measure, as shown in the second row. The red arrows indicated the locations of mis-registration. JT measure is an entropic similarity measure based on JT divergence and Tsallis entropy. The analytical expression of the gradient of JT measure makes image registration efficient and accurate. In comparison with RC measure, there were fewer dark and bright pixels in residual maps when using JT measure, as shown on the third row. However, there were slight amount of dark or bright pixels in the residual maps after applying the proposed EWRC measure as shown on the bottom row. It employed exponential weighting function to constrain the residual term in residual complexity automatically. Intuitively, EWRC measure performed well and outperformed the widely used similarity measure MI, RC, and JT.

The histograms of \( \mu \) and Msim are plotted in Fig. 15. The labels in horizontal axis denote the experimental results for different patients. Fig. 15(a) illustrates that EWRC measure had the smallest registration error followed by JT measure, RC measure, and MI. As is shown in Fig. 15(b), similarity achieved the maximum when...
using EWRC measure followed by JT and RC measure. All of these demonstrated that the proposed EWRC measure outperformed other three similarity measures.

3.5. Patient examples in 3D

To validate the performance of the proposed approach in 3D, a group of pre- and post-contrast enhanced CT data was used in this test. As is shown in Fig. 16, they were acquired using a Philips Brilliance 64-Slice CT scanner at different times from the same

![Fig. 11. Two breast images to be aligned. (a) Reference image. (b) Floating image.](image)

![Fig. 12. Registration results with different mesh spacings. The blank spaces between the rows separate the similarity measures. Rows from top to bottom: RC, JT and EWRC. The blank spaces between the columns separate the mesh spacing: (a) Final warped floating image with $\delta = 6$. (b) Deformed mesh with $\delta = 6$. (c) Final warped floating image with $\delta = 10$. (d) Deformed mesh with $\delta = 10$. (For interpretation of the references to color in this figure caption, the reader is referred to the web version of this article.)](image)

<table>
<thead>
<tr>
<th>Mesh spacing</th>
<th>Method</th>
<th>$\mu$</th>
<th>$\sigma$</th>
<th>$\text{Msim}$</th>
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<tr>
<td>$\delta = 10$</td>
<td>RC</td>
<td>7.1394</td>
<td>483.8234</td>
<td>1.6394</td>
</tr>
<tr>
<td></td>
<td>JT</td>
<td>4.0620</td>
<td>102.5482</td>
<td>1.9992</td>
</tr>
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<td></td>
<td>EWRC</td>
<td>3.5116</td>
<td>42.0778</td>
<td>2.1531</td>
</tr>
<tr>
<td>$\delta = 6$</td>
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<td>2.2655</td>
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<tr>
<td></td>
<td>JT</td>
<td>3.2821</td>
<td>40.2148</td>
<td>2.2694</td>
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<tr>
<td></td>
<td>EWRC</td>
<td>3.1445</td>
<td>38.9338</td>
<td>2.2702</td>
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</tbody>
</table>
patient. The size of each CT data is $512 \times 512 \times 397$, and the voxel size is $0.68 \times 0.68 \times 0.50$ mm. In this experiment, the proposed EWRC measure was compared with RC and JT measures. The three compared similarity measures were run with the same parameter $\sigma = 0.0001$, $\delta = 5$.

For ease of presentation, we demonstrated the residual color maps before and after registration in three views. Fig. 17 shows the registration results obtained from this experiment. The first two rows denote the cross view in 68th slice and 98th slice respectively. The middle two rows demonstrate the 64th slice and 100th slice in coronal view. The 53rd slice and 83rd slice in sagittal view are displayed on the last two rows respectively. Intuitively, the residual color maps before registration showed a relative motion due to considerable patient movement in Fig. 17 (a), see the red arrows. Generally, the motion could be reduced after registration, as shown in Fig. 17(b)-(d). That is, the three algorithms provided improvement. As mentioned above, RC regularizes the intensity correction field automatically. Nevertheless, the poor robustness of RC results in undesirable registration results. Therefore, the images could not be aligned successfully when RC was used as similar measure. The red arrows indicate the locations of mis-registration in Fig. 17(b). JT measure is an extending entropic method, which is deduced from JT divergence and Tsallis entropy. The results also illustrated that the residual color maps obtained by JT measure in Fig. 17(c) show less motion than those obtained by RC measure in Fig. 17(b). That is, most of the visible amount of misalignment has been removed after applying the JT measure, indicating the better performance of the JT measure than RC measure. In this paper, the residual image was weighted by exponential weighting function constructed by local variance of the reference image. We observed that EWRC measure achieved better registration results than those of JT measure, since less motion was found in the residual color maps in Fig. 17(d). In other words, the proposed EWRC was an effective similar measure for the registration of the contrast enhanced images.

Table 2 displays the quantitated results using different similarity measures in this experiment. The first column shows the evaluation criteria, including $\mu$, $\sigma$, and $\text{MIsim}$. The second column displays the statistics before registration. The last three columns list the statistics when using RC, JT and EWRC measures respectively. It can be observed that the values of $\mu$ and $\sigma$ based on EWRC measure were always smaller than those of RC and JT measures, and vice versa in $\text{MIsim}$. The results clearly demonstrated that the registration based on RC measure improved the registration accuracy in a way. Although the results obtained by JT measure outperformed the ones obtained by RC measure, they performed worse than those of the proposed EWRC measure. In a word, experimental results were provided to demonstrate EWRC was a more efficient similarity measure.

4. Conclusion and future research orientation

An intensity-based similarity measure is proposed for medical image registration. The presented EWRC is an extension to residual complexity proposed by Andiry. It employs carefully designed weighting function to constrain the residual term in residual complexity. The residual term is defined as the difference image between reference image and warped floating image. Then, the weighting function is constructed with local variance of the reference image in the form of exponential function. Generally, local variance of noise or outliers is usually large in medical image. We need to reduce the influence of noise or outliers to objective function. Hence, the pixel in residual image will be weighted with a smaller weight if the local variance of the corresponding pixel is larger in reference image.

In this paper, we applied our method on brain magnetic resonance images, dynamic contrast enhanced magnetic resonance image (DCE-MRI) of breast and contrast enhanced 3D CT liver images. Then, comparisons were made to MI, RC and JT, these comparisons were chosen especially because MI is a typical intensity-based similarity measure, and RC is an effective technique to process contrast enhanced images or medical images with intensity non-uniformity in some cases. In particular, the basic ideal of MI relies on the assumption of independence and stationarity of the intensities from pixel to pixel. Such measure cannot capture the complex interactions among the pixel intensities, especially in the presence of noise, intensity distortion and contrast agent. Even though RC performs better than MI, it is sensitive to parameters. Relatively minor modifications of
parameters can generate dramatically different results. JT measure proposed by Khader and Hamza is an extending entropic method, which requires a few iterations. However, it is a time-consuming task. In contrast, the proposed EWRC measure is validated to be robust to parameters. Both qualitative and quantitative experimental results indicate our method has a better performance. In the current form of our work, we only consider the application to areas where images are from monomodality. Generally, multi-modality image registration is an important issue in medical image analysis. Future work will extend the proposed registration algorithm to multi-modality images.

Fig. 14. The residual maps between reference image and warped floating image with registration algorithm based on MI, RC, JT and EWRC. The blank spaces between rows separate the similarity measures. From top row to the bottom row is MI, RC, JT and EWRC. The columns form left to right: (a)–(d) correspond to the registration results from patient 1 to patient 4. (a) Patient 1. (b) Patient 2. (c) Patient 3. (d) Patient 4. (For interpretation of the references to color in this figure caption, the reader is referred to the web version of this article.)

Fig. 15. The histograms of $\mu$ and $M_{\text{Sim}}$. (a) Histogram of $\mu$ using four similarity measures (MI, RC, JT, EWRC) for different patients. (b) Histogram of $M_{\text{Sim}}$ using four similarity measures for different patients. The blue, green, yellow and red colors correspond to MI, RC, JT, and EWRC respectively. (For interpretation of the references to color in this figure caption, the reader is referred to the web version of this article.)
Fig. 16. The pre- and post-contrast enhanced CT data before registration. (a) Post-contrast enhanced CT data used as fixed volume. (b) Pre-contrast enhanced CT data used as moving volume.

Fig. 17. Residual color maps before and after registration in three views. The blank spaces between rows separate views. They are cross view, coronal view and sagittal view, respectively. Columns from left to right: (a) Registration results before registration. (b) Registration results based on RC measure. (c) Registration results based on JT measure. (d) Registration results based on EWRC measure. The red arrows indicate where our method has a best performance than other measures. (For interpretation of the references to color in this figure caption, the reader is referred to the web version of this article.)
Table 2

<table>
<thead>
<tr>
<th>Evaluation criteria</th>
<th>Before registration</th>
<th>RC</th>
<th>JT</th>
<th>EWRC</th>
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<tr>
<td>μ</td>
<td>8.0092</td>
<td>6.7478</td>
<td>6.0428</td>
<td>5.7552</td>
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<td>σ</td>
<td>316.0564</td>
<td>220.8566</td>
<td>173.6521</td>
<td>169.7269</td>
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<tr>
<td>Msim</td>
<td>3.0708</td>
<td>3.0620</td>
<td>3.1342</td>
<td>3.176</td>
</tr>
</tbody>
</table>

Conflict of interest statement

None declared.

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