Registering multiple medical images using the shared chain mutual information

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A new approach to the simultaneous registration of multiple medical images is proposed using shared chain mutual information (SCMI) as the matching measure. The presented method applies SCMI to measure the shared information between the multiple images. Registration is achieved by adjusting the relative position of the floating image until the SCMI between all the images is maximized. Using this measure, we registered three and four simulated magnetic resonance imaging (MRI) images using downhill simplex optimization to search for the optimal transformation parameters. Accuracy and validity of the proposed method for multiple-image registration are testified by comparing the results with that of two-image registration. Furthermore, the performance of the proposed method is validated by registering the real ultrasonic image sequence.

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Image registration is one of the important and fundamental research fields in image processing, pattern recognition, and motion estimation. Over the past few years, various studies have been reported for image registration, so that it can adapt to diverse clinical applications. Mutual information (MI) based registration methods [1−3] have shown great promise. However, MI only can describe the relationship between two random variables, which means that MI only can be used as a similarity measure to register a pair of images.

In certain situations, it is often necessary or desirable to obtain several images of a scene or scans of the same patient. The series of images can reveal the dynamic development and reflect the state of human organs at different times. Comparing the position or state changes between images, which are derived at different times, can facilitate detection of potentially dangerous changes, or success of therapy.

For multiple images registration, generally, the first image is selected as the reference image, the second image can be registered to the first one, and the third image can be registered to the first two pre-registered images, and so on. Based on the above registration scheme of multiple images, we propose a new image registration criterion, which can easily measure the shared mutual information of multiple images according to the chain rule, i.e., it is sensitive to the information of a new image with the pre-registered multiple images, and is called shared chain mutual information (SCMI).

Given two discrete random variables A and B, the mutual information between them is defined as

$$\begin{aligned} I(A;B) &= H(A) + H(B) - H(A,B) \\ &= H(A) - H(A|B) = H(B) - H(B|A), \end{aligned} \quad (1)$$

where $H(A)$ and $H(B)$ are the entropies of A and B. $H(A,B)$ is the joint entropy; $H(A|B)$ and $H(B|A)$ are the conditional entropies, which can measure the uncertainties in A given knowledge of B, and in B given knowledge of A, respectively.

For another discrete random variable C, the conditional mutual information between random variables C and B given knowledge of A is defined as

$$I(C;B|A) = H(C|A) - H(C|B,A), \quad (2)$$

where $H(C|B,A)$ is the conditional entropy, which measures the uncertainty of variable C given knowledge of B and A.

Here we use a Venn diagram, shown in Fig. 1, for visualizing the relationship of mutual information $I(A;B)$ and conditional mutual information $I(C;B|A)$ with the entropies of variables A, B, and C. The area of each circular region represents the entropy of a random variable. The joint entropy is the combined area of the individual entropy. The conditional entropies are the remaining uncertainty in either random variable given knowledge of the other. In Fig. 1(a) the intersecting area represents the mutual information $I(A;B)$, while the dark grey area in Fig. 1(b) represents the conditional mutual information $I(C;B|A)$.

The SCMI of variable C with B and A is defined as

$$I(C;B,A) = I(C;A) + I(C;B|A), \quad (3)$$

where $I(C;A)$ denotes the mutual information between C and A, $I(C;B|A)$ denotes the conditional mutual information described in Eq. (2).

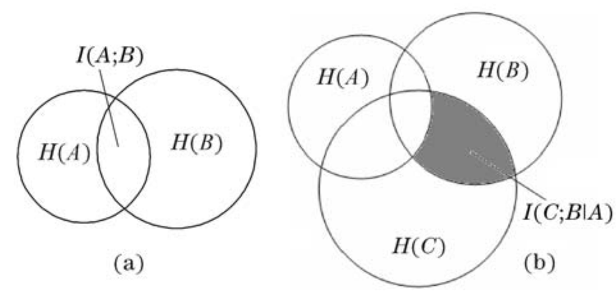

Fig. 1. (a) Mutual information $I(A;B)$ and (b) conditional mutual information $I(C;B|A)$ with the entropies of A, B, and C.

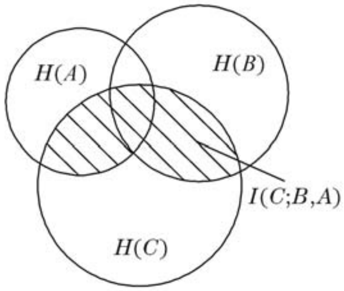

Fig. 2. SCMI $I(C;B,A)$ with the entropies of A, B, and C.

Figure 2 gives the relationship of the SCMI $I(C;B,A)$ with the entropies of A, B, and C. The shadowed area represents $I(C;B,A)$. From Fig. 2 it can be seen that the SCMI can measure the shared information of variable C with B and A simultaneously.

Now let us extend the SCMI of three variables, mentioned above, to more general conditions. Considering multiple variables $U_1, U_2, \cdots, U_n$, the joint entropy of them can be given as

$$H(U_1, U_2, \cdots, U_n) = \sum_{i=1}^{n} H(U_i | U_{i-1}, \cdots, U_1), \tag{4}$$

here, when n is equal to 1, we consider that

$$H(U_1 | U_0) = H(U_1). \tag{5}$$

The conditional mutual information of random variables U_i and U_{i-1} given knowledge of $U_{i-2}, \cdots, U_1$ is equal to

$$\begin{aligned} & I(U_i; U_{i-1} | U_{i-2}, \cdots, U_1) \\ & = H(U_i | U_{i-2}, \cdots, U_1) - H(U_i | U_{i-1}, \cdots, U_1). \end{aligned} \tag{6}$$

Applying Eqs. (1), (4), and (6), the SCMI of variable U_n with variables of $U_{n-1}, \cdots, U_1$ can be written as

$$\begin{aligned} & I(U_n; U_{n-1}, \cdots, U_1) \\ & = H(U_{n-1}, \cdots, U_1) - H(U_{n-1}, \cdots, U_1 | U_n) \\ & = \sum_{i=1}^{n-1} H(U_i | U_{i-1}, \cdots, U_1) - \sum_{i=1}^{n-1} H(U_i | U_{i-1}, \cdots, U_1, U_n) \\ & = \sum_{i=1}^{n-1} I(U_n; U_i | U_{i-1}, \cdots, U_1). \end{aligned} \tag{7}$$

Especially, SCMI of two variables is just MI between them. From Eq. (7) it can be seen that SCMI can be obtained by calculating the sum of a series of conditional mutual information. Because SCMI is a kind of mutual information too, according to the properties of mutual information, we can get the non-negative property of SCMI, i.e.,

$$I(U_n; U_{n-1}, \cdots, U_1) \geq 0, \tag{8}$$

where $I(U_n; U_{n-1}, \cdots, U_1)$ equals zero if and only if U_n and U_i are conditional independent given $U_{i-1}, \cdots, U_1$. In addition, SCMI has symmetry, i.e.,

$$I(U_1, \cdots, U_{n-1}; U_n) = I(U_n; U_1, \cdots, U_{n-1}). \tag{9}$$

Based on above analysis, we investigate a registration method for multiple medical images. Figure 3 shows the diagram of the proposed multiple images registration using SCMI as criterion. It imposes an initial transformation T_0 to floating image U_n, and then calculates SCMI of reference images $U_{n-1}, \cdots, U_1$ with the transformed image $T_0(U_n)$. If SCMI achieves its maximum, the registration process will terminate. Otherwise, an optimization algorithm is used to update the transformation T, until the SCMI of $U_{n-1}, \cdots, U_1$ with $T(U_n)$ gets to the maximum, and the optimal transformation can be received to transform U_n to yield the registered image.

We conduct four simulations to test the validity and accuracy of the proposed method. Figure 4 shows four simulated images. Figure 4(a) is a two-dimensional (2D) magnetic resonance imaging (MRI) image. Figure 4(b) is derived by adding white zero-mean Gaussian noise with variance of 0.007 to Fig. 4(a). Because the difference between Figs. 4(a) and (b) is only the noise, so they can be

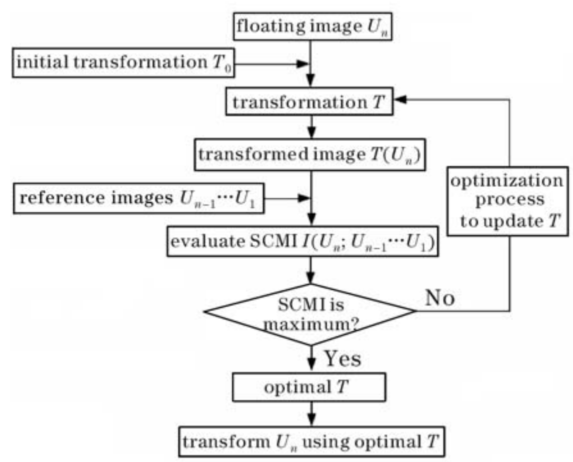

Fig. 3. Flow diagram of multiple images registration using SCMI as criterion.

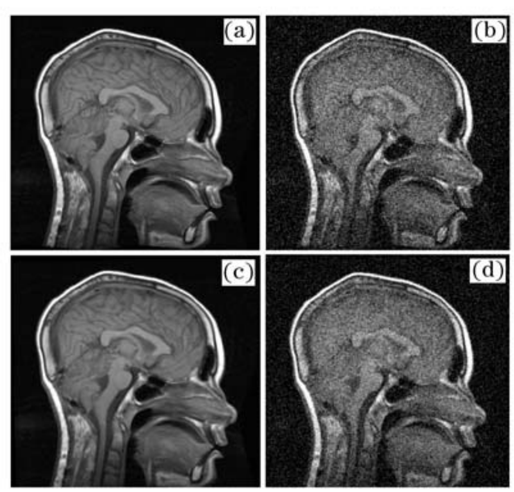

Fig. 4. Simulated MRI images.

considered as spatially pre-registered. Figure 4(c) is derived by transforming Fig. 4(a) by horizontal translation of 2 pixels, vertical translation of 4 pixels and rotation about the image plane 2°. While Fig. 4(d) is derived by adding white zero-mean Gaussian noise with variance of 0.005 to Fig. 4(c). The first two simulations are to register the image Fig. 4(c) to Fig. 4(a) and Fig. 4(b) respectively. The third simulation is to register Fig. 4(c) to the first two images from Figs. 4(a) and (b) using the proposed method. We can evaluate the registration accuracy of multiple images through comparing the results of the third simulation with the first two simulations. The last one is to register Fig. 4(d) to three pre-registered images, including Fig. 4(a), Fig. 4(b), and compensated Fig. 4(c) by the result of the third simulation, to test the registration validity of more than three images.

In our registration process, downhill simplex method is selected as the optimization algorithm to search for the optimal transformation. In N dimensions, a simplex is the geometrical figure consisting of $N+1$ vertices, and every vertex represents one solution of N dimensional space, which is related to the N independent searching variables. In searching process, the vertices of simplex are moving according to the operations of reflections, expansions, and contractions. When the decrease in the SCMI value of every vertex is fractionally smaller than some tolerance ftol, the algorithm is terminated, and the received vertices are the optimal transformation. The detailed information about downhill simplex method can be found in Refs. [4,5]. In our simulation, some initial vertices for simplex must be set first. Under 2D registration process, there are three independent variables, i.e., translation along horizontal direction t_x, translation along vertical direction t_y, and rotation in the plane θ, which are written as $[t_x\ t_y\ \theta]$. Here, four initial vertices vectors are set as $P_0 = [0\ 0\ 0]$, $P_1 = [1\ 0\ 0]$, $P_2 = [0\ 1\ 0]$, $P_3 = [0\ 0\ 1]$. P_0 is denoted as the transformation without any translations and rotation. P_1 is a transformation with translation along horizontal direction of one pixel and without translation along vertical direction and rotation. Analogously, P_3 and P_4 are denoted as transformations with translation along vertical direction of one pixel and rotation of one degree, respectively. Second, a tolerance ftol is set to 0.1.

Table 1 shows the registration results. The registration transformation parameters are obtained using downhill simplex algorithm. The transformation errors are obtained from the theoretical transformation. The images criteria value SCMI when the images are registered, and the calculation iterations are listed. Four vertices of the constructed simplex are listed in each simulation.

From Table 1, it can be seen that, using the proposed method to register three images simultaneously, the registration results (see results of the third simulation) t_x is close to 2, t_y to 4, and ϕ to 2. This is consistent with the theoretical registration results. The registration errors $|\Delta t_x|$, $|\Delta t_y|$, and $|\Delta\phi|$ are less than 0.1, which satisfy the requirement of error tolerance. Moreover, the registration errors are less than that of first two simulations, which are derived by registration of two images individually. This means that the multiple images registration is more accurate than that of only using two images. For registration of four images simultaneously, the results are accurate and can satisfy the sub-pixel accuracy requirement, which indicates that the proposed method is also efficient for registration of more than three images.

For further testing the validity and applicability of the proposed method, we give a sequence of real ultrasonic images in Fig. 5, which are gathered from the ultrasonic phantom using the ultrasonic diagnosis system. The transformations of the image sequence mainly include translations and rotation. The registered images using the proposed SCMI based registration method are shown in Fig. 6. The results using the proposed method to register real ultrasonic image sequence are also satisfactory.

Table 1. Registration Results for the Images in Fig. 4

Simulation	Parameter (unit: pixel, degree)			Error (unit: pixel, degree)			SCMI	Iteration
	t_x	t_y	ϕ	$\|\Delta t_x\|$	$\|\Delta t_y\|$	$\|\Delta\phi\|$		
Fig. 4(c) to Fig. 4(a)	1.9501	3.9169	1.9218	0.0499	0.0831	0.0782	3.8127	50
	1.9313	4.0485	2.0318	0.0687	0.0485	0.0318	4.0353	
	2.0592	4.0579	2.0199	0.0592	0.0579	0.0199	4.0928	
	2.0430	4.0218	1.9108	0.0430	0.0218	0.0892	3.6085	
Fig. 4(c) to Fig. 4(b)	2.0876	3.8704	2.1210	0.0876	0.1296	0.1210	3.4608	67
	2.2119	4.1909	2.1901	0.2119	0.1909	0.1901	3.3574	
	2.1418	4.1708	2.2324	0.1418	0.1708	0.2324	3.5527	
	1.8760	3.8903	2.2319	0.1240	0.1097	0.2319	3.4001	
Fig. 4(c) to Figs. 4(a) and (b)	1.9870	3.9819	1.9883	0.0130	0.0181	0.0117	4.0906	52
	1.9742	4.0364	1.9617	0.0258	0.0364	0.0383	4.0874	
	1.9479	4.0094	2.0051	0.0521	0.0094	0.0051	4.0905	
	2.0204	4.0306	1.9917	0.0204	0.0306	0.0083	4.0894	
Fig. 4(d) to Fig. 4(a), Fig. 4(b) and Compensated Fig. 4(c)	1.9674	4.0566	1.9099	0.0326	0.0566	0.0901	1.3098	44
	1.9255	4.0050	1.9347	0.0745	0.0050	0.0653	1.3107	
	1.9682	4.0672	2.0420	0.0318	0.0672	0.0420	1.3110	
	2.0499	4.0531	1.9708	0.0499	0.0531	0.0292	1.3106	

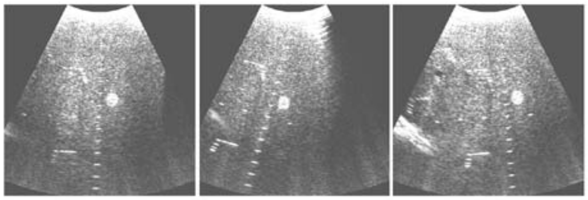

Fig. 5. Real ultrasonic image sequence to be registered.

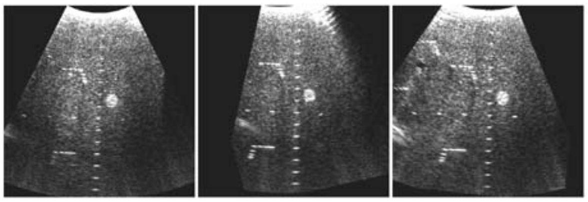

Fig. 6. Registered ultrasonic images.

In this paper, a new multiple-image registration method using SCMI as the measure combined with downhill simplex optimization algorithm is proposed. Unlike MI, which only can be sensitive to the relationship between two images, SCMI can measure the shared information that exists between multiple variables. Therefore, it can be used as a measure to register any finite number of images simultaneously. The experimental results show that the SCMI based multiple images registration presented in this paper allows for sub-pixel accuracy and completely automation. Moreover, the calculation of SCMI is data independent, so the method can be applied to multimodality images, not only to MRI. Furthermore, the method requires no user interaction or preprocessing, so it is well suited to be used in clinical practices.

Note that, theoretically similar to MI, SCMI can be sensitive to any translations and rotation between multiple images, under the condition that there exists overlapping regions between the concerning images. However, in the applications, various manipulations in the registration procedure, such as interpolation and image sub-sampling, generally introduce local extremum in the cost function to result in false registration. Up to now, trapping to local extremum in optimization is an open problem, which can affect the registration accuracy and application range of image registration method. Therefore, obtaining the global extremum and extending the application range of the proposed method are our future work.

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