Using K-means Clustering and MI for Non-rigid Registration of MRI and CT *

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Abstract. Mutual information (MI) based registration methods are susceptible to the variation of the intensity of the image. We present a multi-modality MRI-CT non-rigid registration method by combining K-means clustering technique with mutual information. This method makes use of K-means clustering to determine variant bin sizes in CT image. The resulting clustered (labeled) CT image is non-rigidly registered with MRI by modeling the underlying movement as Free-Form Deformation (FFD). We compare this Cluster-to-Image registration method with Image-to-Image and Cluster-to-Cluster methods. The preliminary experiment shows this method can increase the accuracy of non-rigid registration.

1 Introduction

Image registration can be classified into two categories: mono-modality and multi-modality registration. Multi-modality registration is more complex than mono-modality because the subjects are imaged in different ways, resulting in no direct relation between intensities of two images.

Archip et al. [1] presented a feature point-based method to non-rigidly register pre-procedural MRI with intra-procedural unenhanced CT images for improved targeting of tumors during liver radiofrequency ablations. This method employs block matching to identify deformation on sparsely distributed registration points and then applies this sparse deformation on a biomechanical model to derive the entire brain deformation. This method heavily relies on the result of block matching. However, intensity-based block matching is not effective in estimating the correct displacement between two blocks located in different modality images no matter we use correlation or mutual information as the metric.

Currently, mutual information, presented by Viola and Wells [2], is the most popular similarity measure employed by multi-modality registration. MI measures the statistical dependence of two images and does not rely on the relation of the intensity. Loeckx et al. [3] presented a conditional mutual information measure to deal with spatially-varying intensity inhomogeneity. This method

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extends traditional 2D joint histogram to 3D by incorporating spatial location as an additional dimension along with intensity pair.

Mattes et al. [4] used MI as similarity measure for PET-CT image registration in the Chest. The motions between two images are modeled with a global rigid transformation and local cubic B-splines. This deformation model allows closed-form expression for the gradient of the cost function. The visual inspection, conducted by two experts in specific anatomic locations, reported errors were in the 0- to 6-mm range.

Mutual information requires the number of bins, an interval of intensity, to be decided a priori and then splits the intensity range into equidistant bins. This intensity splitting does not take the intensity distribution into account, and therefore probably leads to misalignment. Z.F. Knops et al. [5] overcame this difficulty by applying K-means on joint histogram. This approach yields variant bin sizes and achieves a more natural clustering of intensities. They evaluated their method on rigid MRI, CT and PET registration. Different from their work, we only apply K-means on CT instead of on both CT and MRI.

In our work, we evaluate the combination of K-means and MI on the non-rigid registration (NRR) of MRI and CT. A Top-to-Down K-means clustering method is developed to generate a clustered CT (labeled CT) and then the resulting clustered CT is non-rigidly registered with MRI, termed as Cluster-to-Image registration, by modeling the underlying movement as Free-Form deformation [6]. We compare this non-rigid Cluster-to-Image registration method with 1) ITK implementation [7], a equidistant bin method, termed as Image-to-Image, and 2) Cluster-to-Cluster method (registration of two clustered images). Our preliminary experiment demonstrates this Cluster-to-Image approach significantly increases the accuracy of NRR.

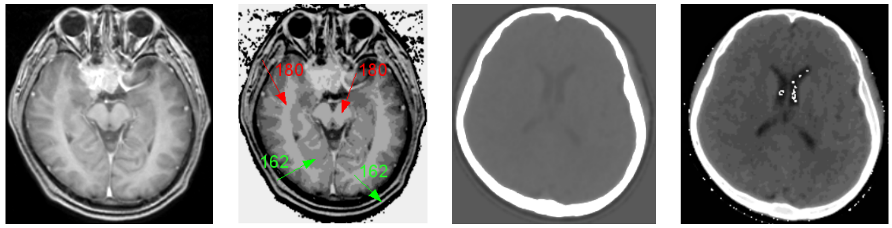
2 Method

We use clustered CT to register with original MRI instead of clustered MRI. CT has large range of intensities, usually from -1000 (Hounsfield units) to positive several thousands, and therefore K-means clustering is able to effectively deal with CT and strengthen the amount of information. On the contrary, MRI has small range of intensities. As a result, different tissues are probably grouped into one cluster, and therefore resulting in the loss of information. We illustrate this point using Fig. 1.

Using clustered CT to register with MRI is equivalent to registering original CT with variable bin sizes, determined by clustering, with MRI. High number of bins, i.e., small bin size is preferred for MRI. Different small bin sizes in MRI do not influence the registration result once the bin sizes of CT are determined using K-means clustering. We clarify this point from the definition of MI [2],

$$I(A, B) = H(A) + H(B) - H(A, B), \tag{1}$$

where $H(A)$ and $H(B)$ are Shannon entropy of image A and B respectively. $H(A, B)$ is joint entropy calculated as $H(A, B) = \sum_{a,b} p(a, b) log p(a, b)$, where



(a) MRI (b) Clustered MRI (c) CT (d) Clustered CT

Fig. 1. K-means clustering. (a) is original MRI and (b) is K-means clustered (labeled) image, in which midbrain and white matter with label 180, gray matter and skin with label 162 fall into the same cluster. (c) is CT, whose window position and width are carefully adjusted, and (d) is clustered CT.

$p(a, b)$ is the joint probability of gray value a in image A and gray value b at the corresponding voxel in image B. The Shannon entropy is a measure of dispersion of a probability distribution. A distribution with a single sharp peak corresponds to a low entropy value, whereas a dispersed distribution yields a high entropy value. In other words, the less the combinations of (a,b) are, the lower the entropy is. Now we are ready to use Fig. 2 to illustrate the influence of the bin size to the registration.

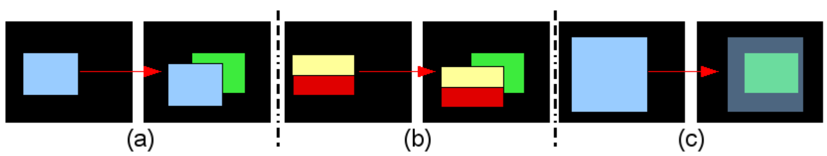


Fig. 2. The influence of the bin size to the registration. (a) shows the misalignment of blue region with green region leads to additional (blue, background) combination, and therefore a higher joint entropy. (b) shows some details of blue region can be distinguished using a small bin size. The misalignment leads to additional (yellow,background), (red, background) and (green, background) combinations. However, a small bin size does not change the registration result. (c) shows a large blue region is produced by a large bin size. The registration result is not unique.

Assume the blue region in the left image of Fig. 2 (a) corresponds to the green region in the right image. For simplicity, the transformation is limited to the translation only. In equation 1, $H(A)$ and $H(B)$ are used to make $I(A, B)$ insensitive to the overlapping region [2], which can be ignored since we only focus on the alignment of the blue region and the green region. If the blue region is totally matched with the green region, $-H(A, B)$ should reach a maximum value because the misalignment (as shown in Fig. 2 (a)) will lead to additional (blue, background) combination, which will disperse the distribution. If we use a small bin size for the left image, some detail structures (yellow and red regions in Fig 2 (b)) are distinguished. However, it does not influence the registration result because any misalignments will lead to additional combinations. The only difference between (a) and (b) is the maximum value of $I(A, B)$ in case (b) is smaller than that in case (a). If we use a large bin size, a possible large grouped blue region is generated. Any translation, which makes the green region totally covered by the blue region (Fig. 2 (c)), is a solution. The above discussion means that if one image is correctly clustered, a small bin size or a large bin number for another image is preferred.

The non-rigid Cluster-to-Image registration is implemented in two steps: cluster CT first, and then non-rigidly register the clustered CT with MRI. We use K-means for CT clustering. K-means requires the number of clusters as input. A small number is likely to combine different tissues together, but a large number is likely to separate one tissue into different clusters. We determine the optimal number of clusters using a Top-to-Down method by initializing K-means with a larger number of clusters and then gradually combining any two sufficiently close clusters.

2.1 Top-to-Down K-means Clustering

Let $\mathbf{x}$ a random variable with N observations: $\boldsymbol{x}_0, ...\boldsymbol{x}_{N-1}$, K-means is used to find the center of the cluster $\boldsymbol{\mu}_k, k = 0, \ldots, K-1$, and the assignment of data points to clusters by minimizing [8]:

$$J = \sum_{n=1}^{N} \sum_{k=1}^{K} r_{nk} \|\boldsymbol{x}_n - \boldsymbol{\mu}_k\|^2, \tag{2}$$

where r_{nk} is a binary indicator variable describing which of the K clusters contains data point $\mathbf{x}_n$. $r_{nk} = 1$ and $r_{nj} = 0$ for $j \neq k$ denotes $\mathbf{x}_n$ is assigned to cluster k.

Expectation and Maximization (EM) algorithm [9] is employed to find r_{nk} and μ_k simultaneously. EM algorithm proceeds iteratively and in each iteration two successive steps are involved:
E step: minimize J with respect to r_{nk} with $\boldsymbol{\mu_k}$ fixed.

$$r_{nk} = \begin{cases} 1 & \text{if} \qquad k = \underset{j}{\operatorname{argmin}} \|\boldsymbol{x}_n - \boldsymbol{\mu}_\mathbf{j}\|^2 \\ 0 & \text{otherwise} \end{cases} \tag{3}$$

M step: minimize J with respect $\boldsymbol{\mu}_k$ with r_{nk} fixed.

$$\boldsymbol{\mu}_k = \frac{\sum_n r_{nk} \boldsymbol{x}_n}{\sum_n r_{nk}} \tag{4}$$

K-means is sensitive to the initialization and requires a priori knowledge on the number of clusters. We overcome these difficulties by initializing K-means with a large number of clusters and then iteratively combining the two closest clusters if the distance between them is below some predefined threshold. This Top-to-Down K-means algorithm is described in Alg. 1.

$[B,\ K]$=*K-means*(A,K,ξ)
Input: A: image, K: the number of initial clusters, ξ: predefined cluster distance
Output: B: clustered image, K: the number of final clusters.

$S \Leftarrow \{0,\dots,K-1\}$
$x_i \Leftarrow A(i)$ // x_i is the gray value at position i of image A
repeat
  Initialize $\boldsymbol{\mu}_k$ with S
  repeat
    E step:
      Estimate r_{nk} according to equation 3
    M step:
      Solve $\boldsymbol{\mu}_k$ according to equation 4
  until no change of the cluster centers
  Find two closest clusters $\boldsymbol{\mu}_i$ and $\boldsymbol{\mu}_j$
  if $\|\boldsymbol{\mu}_i - \boldsymbol{\mu}_j\| < \xi$ **then**
    $S \Leftarrow S - \{\boldsymbol{\mu}_i, \boldsymbol{\mu}_j\}$
    $S \Leftarrow S + \{(\boldsymbol{\mu}_i + \boldsymbol{\mu}_j)/2.0\}$
    $K \Leftarrow K - 1$
  end if
until no two clusters combined
Generate clustered image B: $B(i) = k$, if $r_{ik} = 1$

Algorithm 1: Top-to-Down K-means clustering

2.2 Non-rigid Registration of Clustered CT with MRI

We employ Free-Form Deformation (FFD) [6] as non-rigid transformation to model a 3D deformable object, which can be manipulated by regular control points with spacing $s_x \times s_y \times s_z$. FFD is computationally efficient because the deformation at one point is only influenced by its neighboring control points. For a 3D image, the deformation of a point is influenced by its surrounding $4 \times 4 \times 4$ control points.

For a point p with coordinate (x, y, z), assume its $4 \times 4 \times 4$ control points are p_{ijk}. $i, j, k = 0, \dots, 3$. Denote d_{ijk} as the displacement vector associated with the control point p_{ijk} , the interpolation at point p is,

$$T(x, y, z|d_{ijk}) = \sum_{i=0}^{3}\sum_{j=0}^{3}\sum_{k=0}^{3} B_i(u)B_j(v)B_k(w)d_{ijk}, \tag{5}$$

where $u = x/s_x - \lfloor x/s_x \rfloor$, $v = y/s_y - \lfloor y/s_y \rfloor$, $w = z/s_z - \lfloor z/s_z \rfloor$. B_i is the i-th basis function of the B-splines [6].

Mutual information is used to measure the statistical dependence between two images. The mutual information between reference image R, a clustered CT, and transformed floating image $F(T(x, y, z|d_{ijk}))$, a pre-operative MRI, can be expressed as a function of the transformation parameter vector D, a concatenation of all control point displacements d_{ijk} [4].

$$S(D) = -\sum_{l}\sum_{k} p(l,k|D) log \frac{p(l,k|D)}{p_F(l|D)p_R(k)} \quad (6)$$

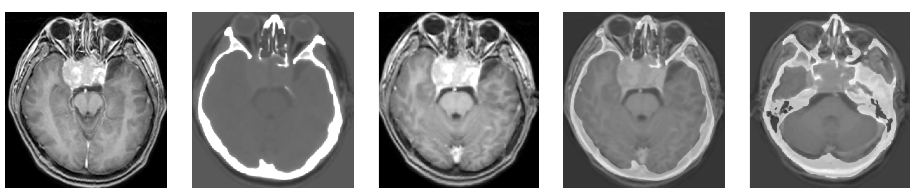
where $p(l,k|D)$, $p_F(l|D)$ and $p_R(k)$ are joint probability distribution, marginal distribution of floating image and marginal distribution of reference image, respectively.

$l, 0 \leq l \leq L_F$, and $k, 0 \leq k \leq L_R$, are histogram bin indexes in the floating image and the reference image, respectively. For the reference image, L_R is set to be equal to the number of the clusters, i.e., K. For the floating image, a large bin size is preferred. We conducted experiments on different bin sizes: $K, 2K, 3K, 4K, 5K$ and found there was little difference for the results if $L_F \geq 2K$.

The solution of function 6 can be resolved by L-BFGS-B optimization, which is particularly suited for high dimensional optimization problems [10].

3 Results

We conduct experiment on the non-rigid registration of MRI (dimension: $256 \times 256 \times 76$, spacing: $0.9375 \times 0.9375 \times 2$) and CT (dimension: $512 \times 512 \times 75$, spacing: $0.453 \times 0.453 \times 2$). MRI has been rigidly registered with CT. The Top-to-Down K-means clustering results, non-rigid registration results and the comparisons among Cluster-to-Image, Image-to-Image and Cluster-to-Cluster methods are presented in this section.



(a) Rigid MRI (b) CT (c) NRR MRI (d) Merged55 (e) Merged42

Fig. 3. The rigidly registered MRI (a) is non-rigidly registered with CT (b). The resulting MRI (c) is merged with CT and two merged slices are shown as (d) and (e).

3.1 K-means Results

The results of Alg. 1 with different inputs $A = MRI$, $K = 32$, $\xi = 2$ and $A = CT$, $K = 32$, $\xi = 2$ are shown in Fig. 1. For MRI, 19 clusters out of initial 32 clusters are combined with others even with a very small cluster distance 2. For CT, 31 clusters are generated, including some unremoved noises (scattered small white regions in Fig. 1). The clustered CT will be used in both Cluster-to-Image and Cluster-to-Cluster registration, and the clustered MRI will be used in Cluster-to-Cluster registration.

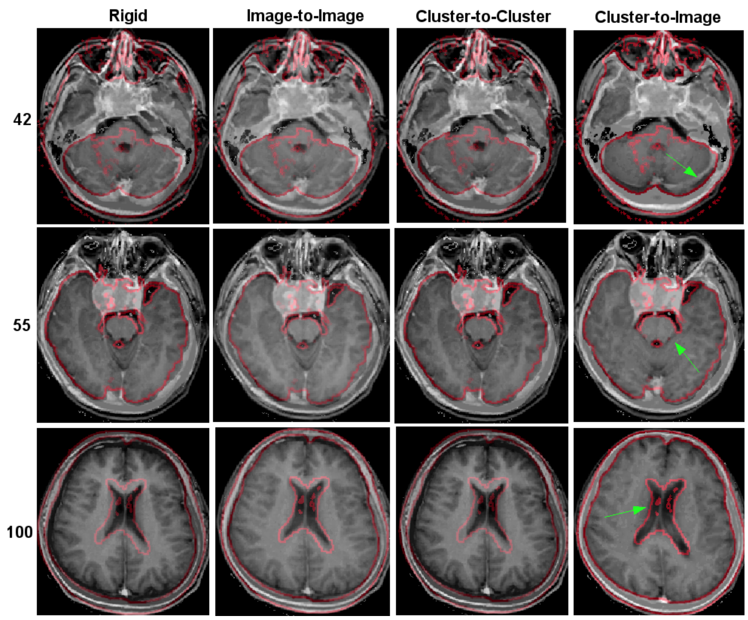


Fig. 4. The comparison of the results. The row is the index of the slice and the column is the registration method. The bin number we use in the Image-to-Image method is 256, which yields the best result among $32, 64, 128, 256$. The bin number in the Cluster-to-Image method is 31 (the number of clusters) for clustered CT, and $2K = 62$ for MRI. For the Cluster-to-Cluster method, the bin numbers are 31 for clustered CT, and 13 for clustered MRI respectively. Some detectable boundaries of soft tissues of CT such as the cerebellar hemisphere, the midbrain and the ventricles are extracted, highlighted and overlapped on registered MRI. The green arrows point to the boundaries exhibiting significant improvement of the accuracy using the Cluster-to-Image method.

3.2 Non-rigid registration Results

Non-rigidly registered MRI and its fusion with CT are shown in Fig. 3. We qualitatively compare our non-rigid registration method with Cluster-to-Cluster and traditional equidistant bin (Image-to-Image) methods. The results are presented in Fig. 4. It shows clearly that the Cluster-to-Image method matches the soft tissue boundaries better than the other two methods.

To quantitatively evaluate the result, we select 7 detectable feature points in CT and compare the registration accuracy among different registration methods with respect to these anatomical points. The Cluster-to-Image method demonstrates the highest accuracy as shown in Table 1.

4 Conclusion

We present a Cluster-to-Image non-rigid registration method to register MRI with CT. A Top-to-Down K-means method is developed to cluster CT. The clustered CT is non-rigidly registered with MRI by employing FFD as non-rigid

Table 1. Accuracy evaluation (mm) on 7 detectable feature points of CT: 1) anterior horn of right lateral ventricle (AHRLV), 2) pons (PONS), 3) anterior horn of left lateral ventricle (AHLLV), 4) posterior horn of right lateral ventricle (PHRLV), 5) posterior horn of left lateral ventricle (PHLLV), 6) septum pellucidum (SP), and 7) splenium of corpus callosum (SCC).

Anatomical points	AHRLV	PONS	AHLLV	PHRLV	PHLLV	SP	SCC
Rigid registration	7.55	3.61	6.32	6.71	6.40	7.14	4.59
Non-rigid Cluster-to-Image	2.45	1.00	1.41	1.73	0.71	2.00	1.41
Non-rigid Image-to-Image	4.69	2.24	3.0	3.16	5.74	2.00	2.45
Non-rigid Cluster-to-Cluster	7.35	2.83	6.08	6.40	5.48	7.14	4.36

transformation. This method overcomes the difficult of Image-to-Image method to determine the bin size in MRI in the absence of the knowledge of the bin size in CT. Moreover, it also avoids the shortcoming of the Cluster-to-Cluster method regarding the loss of information. The preliminary experiment demonstrates this method is capable of increasing the accuracy of the non-rigid registration of MRI and CT.

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