

# Multimodal Image registration for medical images

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## ABSTRACT

In this paper, a technique for registering medical images captured through different modalities with focus on portal image is been discussed. Earlier template matching was used to register satellite images, but it does not serve the purpose as images are from different modalities and same objects are represented with different intensity values. Mutual information based techniques outperform other multimodal techniques for this application because of inherently poor quality acquired image through MV image during patient treatment. This technique will suffer if image is very blurry. The technique is to maximize the mutual information between two images using gradient ascent method.

## Keywords

registration; computer vision; information theory; optimisation; entropy

## 1. INTRODUCTION

Registration is a prime task in image processing which is used to match two or more images taken, for example, from different sensors, at different sensors, or from different viewpoints [1], [2]. The large systems which evaluate images require registration of images, or a similar operation, as an intermediate step [3]. Examples of systems where image registration is a prime component includes matching a target with a real-time image of a scene for target recognition, alignment of images from different medical modalities for diagnosis, matching stereo images to recover shape for autonomous navigation and monitoring global land usage using satellite images. Nowadays, medical images are being widely used in healthcare, bio-medical research and a very wide range of imaging modalities are now available, such as SPECT, PET, MRI, CT, and so on [4],[5]. In some scenarios, it is required that the information obtained from several different imaging modalities needs to be integrated to deduce some very useful clinical conclusions. Image registration aligns the images and hence establishes correspondence between different features contained on different imaging modalities [5]. It allows monitoring of subtle changes in intensity or size over time or across a population and establishes correspondence between images and physical space in image guided radiation therapy or in image guided interventions. Image registration is the process of determining the spatial transform that maps points from one image (defined as the floating image) to homologous points on an object in the reference image (called as the fixed image). The similarity of the two images will be calculated and checked after each transform unless they are registered. Mutual information is the used measure for checking the alignment of images. This draws our attention which is a logical consequence of both the favourable characteristics of the measure and the good registration results. Mutual information is an intensity-based metric and automatic, which does not require landmarks or features such as surfaces and hence it can be applied [6]. Additionally, it is the intensity-based measure suited to alignment of multimodal images. Unlike measures based on differences of gray values or correlation of gray values, it does not assume a linear relationship among the gray values in the

images [7]. Furthermore, mutual information registration function is well-defined, which consists of local maxima [8]. The drawback of mutual information is that it is calculated on the basis of pixel-by-pixel, applying which tasks into relationship between corresponding individual pixels and not each pixel's respective neighbourhood. Due to this, much of the global spatial information inherent in images is not utilized. Additionally, it is a time-consuming work, specifically for high resolution images, because mutual information of the two images has to be calculated for each iteration. In the next section the methodology is been discussed.

## 2. METHODOLOGY

### 2.1 Entropy and Mutual information

Entropy is defined as measure of randomness. Entropy for a random variable  $x$  is given as [9]:

$$h(x) = - \int p(x) \ln p(x) dx \quad (1)$$

Joint Entropy for a random variable  $x$  is given as:

$$h(x, y) = - \iint p(x, y) \ln p(x, y) dx dy \quad (2)$$

Mutual Information is given as:

$$I(x, y) = h(x) + h(y) - h(x, y) \quad (3)$$

### 2.2 Registration By Maximisation Of Mutual Information

Estimate of  $T$  registers reference object  $u$  and test object  $v$  by maximizing their mutual information [12].

$$\hat{T} = \arg \max_T I(u(x), v(T(x))) \quad (4)$$

$T$  is a transformation from the coordinate frame of the reference object to the test object.  $v(T(x))$  is the test object pixel associated with reference object pixel  $u(x)$ .

Mutual information in terms of entropy is defined as [10]:

$$I(u(x), v(T(x))) \equiv h(u(x)) + h(v(T(x))) - h(u(x), v(T(x))) \quad (5)$$

Papoulis depicts this with examples,  $h(\cdot)$  is the entropy of a random variable.

### 2.3 Probability Estimation Using Parzen Window

Probability density function can be found by parzen density function,  $R$  is Gaussian window [11]. First step for estimating entropy from a sample is to approximate probability density  $p(z)$  by a superposition of functions centered on the elements of a sample  $A$  drawn from  $z$ ;

$$p(z) \approx P^*(z) \equiv \frac{1}{N_A} \sum_{z_j \in A} R(z - z_j) \quad (6)$$

Window function R is Gaussian density function given as:

$$G_{\psi}(z) \equiv (2\pi)^{-\frac{n}{2}} |\psi|^{-\frac{1}{2}} \exp\left(-\frac{1}{2} z^T \psi^{-1} z\right) \quad (7)$$

Where,  $\psi$  is the co-variance of the Gaussian. Probability of image is estimated using parzen window method using Gaussian density function. The kernel is moved over the image based on which the resultant probability image is formed. The intensity value of center pixel of the kernel at a given location is subtracted from the neighbouring pixel value and is substituted in Gaussian equation. The same is computed over the whole image by moving the kernel over the complete image.

## 2.4 Entropy Estimation

Entropy can be interpreted as a measure of randomness, variability or uncertainty [9].

$$h(z) \approx -\frac{1}{N_B} \sum_{z_i \in B} \ln P^*(z_i) \quad (8)$$

where,  $N_B$  is the size of sample B.

After substituting approximation for entropy of a random variable z, we get,

$$h(z) \approx h^*(z) \equiv -\frac{1}{N_B} \sum_{z_i \in B} \ln \frac{1}{N_A} \sum_{z_j \in A} G_{\psi}(z_i - z_j) \quad (9)$$

After estimating the probability, its entropy is been estimated by using equation 9 on the image. In this, kernel is again moved over the complete image to get the entropy of the image.

r x c is size of image, k x l is size of kernel. f1 is the kernel image. G is probability matrix. H is entropy matrix.

Input: Image, Sample sets A and B

Output: Entropy of image

1. Initialise kernel to 0;
2. for i: 1 to r-k+1
3. for j: 1 to c-l+1
4. Initialize temp to 0.
5. for x: 1 to k
6. for y: 1 to l
7. store pixels from image location x+i-1, y+j-1 to kernel location x,y
8. temp ← temp+(2\*pi\*sigma)^-0.5\*exp(-(f1((p+1)/2, (q+1)/2)- f1(x,y))^2/2)/sigma
9. end
10. end
11. G(i+(k+1)/2-1, j+(l+1)/2-1)← temp/(total number of pixel in kernel)
12. end
13. end
14. for i: 1 to gr-k+1,
15. for j: 1 to gc-l+1,
16. for x: 1 to k,
17. for y: 1 to l,
18. store pixels from image location x+i-1, y+j-1 to kernel location x,y
19. Sum all values of (log(kernel location(x,y))) and store in temp
20. end
21. end
22. H(i+(k+1)/2-1, j+(l+1)/2-1)← -temp/(total number of pixel in kernel)

23. end

24. end

## 2.5 Derivative Of Entropy

Entropy of  $v(T(x))$  is found, which is a function of the transformation T. To find maxima, gradient is ascended w.r.t. transformation T. T is a vector consisting parameters such as translation, rotation and scaling.

$$\frac{d}{dT} h^*(v(T(x))) = \frac{1}{N_B} \sum_{x_i \in B} \sum_{x_j \in A} W_v(v_i, v_j) (v_i - v_j)^T \psi^{-1} \frac{d}{dT} (v_i - v_j) \quad (10)$$

Where,

$$v_i \equiv v(T(x_i)), \quad v_j \equiv v(T(x_j)), \quad v_k \equiv v(T(x_k))$$

Weighting factor

$$W_v(v_i, v_j) \equiv \frac{G_{\psi_v}(v_i - v_j)}{\sum_{x_k \in A} G_{\psi_v}(v_i - v_k)}$$

## 2.6 Derivative Of Mutual Information

Mutual information equation is given in equation 5. After differentiating mutual information as given in equation 5 w.r.t. T, we get,

$$\begin{aligned} \frac{d}{dT} I(u(x), v(T(x))) &= \frac{d}{dT} h(u(x)) + \frac{d}{dT} h(v(T(x))) \\ &\quad - \frac{d}{dT} h(u(x), v(T(x))) \end{aligned} \quad (11)$$

Object  $u(x)$  is independent of transformation T [25]. As a result of which its derivative is zero. Joint entropy of two random variables, can be evaluated by

$$w = [u(x), v(T(x))]^T \rightarrow h(w)$$

Where w is a vector.

## 2.7 Maximising Mutual Information

Stochastic gradient ascent algorithm is been used for finding derivative of mutual information for finding the maximum [12].

$$\begin{aligned} \frac{dI}{dT} &= \frac{1}{N_B} \sum_{x_i \in B} \sum_{x_j \in A} (v_i - v_j)^T [W_v(v_i, v_j) \psi_v^{-1} \\ &\quad - W_w(w_i, w_j) \psi_w^{-1}] \frac{d}{dT} (v_i - v_j) \end{aligned} \quad (12)$$

Weighting factors are defined as follows:

$$W_v(v_i, v_j) \equiv \frac{G_{\psi_v}(v_i - v_j)}{\sum_{x_k \in A} G_{\psi_v}(v_i - v_k)}$$

$$W_w(w_i, w_j) \equiv \frac{G_{\psi_w}(w_i - w_j)}{\sum_{x_k \in A} G_{\psi_w}(w_i - w_k)}$$

Following notations are used for j and k as well

$$u_i \equiv u(x_i), \quad v_i \equiv v(T(x_i)), \quad w_i \equiv [u_i, v_i]^T$$

The search for local maxima is done using stochastic gradient descent algorithm.

The function is then updated using the following formula:

$$T \leftarrow T + \lambda \frac{\partial T}{\partial T} \quad (13)$$

In this, lambda is selected as 0.01 to 0.05 as reported. If lambda is low then excess mean square error is less and convergence is slow and if lambda is high then excess mean squared error is more and convergence is fast.

### 2.8 Summary Of Methodology

With the help of above mentioned equations, the images are registered. Probability of image is estimated using parzen window method using Gaussian density function. The kernel is moved over the image based on which the resultant probability image is formed. The intensity value of center pixel of the kernel at a given location is subtracted from the neighbouring pixel value and is substituted in Gaussian equation. The same is computed over the whole image by moving the kernel over the complete image. After this the entropy of the image is estimated using equation 9. Mutual information is calculated of the images using equation 5 and then it is differentiated with respect to transformation vector. The reference image is the one which is fixed and its derivative will be zero and floating image will be considered in the equation 11. Later on the maxima is found for getting good registration. This can be achieved using stochastic gradient ascent algorithm. The maxima which is obtained by this method is the local maxima. Then the function mentioned in equation 13 is been updated and the floating image is transformed. This gives the registration of floating and reference images.

### 3. RESULTS

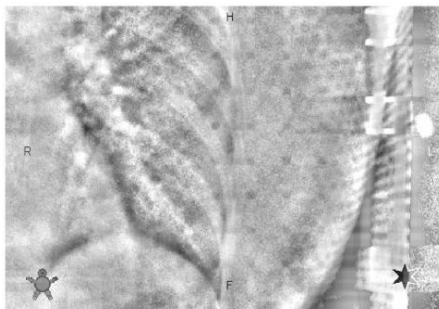


Figure 1. Floating image

Figure 1 is the EPID(electronic portal imaging device) image formed from high energy beam of LINAC.

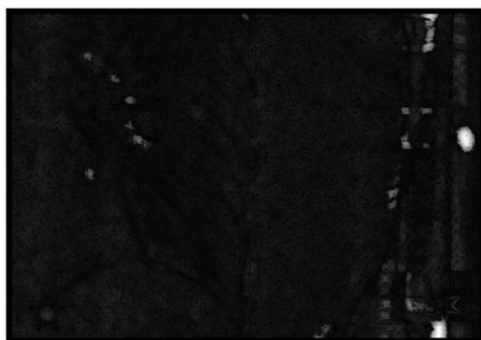


Figure 2. Probability of floating image using parzen method

Figure 2 is the probability of floating image obtained after applying equation 6 and assuming psi=1.

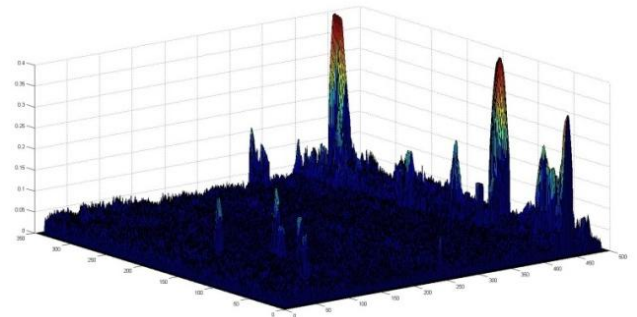


Figure 3. Surface of probability floating image

Above figure is the 3 dimensional surface contour image of figure 2, where x and y axis represents the pixel values and z axis represents the probability value. Above figure is the CT image.



Figure 4. Reference image

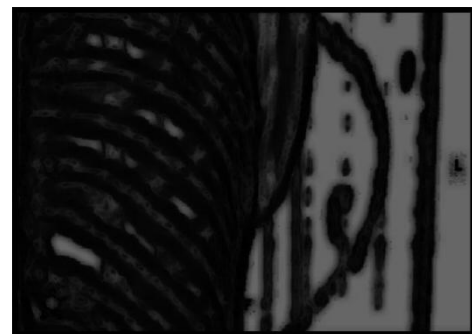


Figure 5. Probability of reference image using parzen window method

Above figure is the probability of reference image obtained after applying equation 6 and assuming psi=1.

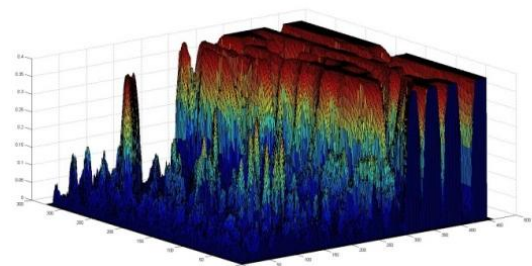
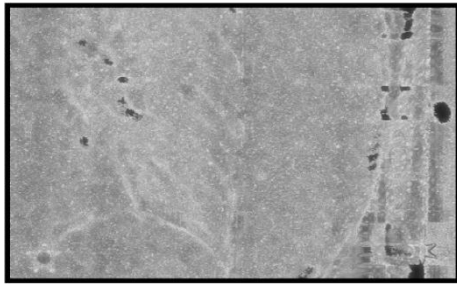


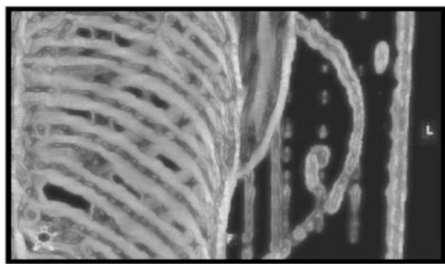
Figure 6. Surface of probability reference image

Above figure is the 3 dimensional surface contour image of figure 6, where x and y axis represents the pixel values and z axis represents the probability value.



**Figure 7. Entropy of floating image**

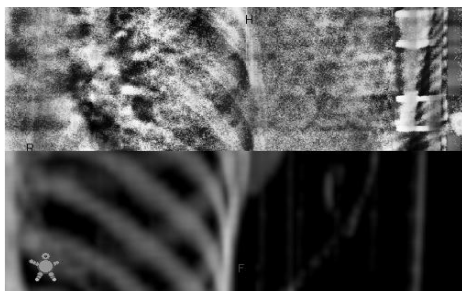
Above figure is the entropy of floating image obtained after applying equation 9 and assuming  $\psi=1$ . The image looks homogenous due to noise present in original image. We can also see that the image has lot of local minima, hence it is natural to have lot of maxima. Whenever probability is high or low, entropy is low.



**Figure 8. Entropy of reference image**

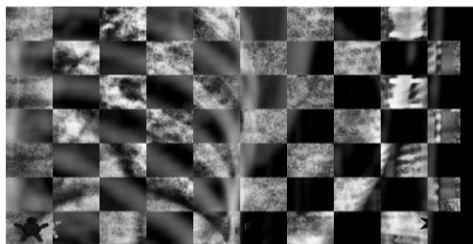
Above figure is the entropy of reference image obtained after applying equation 9 and assuming  $\psi=1$ .

In the 3 dimensional surface image the x and y axis are the pixel values and z axis defines the probability or entropy value of the image. Floating image is the EPID image and reference image is the CT image.



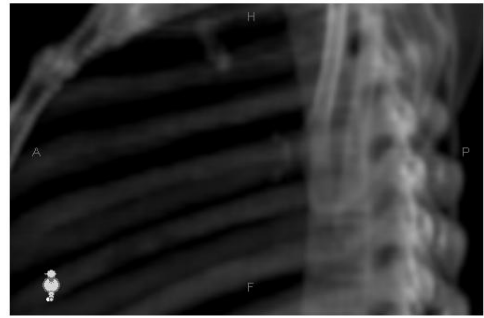
**Figure 9. Visualisation before registration**

Above image is the visualization showing floating image and reference image alternately before registration.



**Figure 10. Checkerboard visualisation after registration**

Above image is the checkerboard visualization showing floating image and reference image alternately after registration.

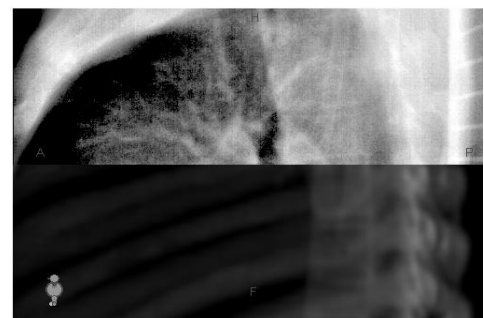


**Figure 11. Reference image**

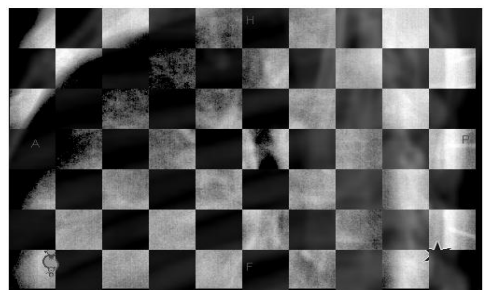


**Figure 12. Floating image**

Above figure is the EPID (electronic portal imaging device) image formed from high intensity beam of LINAC. Above image is the checkerboard visualization showing floating image and reference image alternately after registration.



**Figure 13. Partially overlapped images after registration**



**Fig 14. Checkerboard visualisation after registration**

#### 4. CONCLUSION

Here, one of the methodologies for registering multimodal medical images has been discussed. Reference image is Computed Tomography (CT) diagnostic high contrast image. Floating image is portal image captured using Mega Voltage

treatment beam thus inherently poor quality image. Portal image is having low contrast and highly noisy. Here, image registration involves challenges to register images with good accuracy in present of large amount of noise and poor edge information. The above mentioned algorithm has worked satisfactorily because of the fact that the algorithm is not strictly dependent on edge information or other similar local features. In this methodology because of noisy estimate of derivative, algorithm is able to come out of local maxima. Due to the presence of noise, outlier and multimodal nature of registration Mutual information surface may not be smooth enough and may result in slow registration and stuck to local maxima occasionally. Further efforts will be put to overcome the same in future. Overall, image registration results are accurate and the above method has the potential to be applied for portal image registration application. The overlapping can be seen clearly from the checkerboard visualization method.

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