

# 3D Voxel-Based Volumetric Image Registration with Volume-View Guidance

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In this article, we will present a novel interactive image registration technique using the 3D volumetric view as guidance throughout the registration process. The registration criterion used in this technique is the homogeneity of the color distribution on any given anatomic landmark, usually the skin/muscle voxels. This registration criterion has been validated using two different approaches, including comparison with automatic registration using mutual information based on the Insight Toolkits (ITK) and comparison with “registered” MR images with different pulse sequences acquired directly from the same MR scanner less than 5 minutes. An investigation is also made to compare this technique with the conventional interactive image registration using three orthogonal planar (3P) views, which is predominantly used in the current treatment planning clinic. This 3D technique has shown several advantages, including improved registration accuracy and accelerated registration speed. It has also found that the 3P pixel registration technique often “inherits” a global positioning error, due to its partial 3D visual presentation. In addition, unlike the 3P technique, which generally cannot be used to register more than 2 images simultaneously and low resolution PET images, this 3D technique can register up to 4 imaging modalities simultaneously, including PET images, with both global view guidance and detail checking capability.

## Introduction

Multi-modality image registration has become increasingly employed in the routine clinical diagnosis and radiotherapy, and there is a trend to incorporate more and more imaging modalities into the radiation treatment planning. For instance, physician may use the T2-based MR image to determine initial irradiation target volume and cone down the treatment volume based on T1-based MR image in brain cancer patients. All these images must be registered with the treatment planning CT image that is used for radiation dosimetry calculation and patient setup prior to the treatment.

Currently, the conventional interactive image registration using the 3 orthogonal planar (3P) views is still predominantly used in the clinic, although the automatic registration using mutual information (MI) has been increasingly recognized and used in the clinic recently [1-3]. The 3P pixel-based image registration has been reported

for large variance and long registration time [4]. To overcome this problem, we have developed the 3D voxel-based image registration technique [5, 6]. Here, we will discuss the validation of this 3D technique, the comparison with the 3P registration and the MI automatic registration, and the registration of PET images using this 3D voxel technique. In future, non-rigid image registration will be investigated.

## Methods and Materials

The 3D voxel-based image registration software is supported by a PCI volume rendering board (VolumePro1000-4GB) and run on a PC computer (dual PentiumIV-2.8GHz Xeon and 2GB RAM) under Windows 2000 operation system. In the volume rendering pipeline using the ray casting algorithm, the transformation for registration is performed in the early stage using the host computer resources [5, 6].

A simplified affine transformation is used with six degrees of freedom, and the transformed voxel volume is then inversely reassigned back to the original volume matrix under the original volume coordinate with linear interpolation and precision of one decimal point. Thus, it allows user to shift and/or rotate the active volume with fraction of voxel or degree, relative to the other rendered volumes. The three rotation angles are set in such way that they are corresponding to the gantry, table and tilt rotations, as specified by the Varian's 21ex radiotherapy treatment unit.

The most useful color visual representation of the volumetric image is the mono-color representation, which assigns a single color to each of the imaging modalities, such as red (R), green (G), blue (B) or white (W), as shown in Fig. 1. The image visibility is controlled by alpha (A) value overlaid to the image histogram. This mono-color representation provides a practical way to distinguish each imaging modality, as well as serves as guidance for evaluating the current alignment and for estimating the next potential adjustment. Other color visual representations can be also achieved using this program, such as pseudo-color representation, where the visibility of any voxel with a given intensity is controlled by 4 lookup tables (R, G, B and A), providing a comprehensive way to perform window/level adjustment.

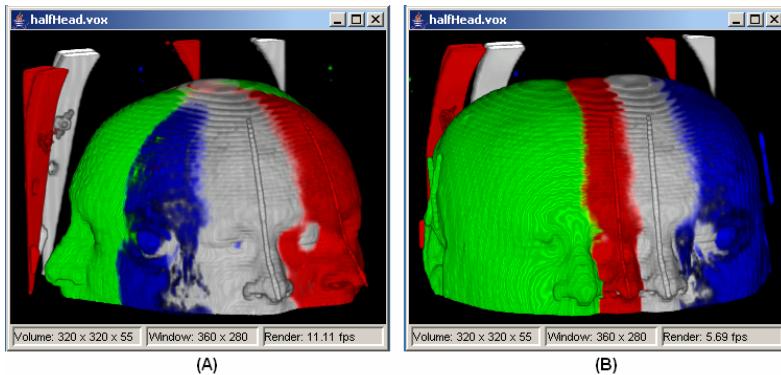


Figure 1. Demonstration of registration of 4 volumetric images: CT-1 (red), MR-T1 (green), MR-T2 (blue) and CT-2 (white). (A) rotation and (B) translation.

The original imaging modalities ( $\leq 4$ ) must be pre-processed in order to meet the volume rendering and registration requirements, including the same image size, same voxel size and compressed gray scale from 16 bits to 8 bits with optimal visibility. This pre-process is not image specific and therefore can be done using the software without intensive user's intervention.

For the conventional 3P image registration, the technique and software has been developed and used in the clinic for many years. It provides detailed comparison slice-by-slice in three orthogonal directions and is useful for checking details along the edge of display windows, where the two registering images are shown alternately.

For automatic image registration using maximization of mutual information, the software is developed based on the Insight Toolkit (ITK, version 2.0.0) [7]. A mutual information metric [8] and an evolutionary optimizer [9] are used. Detailed parameter settings are reported previously [6]. Also, in some calculation, the multi-resolution strategy [7] is applied, aiming to reduce the chance of reaching a local maximum and improve the optimization performance.

14 sets of CT/MR images and 7 sets of multiple MR images with different pulse sequences acquired within 5 minutes are used in this study. A CT/PET image is also used. All of the images are head images, where deformation can be negligible.

## Results

### *Real-time image registration of up to four image sets*

Each of image voxel of 32 bits is divided into 4 (8 bits) fields, and 4 image sets can be simultaneously loaded into the volume buffer. The 4-field volume can be rendered with proper classifications so that different display modes can be set interactively based on the graphic user interface (GUI). Any voxel field can be turned on or off as desired through GUI control. Four image lookup tables (R, G, B and A) are dedicated for each volume field for visualization.

The key to registration is the ability to shift an individual image volume relative to others in real-time prior to the rendering. With the volume rendering board, real-time performance can be achieved with 5-20 frames per second (fps). However, the transformation of a volume is done using the host computer resources and is the bottle neck for the entire process. With the current computer setting, the performance achieved is in the range of 100-600 ms per operation, depending on the availability of the computer resources, as well as the size of the volumetric images. Therefore, for an interactive registration, this performance is satisfied as a real-time operation.

The GUI panel is set to allow user to do coarse, normal or fine adjustment for any transformation. A test for the visual sensitivity is done using 2 identical images on computer monitors with resolutions of 1280x1024 and 1600x1200. In this ideal case, the smallest visually-detectable change is about  $0.1^\circ$  for rotational shift and 0.1 voxel unit for translational shift. Therefore, they are set as the minimum increments.

### *Validation of the 3D voxel image registration criterion*

The registration criterion has been set as “the highest achievable homogeneity of the color distribution on a given anatomic voxel landmark” [6]. This criterion is true

for the registration of 2 identical images: when they are superimposed, a color change effect (the highest color homogeneity) can be observed. In this ideal case, if the 2 images are colored with red and green, then when superimposed, the equally weighted red and green contributions in the same voxel will synthesize the color of yellow. When images from different imaging modalities are used, this criterion should still be true, but the quality of the homogeneity will be reduced and be modality dependent, due to different voxel signals, noise levels, as well as correlations to anatomy.

To validate the criterion, 7 sets of two different MR images: Flair and T1-based, acquired within 5 minutes in the same MR scanner, are used as registered images, where patient motion can be negligible, as shown in Fig. 2. The deviations between the original images and the 3D voxel registration are  $0.2^{\circ} \pm 0.4^{\circ}$  in rotation and  $0.4 \pm 0.3$  voxel unit in translation. The “distance” ( $\sqrt{\sum x_i^2}$ ) is used for evaluating the deviations.

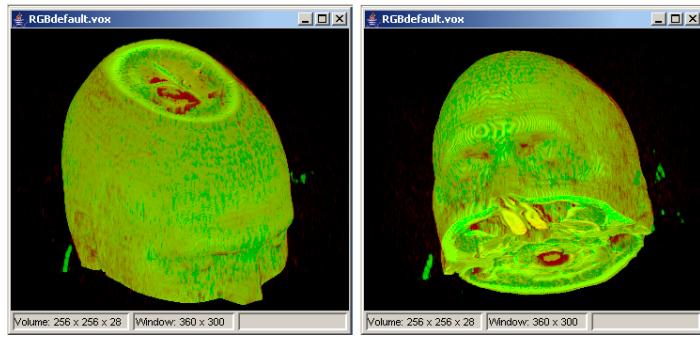


Figure 2. The homogeneity of color distribution on skin/muscle voxel volume in two different views of the original MR-Flair (red) and MR-T1 (green) images.

The comparison with the MI automatic registration is also performed using the 14 sets of CT/MR images. An excellent agreement with the 3D voxel registration is also found: the deviations are  $0.4^{\circ} \pm 0.7^{\circ}$  in rotation and  $0.3 \pm 0.5$  voxel unit in translation.

#### *Comparison with the 3P registration technique*

The same 14 sets of CT/MR images have been registered using 3P registration technique by 2 medical physicists who routinely perform the image fusion in clinic. When displaying the registered images using the 3D voxel technique, misalignments are readily identified for 13 out of 14 image sets (92%). A typical case is shown in Fig. 3. It is further found that these misalignments have rather large amplitudes:  $1.8^{\circ} \pm 1.2^{\circ}$  in rotation and  $2.0 \pm 1.3$  voxel unit in translation.

Cross-verification has been done in 3D voxel registration using different anatomic landmark, in addition to skin/muscle voxel landmark. When eyeballs are used as the landmark, the superimposed voxels can have the color change effect, indicating a good alignment. In addition, all of the 3D voxel registration results are verified with the planar views and considered good registration based on the conventional registration criteria. Therefore, with these cross-verifications, the reliability of the 3D voxel image registration results should become much higher statistically.

The large deviations (error distributions) indicate that the 3P pixel registration technique may be rooted with some fundamental problems, which have not been seen

in the literature. It also suggests that the 3D voxel registration is superior to the 3P pixel registration with improved registration accuracy.

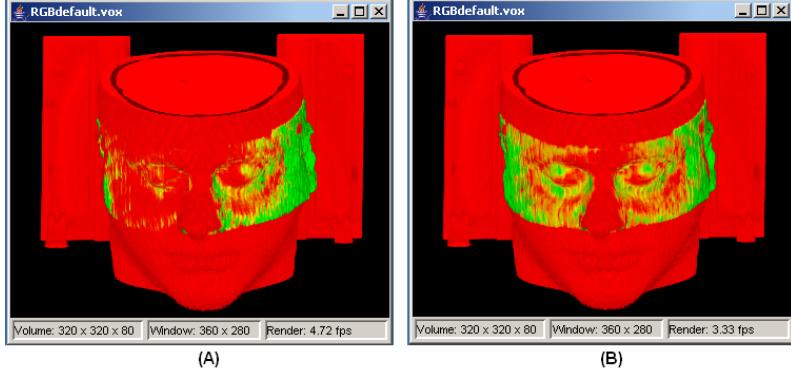


Figure 3. Global positioning error found in the 3P registration (A) and corrected by the 3D registration (B). CT (red) and MR (green) are used.

#### *Registration of functional image to anatomical image*

Because the poor resolution of the functional images, such as PET images, it is almost impossible for the conventional 3P registration technique to perform such task, since there is often little detailed anatomic structure in PET images comparing with the anatomical images, such as CT images.

However, using the 3D voxel registration technique, the fuzzy volumetric views of PET images can reflect some global geometric information when using skin/muscle voxels as the volumetric registration landmark. For head images, the brain voxels in PET is rather strong and it can be used to register with the inner surface of the skull in CT image. So, the matched surface indicates a good registration, as shown in Fig. 4.

Preliminary results have shown that the 3D voxel registration technique can be practically used for registering PET images to CT images with accuracy of about a single degree in rotation and single PET voxel unit in translation. Therefore, this technique can be applied to the functional image registration in clinic.

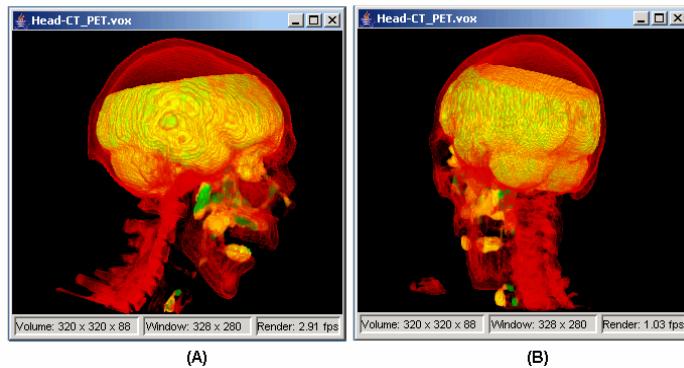


Figure 4. Functional image registration by the 3D voxel technique using transparent CT bone voxel (red) and the most intense PET brain voxel (green) for surface matching. (A) side view and (B) back view.

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## Discussion

### *The 3D voxel image registration criterion*

The best achievable homogeneity of color distribution on a given anatomic voxel landmark is set to be a robust criterion to use and the skin/muscle voxels are often serve as such anatomic landmark really well as they are residing on the surface of the image volume and readily distinguishable from the surrounding air voxels.

Visually, it is a direct derivation from the alignment of identical images. Using different images from different modalities, different signals and noises are expected. Therefore, the color changing effect is no longer uniformly distributed in all voxels and the criterion is “downgraded” from the color changing effect in identical images to best homogeneous color distribution that can be achieved.

Mathematically, when two voxel volumes with different level of signals and noises superimpose to each other, on any given anatomical volume, in which similar voxel intensity can be found, the best homogeneous color distribution is actually reflecting the randomness of the fitting “curve” - volumetric surface. In this sense, the 3D voxel registration criterion reflects the fitting residue “curve”. Although the randomness may only be viewed partially, this attempt has not been seen in the literature.

Therefore, the 3D voxel registration criterion is sound, as long as common visible voxels reside in the multimodal images. When multiple anatomic landmarks are used for cross-verification, the reliability of the result should be increased dramatically.

Practically, in any stages of the registration, user is guided with the global views, aiming to achieve the fit described by the criterion. Therefore, the 3D registration is volume-view-guided and found accelerated by as much as 2-3 folds on average with improved accuracy, comparing with the 3P registration.

### *Global positioning error in 3P pixel image registration*

By carefully evaluating the two different results from the 3P and 3D registration techniques, it is found that both registrations are acceptable under the 3P registration criteria without exhaustive correlating all slices in all 3 orthogonal directions. This exhaustive checking is often ignored as it is quite tedious, very difficult in detecting small difference, as well as intensive in user involvement and demanding for strong cognitive ability. It is very time consuming with little gain but large variance [4, 6].

Therefore, there is often an ambiguity in the 3P technique that fails to distinguish the best fit among candidates. In addition, the 3P technique has poor sensitivity and can only handle integer increments in registration [4]. We found that user often drops their effort in further improving the registration as soon as a satisfied registration result is found. This is similar to the local minimum that an automatic registration may encounter. So, it is suggested that the 3P technique has a high probability (92%) to lead to a registration result that is nothing but a “local minimum”.

What the 3P pixel technique is really missing is the tissue continuity or tissue integrity. Users have to put the 3P partial views together using their own imaginary thinking in order to sense any global misalignment. Therefore, it is very time consuming and user’s cognitive ability dependent. In contrast, the 3D voxel technique presents such tissue integrity to the users, so that they are released from such burden but guided with the visual registration criterion throughout the process.

Visual confirmation of the image registration is important not only for interactive technique but also for any automatic technique [10]. We have found 2 cases where the automatic registration failed possibly due to anatomical changes resulted from surgery between image acquisitions. Based on the above discussion, we strongly recommend to use the 3D voxel registration technique for visual verification, because it is the super set of the two, containing both volumetric views and planar views.

#### *Functional image registration using the 3D voxel technique*

It is beyond the capability of the 3P pixel technique to register PET image because it contains little anatomical details, which are often incomplete. Therefore, it is very difficult for a detail-oriented technique to fulfill such registration. However, the 3D voxel technique can perform the registration based on volume information, although blurry, in addition to detailed voxel information, making the registration feasible.

Two common ways, surface-based and volume-based [11], have been studied for the registration of CT/PET images. Both of the approaches can be done, as long as a definable volume can be identified in the modalities involved.

## Conclusion

The 3D voxel-based image registration technique is developed for volume-view-guided registration of up to 4 concurrent imaging modalities. This technique has been validated by registered images acquired at the scanner level and/or obtained from automatic registration using mutual information. Comparing with the conventional 3P pixel-based technique, the 3D voxel-based technique has four advantages: the improved registration accuracy, accelerated registration speed, up to four concurrent image registration and functional image registration.

It has found that global positioning error is often associated with the 3P registration technique, and therefore it should be cautious when using this conventional technique. It is suggested that the 3D voxel technique is a good safe-guard for other registrations.

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