

RESEARCH ARTICLE

Medical Image Enhancement Based on Volumetric Tissue Segmentation Fusion (Uni-Stable-3D Method)

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HIGHLIGHTS

- *The Uni-Stable-3D is a new method for 3D medical image enhancement.*
- *The Uni-Stable-3D image is almost universal as it combines variety of algorithms points of views into one 3D probability map*
- *Uni-Stable-3D Images reduces boundary-overlapping among different tissues.*

GRAPHICAL ABSTRACT

The Uni-Stable-3D is a new method for 3D medical image enhancement which produces 3D Images of high contrast from the scanned anisotropic scaling images.

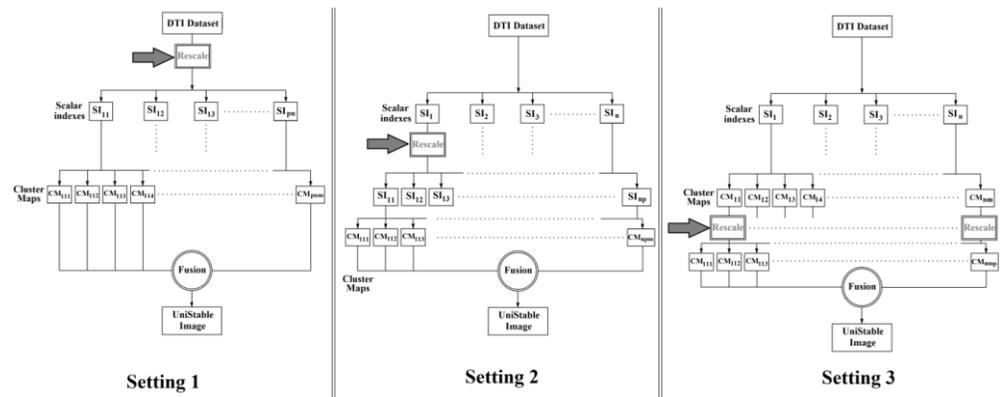


Figure Different settings of Uni-Stable-3D method

Keywords:

- Uni-Stable
- WM
- GM
- CSF
- Brain Segmentation
-

Article Info:

Received : 11 February 2023
 Accepted : 6 June 2023

DOI:
 10.53525/jster.1250050

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Aim of Article: Medical image enhancement based on 3D reconfiguring of anisotropic images scans to produce images of high contrast which are suitable for segmentation using any clustering algorithm.

Theory and Methodology: This is done by estimating some intermediate slices through resizing the original DTI scans. Rescaling has been achieved at three different levels: rescaling of eigenvalues of diffusion, rescaling the Scalar Indexes from the original eigenvalues, and rescaling the cluster maps of the segmentation of the original Scalar Indexes. Four interpolation methods have been employed at each level and four clustering algorithms have been employed in the process.

Findings and Results: Univeral and stable 3D medical images with high contrats.

Conclusion : The Uni-Stable-3D images are almost universal as they combine a variety of algorithms points-of-views into one 3D probability map. This reduces boundary-overlapping among different tissues, and hence improves the uniqueness of the segmentation problem solution.



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Citation:

Elaff, I. (2023). *Medical image enhancement based on volumetric tissue segmentation fusion (Uni-Stable 3D method)*, Journal of Science Technology and Engineering Research, 4(2): 78-89. DOI: 10.53525/jster.1250050

HIGHLIGHTS

- *Novel technique for 3D medical image enhancement that is titled as: Uni-Stable-3D Images.*
- *The Uni-Stable-3D image is almost universal as it combines variety of algorithms points of views into one 3D probability map*
- *Uni-Stable-3D Images reduces boundary-overlapping among different tissues*

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ABSTRACT

The Uni-Stable-3D is a new method for 3D medical image enhancement which produces 3D Images of high contrast from the DTI anisotropic images. This is done by estimating some intermediate slices through resizing the original scans. Rescaling has been achieved at three different levels: rescaling of eigenvalues of diffusion, rescaling the Scalar Indexes from the original eigenvalues, and rescaling the cluster maps of the segmentation of the original Scalar Indexes. Four interpolation methods have been employed at each level and four clustering algorithms have been employed in the process. The Uni-Stable-3D produces images which are almost universal as the method combines a variety of algorithms points-of-views into one 3D probability map. This reduces boundary-overlapping among different tissues, and hence improves the uniqueness of the segmentation problem solution. The stability factor of the Uni-Stable-3D images has been measured using maximum match analysis between the cluster maps which are generated from Uni-Stable-3D images by a variety of clustering methods with respect to true fact references for 5 different brains. The resultant standard deviations of Uni-Stable-3D images maximum match analysis in both threshold and tissue to brain ratio are much lower than Mean Diffusivity and Fractional Anisotropy scalar indexes for both CSF/non-CSF and WM/non-WM respectively.

Keywords: *Uni-Stable, WM, GM, CSF, Brain Segmentation*

I. INTRODUCTION

Computer-aided diagnosis (CAD) is considered one of the major research subjects in medical imaging and diagnostic radiology [1, 2]. With CAD, radiologists use the computer output as a "second opinion" and make the final decisions. The ability to produce high contrast medical images has its importance in diagnosing, evaluation and computer-based simulation of a certain tissue or organ.

Medical imaging such as CT-scan and MRI are

usually accomplished in an anisotropic manner where the planer resolution spacing and slice to slice spacing are (usually) different [3]. This makes the 2D based segmentation process of scans not able to provide the accurate 3D bounds of the tissues, where this shows the necessity for estimating some intermediate plans to solve that problem. The estimation of some intermediate plans requires 3D image resizing to be involved in the process.

In addition to the anisotropic spacing problem, the macroscale resolution of scanners [4, 5] causes



boundary-overlapping between neighbor tissues in medical images [6 – 8]. With those 2 problems, the estimation of an accurate 3D tissue's boundary becomes in demand.

When only 2D images of the original scans are employed for processing tissue in 3D, it would act like resizing this image using the nearest interpolation method. However, by applying other interpolation methods such as Linear, Cubic, Lanczos2 or Lanczos3 [9, 10], more accurate estimation for the intermediate plans would be expected. Linear interpolation estimates intermediate states over a tangent line between two measured states, while Cubic uses Gaussian smoothing curve and Lanczos methods depend on the Sinc function.

The most important image segmentation techniques are: threshold based methods, clustering based methods, edge based methods, region based methods, watershed based methods, Partial Differential Equation (PDE) based methods and Artificial Neural Network (ANN) based methods [11]. Clustering base methods such as Otsu algorithm [12], K-Means algorithm [13], Expectation Maximization (EM) algorithm [14], C-Means algorithm, Fuzzy C-Means (FCM) algorithm and Spatial constrained Fuzzy C-Means (SFCM) algorithm [15], Markov Random Field (MRF) algorithm and Iterated Conditional Modes (ICM) algorithm [16] are widely used with medical images.

It was reported that there is no unique solution to the segmentation problem, because of the effect of the used imaging modality on the segmentation process; different results are obtained by changing clustering method and/or the selected numbers of clusters [5, 7, 8, 15, 16]. Many models have been represented for 3D brain segmentation. Duy M. H. Nguyen et. al. produces a 3D brain tissue segmentation using Gaussian Mixture Models (GMMs), Convolution Neural Networks (CNNs) and Deep Neural Networks (DNNs)[17]. Yuankai Huo et.al. proposed the Spatially Localized Atlas Network Tiles (SLANT) method to distribute multiple independent 3D Fully Convolutional Networks (FCN) for high-resolution whole brain segmentation[18]. Fareeen Ramzan et.al. employ a network for the segmentation of multiple brain regions has been proposed that is based on 3D convolutional neural networks and utilizes residual learning and dilated convolution operations to efficiently learn the end-to-end mapping from MRI volumes to the voxel-

level brain segments[19]. Youyong Kong et.al. presents a novel algorithm for brain tissue segmentation based on supervoxel and graph filter. Firstly, an effective supervoxel method is employed to generate effective supervoxels for the 3D MRI image. Secondly, supervoxels are classified into different types of tissues based on filtering of graph signals [20]. Kamarujjaman represents a novel 3D unsupervised spatial fuzzy-based brain MRI volume segmentation technique in the presence of intensity inhomogeneity and noise. Instead of static masking, dynamic 3D masking has been proposed to measure the correlation among neighbors [21]. Results from stated methods targeting either high resolution scans or depend on one segmentation technique. According to our best knowledge, the present 3D segmentation methods don't consider the lost information in the spacing between slices, which in turn produce approximate results for volumetric shapes.

One solution in a former research [22] that has been developed to produce Uni-Stable images where segmentation results are relatively stable regardless of the use of the clustering method. The maximum match analysis of 5 brains for CSFUni and WMUni gives values 0.29 ± 0.002 and 0.39 ± 0.003 respectively. However, the Uni-Stable method, also, did not consider the spacing between slices. This research represents an improvement to the Uni-Stable method by re-producing medical image slices in a way to cover spaces between scanned slices using combinations of interpolation methods and cluster maps. This will re-generate volumetric 3D images which are universal and stable for the segmentation process using any algorithm and produce fewer overlapping errors.

II. MATERIALS AND METHODS

A. Dataset

Datasets of this study have been obtained from John Hopkins Medical Institute website. These datasets consist of brains' DTI volume data where each brain is scanned in 50 slices with a resolution of 256×256 voxels per slice. In every slice, the voxel width and height are 0.9375 mm and the spacing between each successive slice is 2.5mm. Some scalar Indices (SI) for those DTI images have been generated, namely: Mean Diffusivity (MD), Fractional Anisotropy (FA), Rational Anisotropy (RA), Matisuia Anisotropy (MA), Linear Anisotropy (Cl), Spherical Anisotropy (Cs) , Volume Ratio (VR), Angular Anisotropy (AA), and Diffusion

Volume (DV) [4, 5, 6, 23 - 27].

B. Uni-Stable-3D Images

The lack of solution uniqueness in the medical image segmentation problem is because of different medical imaging types, the selected clustering algorithm, and interpolation method of rescaling its order where each setting has its own estimate. A new approach for 3D brain image segmentation based on interpolating anisotropic brain scans from Diffusion Tensor Imaging modality. As axial brain scans are usually accomplished in anisotropic spacing where the plane resolution spacing and slice to slice spacing are usually different, then 2D-based segmentation of brain tissues cannot provide accurate 3D bounds of the tissues. This is where 3D image interpolation should be involved in the process. The main concerns of the accurate 3D brain tissues are the suitable stage order of the interpolation in the process, the suitable interpolation methods and the suitable Scalar indexes for that job.

The Uni-Stable method [17] was originally developed for generating high contrast 2D images based on DTI scans, where the Uni-Stable method has been proved to be universal where many segmentation settings are considered, and their segmentation results are relatively independent of the applied clustering method, which makes it relatively stable. The process starts by producing different SI from eigenvalues of the DTI data, generating Cluster Maps (CM) from the generated SIs and finally fusing the generated CMs into one probability map, which is the Uni-Stable Image, where this process makes sure that common points will have more probability than less common points.

In the way to upgrade this method to a 3D version, a resizing stage would be added to estimate some intermediate slices between originally scanned ones, which in turn will solve the anisotropic spacing problem. The selected interpolation method of the resize operation and its order in the process plays a basic role that affects the Uni-Stable-3D image generation as shown in Figure 1. The first setting (Setting 1) is resizing the eigenvalues of the DTI images before the other stages. The 2nd (Setting 2) is to generate SI's from the original eigenvalues and then resize the SI maps. The last one (Setting 3) is to generate the CM's from the original SIs and then resize them before the fusion process. Four interpolation methods are tested for 3D image resizing: Linear, Cubic, Lanczos2 and Lanczos3. For N SIs, which contain clear features about the required tissues; M

clustering methods with P different Interpolation methods generate $N \times M \times P$ estimates of normalized CMs. Normalized Uni-Stable-Image IMGUni is generated by fusing these CMs together, where:

$$IMG_{Uni} = \frac{\sum_{n=1}^N \sum_{m=1}^M \sum_{p=1}^P CM_{nmp}}{\text{Max}(\sum_{n=1}^N \sum_{m=1}^M \sum_{p=1}^P CM_{nmp})} \dots\dots\dots (1)$$

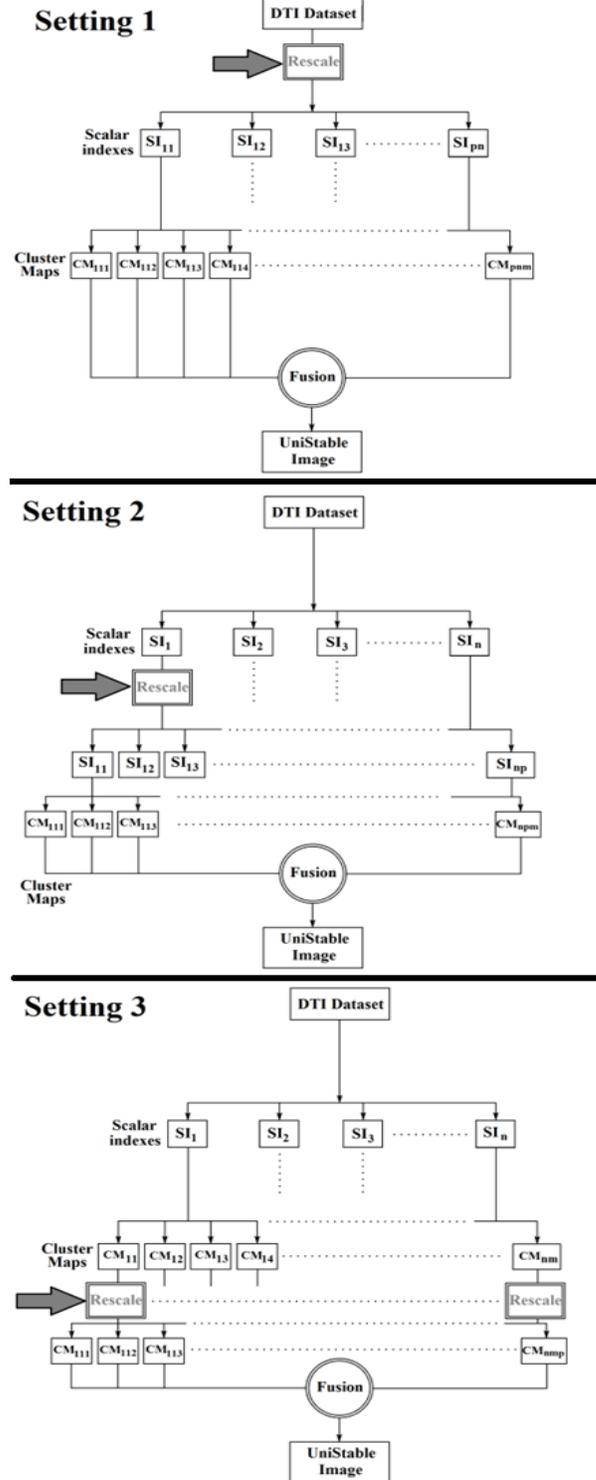


Figure 1 Different settings of Uni-Stable-3D method
 In this study, brain data has been resized from 256x256x50 to 256x256x200 using three different settings to estimate some intermediate slices between originally scanned ones.

C. CSF/non-CSF 3D Uni-Stable-Image generation

For generating CSF/non-CFS 3D-Uni-Stable-Images (CSFUni), some SI's are used, namely: MD, DV, λ_1 , λ_2 , and λ_3 . Those SI has been clustered using 4 different clustering algorithms, namely: Otsu, KM, FCM and SFCM. Rescaling using four interpolation methods has been tested in the process with the different location. For each setting, 80 different cluster maps are produced. Cluster maps are then fused into one image as shown in Figure 2.

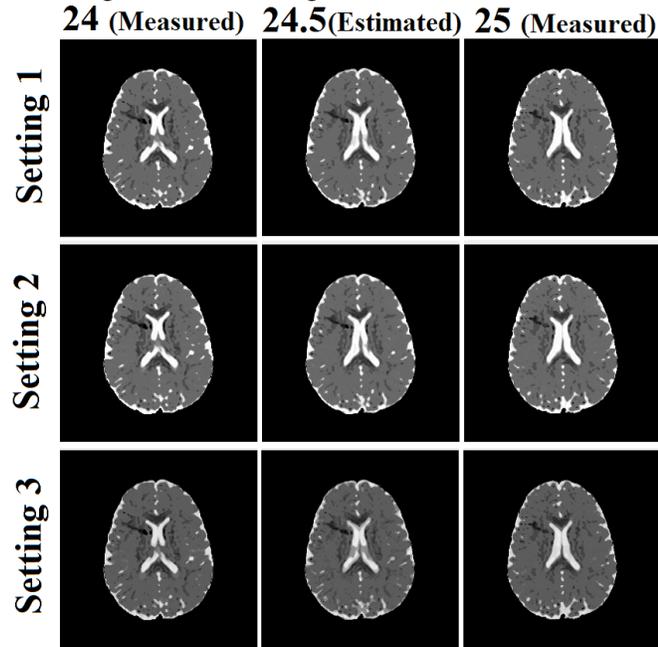


Figure 2 CSF/non-CSF Uni-Stable-3D images using different settings for 2 measured slices and one estimated slice in the middle.

Table 1. Different Settings for CSF/non-CSF Uni-Stable-3D Image Generation.

	Rescale Level	Interpolation Methods	Clustering Methods	Scalar Indexes	Number of Fused Cluster Maps
Setting 1	Eigenvalues Rescale	Linear, Cubic, Lanczos2, Lanczos3	Otsu, K-Means, FCM, SFCM	MD, DV, λ_1 , λ_2 , λ_3	80
Setting 2	Scalar Indexes Rescale	Linear, Cubic, Lanczos2, Lanczos3	Otsu, K-Means, FCM, SFCM	MD, DV, λ_1 , λ_2 , λ_3	80
Setting 3	Cluster Maps Rescale	Linear, Cubic, Lanczos2, Lanczos3	Otsu, K-Means, FCM,	MD, DV, λ_1 , λ_2 , λ_3	80

		SFCM	
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D. WM/non-WM 3D Uni-Stable-Image generation

For generating WM/non-WM 3D-Uni-Stable-Images (WMUni), some SI's are used, namely: FA, RA, AA, MA, and CI. Those SI has been clustered using 4 different clustering algorithms, namely: Otsu, KM, FCM and SFCM. Rescaling using four interpolation methods has been tested in the process with the different location. For setting 1, 40 different cluster maps are produced because only two interpolation methods re used and 80 different cluster maps are use in other settings. More justification would be indicated in the discussion and conclusion part about that. Finally, cluster maps are then fused into one image as shown in Figure 3.

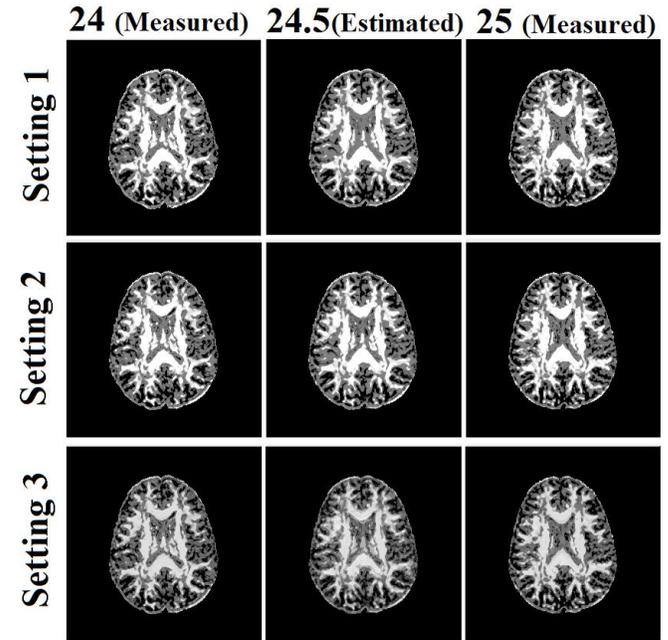


Figure 3 WM/non-WM Uni-Stable-3D images using different settings for 2 measured slices and one estimated slice in the middle.

Table 2. Different Settings for WM/non-WM Uni-Stable-3D Image Generation

	Rescale Level	Interpolation Methods	Clustering Methods	Scalar Indexes	Number of Fused Cluster Maps
Setting 1	Eigenvalues Rescale	Linear Cubic	Otsu, K-Means, FCM, SFCM	FA, RA, AA, MA, CI	40
Setting 2	Scalar Indexes Rescale	Linear Cubic, Lanczos2, Lanczos3	Otsu, K-Means, FCM, SFCM	FA, RA, AA, MA, CI	80
Setting 3	Cluster Maps Rescale	Linear Cubic, Lanczos2,	Otsu, K-Means, FCM,	FA, RA, AA,	80



		Lanczos3	SFCM	MA, CI	
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III. RESULTS

A. Reference Model

The usual SIs which are used in the brain image segmentation are FA and MD. For normalized MD images, a threshold with values around 0.3 can efficiently separate CSF/non-CSF [28] and for normalized FA images, a threshold with values between 0.25 and 0.45 can separate WM/non-WM [29]. As the original scans reflect the solid facts about the scans, so they should be taken as a comparison reference. For size consistency, the nearest interpolation is applied to resize the original FA and MD.

B. Non-Uni-Stable 3D images Segmentation

For the regular process, FA and MD are resized using linear interpolation or cubic interpolation after being calculated from the original eigenvalues [30]. However, more settings have been explored where FA and MD are resized according to the following tables:

Table 3. Different Settings for MD rescaling.

	Rescale Level	Interpolation Methods
MD1.1	Eigenvalues Rescale	Linear
MD1.2	Eigenvalues Rescale	Cubic
MD2.1	Scalar Indexes Rescale	Linear
MD2.2	Scalar Indexes Rescale	Cubic

Table 4. Different Settings for FA rescaling.

	Rescale Level	Interpolation Methods
FA1.1	Eigenvalues Rescale	Linear
FA1.2	Eigenvalues Rescale	Cubic
FA2.1	Scalar Indexes Rescale	Linear
FA2.2	Scalar Indexes Rescale	Cubic

And the four mentioned clustering methods are also applied on those images with maximum match as shown in Figure 4 and Figure 5. It is noticed that each clustering method has different threshold point and this is the normal case where non unique solution is obtained.

Referring to Maximum-Match analysis for 5 brains, the average mean and the average standard deviation of the clustering algorithm and regular threshold method and the CSF to Brain and WM to Brain ratios are given in Tables 5 and Table 6

Table 5 Average Mean and Average standard deviation of 5 human brains for maximum match Threshold value and CSF to Brain ratio based on MD Images of different settings

	Threshold	CSF to Brain Ratio
MD1.1	0.306±0.0118	18.75±1.07
MD1.2	0.306±0.0125	18.64±1.06
MD2.1	0.306±0.0118	18.75±1.07
MD2.2	0.306±0.0125	18.64±1.06

Table 6 Average Mean and Average standard deviation of 5 human brains for maximum match Threshold value and WM to Brain ratio based on FA Images of different settings

	Threshold	WM to Brain Ratio
FA1.1	0.371±0.0127	29.15±1.80
FA1.2	0.375±0.0142	28.57±1.92
FA2.1	0.355±0.0203	32.71±8.58
FA2.2	0.368±0.0109	28.26±1.56

C. 3 Uni-Stable 3D images Segmentation

Maximum-Match analysis for 5 brains is repeated again for 3D Universal images under the 3 settings (Figure 6, Figure 7, Table 7 and Table 8). In both Figure 6 and Figure 7: Otsu, K-Means and FCM curves are overlapping. The SFCM is shifted a little bit downward below them; however, all of them are aligned almost to the same threshold point. This indicates that segmentation results are almost independent from the clustering algorithm.

Quantitatively, the average mean and average standard deviation of 5 human brains for maximum match the threshold value and CSF to brain ratio based on 3D Universal images of both CSF/non-CSF and WM/non-WM under the different three settings are demonstrated in Table 7 and Table 8 respectively. The average mean values are almost the same such as Table 5 and Table 6; however, the average standard-deviation values are much lower than in the MD and FA cases. This indicates that segmentation of the Uni-Stable-3D images is almost independent of the clustering method.

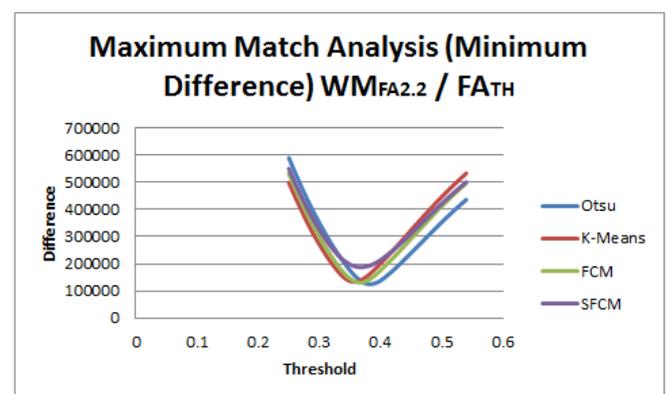
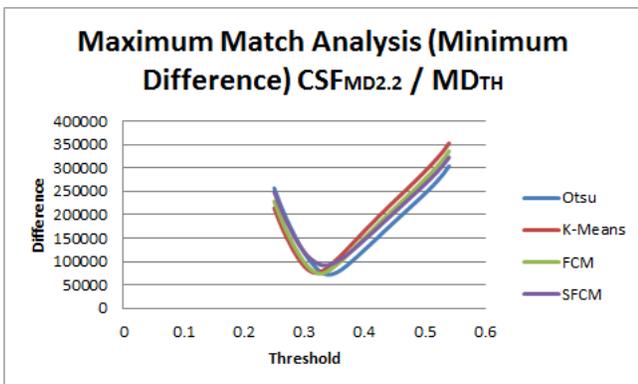
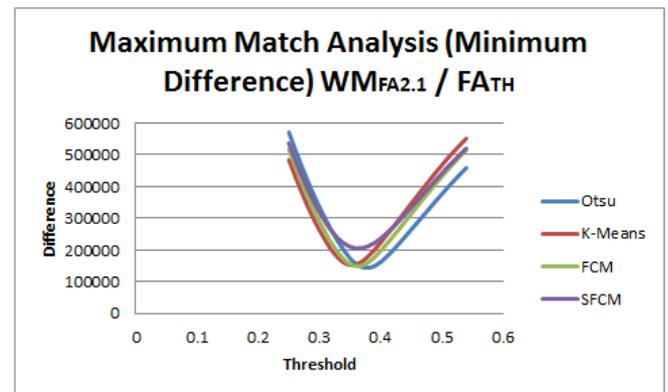
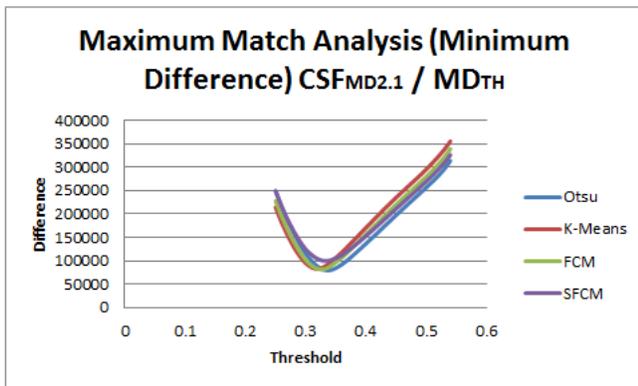
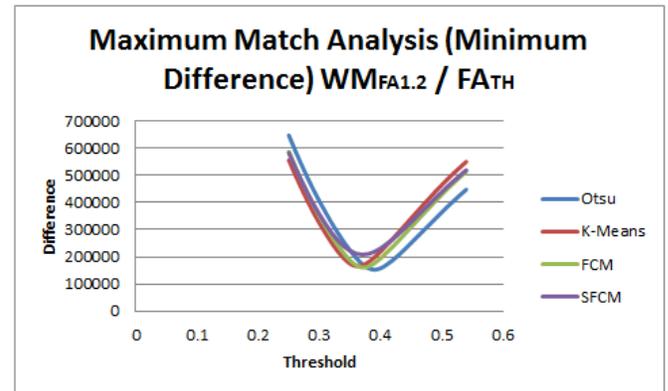
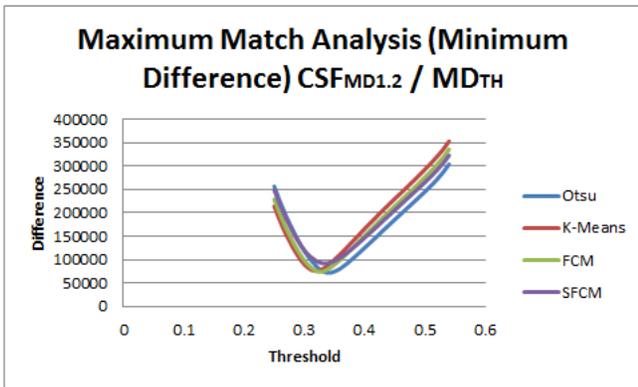
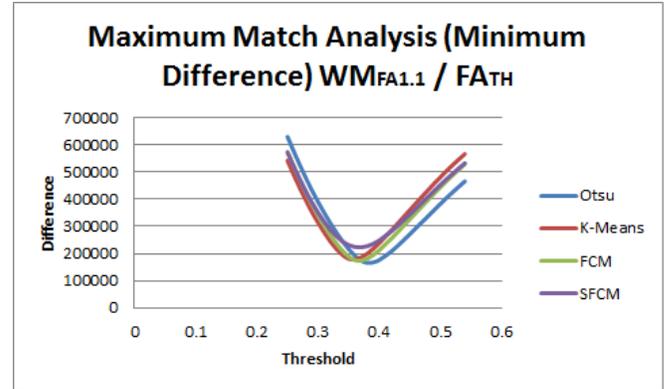
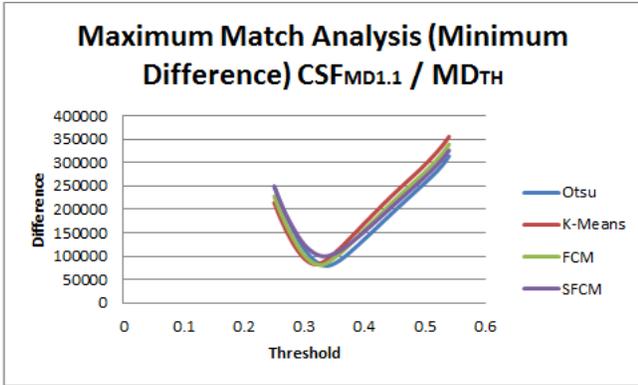


Figure 4 Maximum match analysis for CSF using MD Cluster Maps.

Figure 5 Maximum-Match analysis for WM using FA Cluster Maps.

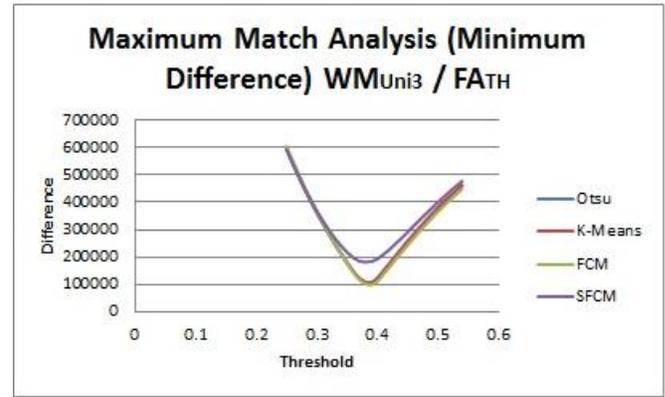
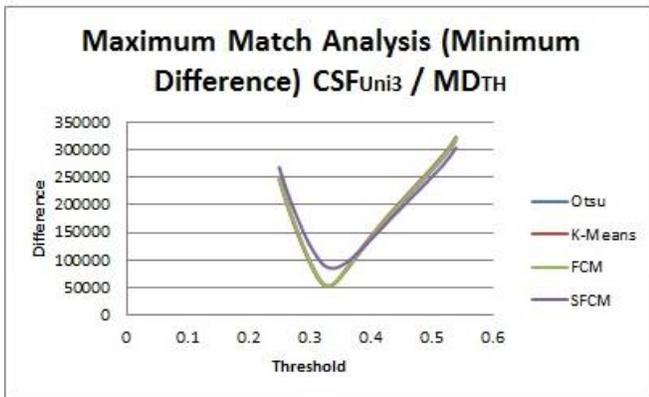
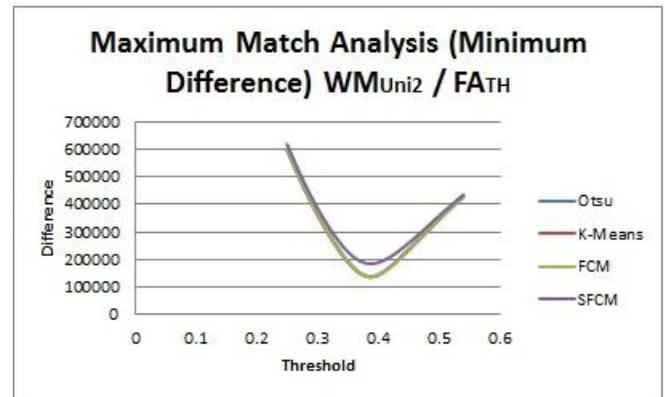
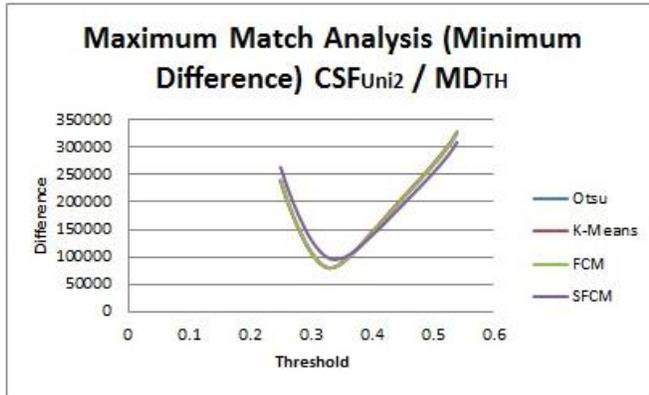
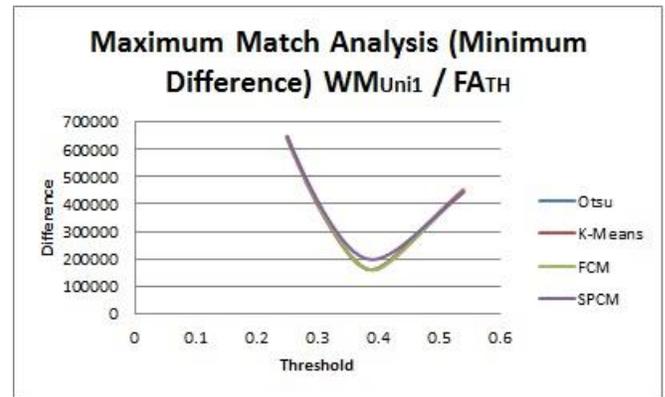
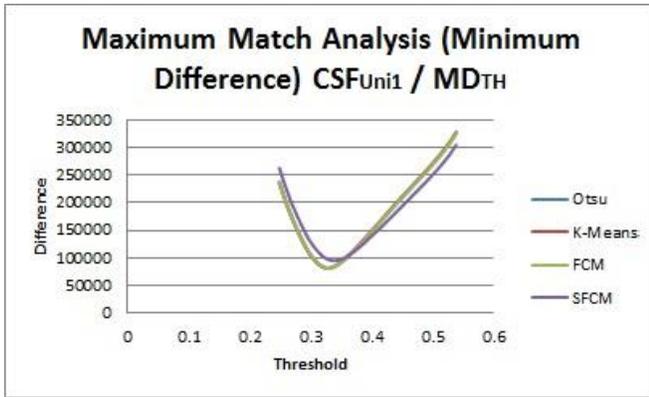


Figure 6 Maximum match analysis for CSF using CSF_{Uni} Cluster Maps

Figure 7 Maximum match analysis for WM using WM_{Uni} Cluster Maps



Table 7 Average Mean and Average standard deviation of 5 human brains for maximum match Threshold value and CSF to Brain ratio based on 3D Universal CSF/non-CSF Images of different settings

		Threshold		CSF to Brain Ratio	
		AVG	STD	AVG	STD
CSF _{Uni1}	Brain1	0.3325	0.0050	17.80%	0.4570
	Brain2	0.2925	0.0050	17.82%	0.5550
	Brain3	0.3075	0.0050	18.99%	0.4440
	Brain4	0.3025	0.0050	21.59%	0.4890
	Brain5	0.3125	0.0050	16.01%	0.4200
	Average	0.310 ± 0.0050		18.44% ± 0.4730	
CSF _{Uni2}	Brain1	0.3325	0.0050	17.83%	0.3450
	Brain2	0.2925	0.0050	17.72%	0.4740
	Brain3	0.3075	0.0050	19.09%	0.4140
	Brain4	0.3025	0.0050	21.64%	0.4260
	Brain5	0.3125	0.0050	16.03%	0.3550
	Average	0.310 ± 0.0050		18.46% ± 0.4028	
CSF _{Uni3}	Brain1	0.3325	0.0050	17.12%	0.2830
	Brain2	0.2925	0.0050	17.20%	0.4300
	Brain3	0.3025	0.0050	18.42%	0.3100
	Brain4	0.295	0.0058	21.13%	0.3790
	Brain5	0.3025	0.0050	16.10%	0.2740
	Average	0.305 ± 0.0052		17.99% ± 0.3352	

Table 8 Average Mean and Average standard deviation of 5 human brains for maximum match Threshold value and WM to Brain ratio based on 3D Universal WM/non-WM Images of different settings

		Threshold		WM to Brain Ratio	
		AVG	STD	AVG	STD
WM _{Uni1}	Brain1	0.39	0.0000	26.03%	0.3980
	Brain2	0.39	0.0000	28.41%	0.4230
	Brain3	0.39	0.0100	29.34%	0.8500
	Brain4	0.41	0.0050	25.31%	0.2360
	Brain5	0.36	0.0000	26.34%	0.5250
	Average	0.3865 ± 0.0030		27.085% ± 0.4864	
WM _{Uni2}	Brain1	0.39	0.0000	25.47%	0.3030
	Brain2	0.38	0.0000	27.80%	0.3550
	Brain3	0.38	0.0096	28.45%	0.7580
	Brain4	0.40	0.0000	24.81%	0.1660
	Brain5	0.36	0.0000	25.50%	0.3250
	Average	0.3825 ± 0.0019		26.4065% ± 0.3814	
WM _{Uni3}	Brain1	0.39	0.0050	26.14%	0.2620
	Brain2	0.39	0.0058	27.57%	0.2810
	Brain3	0.36	0.0350	33.39%	4.3550
	Brain4	0.40	0.0050	24.69%	0.2650
	Brain5	0.36	0.0000	25.46%	0.2100
	Average	0.38 ± 0.0102		27.4505% ± 1.0746	

For CSF/non-CSF Uni-Stable-3D images, Setting 3 provides the lowest average standard deviations and hence the most stable setup. For WM/non-WM Uni-Stable-3D images, Setting 2 provides the most stable setup.

IV. RESULT AND DISCUSSIONS

The Uni-Stable-3D is a new method for 3D medical image enhancement which produces images of high contrast from the scanned anisotropic images. It is basically an upgraded version of the former Uni-Stable method. This is done by estimating some intermediate slices by resizing the original scans. Rescaling has been achieved at three different levels: rescaling of eigenvalues of diffusion, rescaling the Scalar Indexes from the original eigenvalues, and rescaling the cluster maps of the segmentation of the original Scalar Indexes. Four different interpolation methods and four

different clustering algorithms have been employed in the process.

The Uni-Stable-3D images are almost universal as they combine a variety of algorithms point-of-view into one 3D probability map. This reduces boundary-overlapping among different tissues, and hence improves the uniqueness of the segmentation problem solution.

The stability factor of the Uni-Stable-3D Images is measured by maximum match analysis between the cluster maps which are generated from Uni-Stable-3D images using a variety of clustering methods with respect to true fact references. For CSF/non-CSF, the true fact reference is taken as the threshold of MD scalar index's histogram after being resized using the nearest interpolation and again, for WM/non-WM, the true fact reference is taken as the threshold of FA scalar index's histogram after being resized using nearest

interpolation. The same is repeated again but using cluster maps which are generated by applying some clustering methods to MD and FA.

The resultant standard deviations of Uni-Stable-3D images maximum match analysis in both threshold and tissue to brain ratio (tables 7 and 8) are much lower than MD and FA (tables 5 and 6). This reflects the stability of the Uni-Stable-3D images and indicates that they are almost clustering-algorithm-independent. The same process was repeated for 5 brains and the results were also the same.

Referring to the former research [22] that has been developed to produce Uni-Stable images based on multi-2D slices; for the same 5 brains, maximum match analysis for CSFUni and WMUni, there are no significant changes compared to Uni-Stable-3D method in mean values and SD values are still relatively very small in both cases (Table 9). Those minor differences are due to the interpolation process used in the Uni-Stable-3D with the advantage of covering the gaps between 2 successive slices.

Table 9 Comparison between clustering results of Uni-Stable method and Uni-Stable-3D method.

CSF/non-CSF		WM/non-WM	
CSF _{Uni}	0.29±0.002	WM _{Uni}	0.39±0.003
CSF _{Uni1}	0.310 ± 0.0050	WM _{Uni1}	0.3865 ± 0.0030
CSF _{Uni2}	0.310 ± 0.0050	WM _{Uni2}	0.3825± 0.0019
CSF _{Uni3}	0.305 ± 0.0052	WM _{Uni3}	0.38 ± 0.0102

Cubic, Lanczos2 and Lanczos 3 produce some negative values because of their kernel function, which can be eliminated. However, Lanczos2 and Lanczos3 Interpolation methods might not be suitable to be used in the level of resizing the eigenvalues because they depend on Sinc function. As the Sinc function oscillates, some small positive values could be produced in the background zone. Because of the rational nature of WM/non-WM scalar index calculations, extra regions would be generated in the background zone such as FA images (Figure 8). However, for integration based scalar indexes which are used to find CSF/non-CSF scalar indexes such as MD, these small values have almost no effect (Figure 8).

Finally, it is concluded that the Uni-Stable-3D method might be a straightforward solution for the

segmentation problem of medical images, where the segmentation process can be achieved using only one Uni-Stable-3D image and any clustering method.

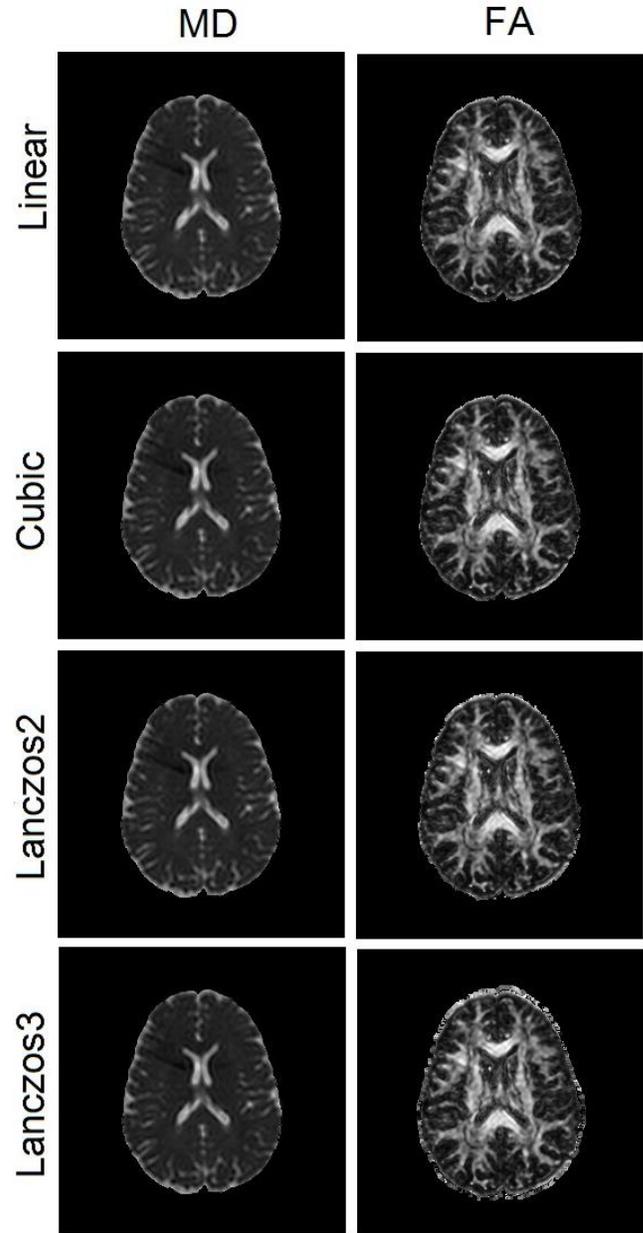


Figure 8 The Effect of some Interpolation methods for eigenvalues on the generated scalar indexes.

CONFLICTS OF INTEREST

They reported that there was no conflict of interest between the authors and their respective institutions.

RESEARCH AND PUBLICATION ETHICS

In the studies carried out within the scope of this article, the rules of research and publication ethics were followed.



ACKNOWLEDGMENT

Laboratory of Brain Anatomical MRI – Johns Hopkins Medical Institute at Johns Hopkins University for provision of DT-MRI data and DTI-Studio utility.

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