AN ALGORITHM TO SEGMENT THE MID-BRAIN STRUCTURES USING MULTI-RESOLUTION NON-RIGID REGISTRATION

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ABSTRACT: In present study, a reference based technique has been proposed to segment mid-brain structures in 3D Magnetic Resonance (MR) images using multi-resolution non-rigid registration. The proposed scheme segmented the mid-brain structures in two stages. During first stage, a target image was registered to an already segmented reference image while in second stage, segmentation information was mapped from reference to target medical image. Using this scheme, the aim was to segment nine mid-brain structures including left ventricle, right ventricle, third ventricle, anterior commissure, posterior commissure, left putamen, right putamen, left caudate nucleus and right caudate nucleus. Results of automatic segmentation achieved through reference based non-rigid registration were validated by comparing with the manual segmentation, considered as ground truth. Three metrics namely Dice Coefficient, Sensitivity and Positive Predictive Values were used for assessing the segmentation results. The proposed algorithm showed the satisfactory segmentation of mid-brain structures by achieving a mean sensitivity of 89. 85 % for five target MR images. The results indicated that the proposed scheme performed accurate segmentation of mid-brain structures.

Keywords: Segmentation, Non-Rigid Registration, Magnetic Resonance Images, Mid-Brain Structures.

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INTRODUCTION

Accurate segmentation of medical images is very important to localize specific mid-brain structures in Deep Brain Stimulation (DBS) surgery, treatment planning, gamma knife radio surgery and study of anatomical structures (Doshi *et al*., 2016; Khan *et al*., 2008; Hamid *et al*., 2005). Prominent image segmentation techniques normally involve pixel-classification methods (Pham *et al*., 2000). These methods are based upon the location and shape of the structures of interest but do not take the spatial relationship between them into consideration. This often leads to less precise segmentation of medical images in general and brain structures in particular. Reference-guided approaches are a powerful tool for medical image segmentation when a standard reference or atlas is available (Doshi *et al*., 2016; Iglesias and Sabuncu, 2015; Tang *et al*., 2015 and Yousefi *et al*., 2010). Reference or atlas is generated by compiling information on the anatomy requiring segmentation. This atlas is then used as a reference frame for segmenting new images. Unlike the pixel classification methods, reference-guided approaches take the spatial domain of the image into consideration (Ji *et al*., 2014; Ji *et al*., 2012; Tsai *et al*., 2003). These approaches vary in terms of image registration methods employed to relate spatial locations of target image to reference image by finding a geometrical transformation (Rueckert and Aljabar, 2010). In the present study, segmentation of nine mid-brain structures is proposed by registering the 3D target MR images with a high quality 3D reference MR image. Delineation of these brain structures can be difficult due to similar intensities of surrounding issues. Proposed non-rigid registration scheme ensures automatic segmentation of desired structures with satisfactory degree of accuracy.

MATERIALS AND METHODS

A three step scheme was proposed for segmentation of mid-brain structures. In the first step, reference image and target image were globally aligned using affine transformation. Region of interest was selected and a mesh of control points was initialized over the region using the affine transformation. In the second step, an intensity based non-rigid registration was employed at three resolutions ie 20 mm, 10 mm, 5 mm successively to cater for local deformations and warping. Cubic B-spline was used as a non-linear transformation model, which was optimized by GD method at all the three resolutions by maximizing image similarity (NCC). In the third step, segmented mid-brain structures in the reference image were mapped to the target image by using the final transformation achieved in the second step (Fig. I).

Affine registration: Proposed programe was started with the global alignment of reference image M and target image N using affine transformation. Landmark based approach was used and landmark points were marked in both the images. These landmarks were used to determine the affine parameters for translation, rotation, scaling and shearing effect. Let matrix A denote the combined effect of rotation, scaling and skewing as is shown in (1) (Jenkinson and Smith, 2001)

$$A = \begin{bmatrix} a & b & c \\ d & e & f \\ g & h & i \end{bmatrix} \qquad (1)$$

Where $a - i$ represent the affine parameters. The transformation function T_{Affine} can be represented as in (2)

$$T_{Affine}(\mathrm{X}) = \mathrm{AX} + \mathrm{t} \qquad (2)$$

Where $\boldsymbol{t} = [t_x\ t_y\ t_z]^T$ and $\boldsymbol{X} = [x\ \ y\ \ z]^T$. The affine parameters thus obtained were used to globally register the two images.

Multi-Resolution Non-Rigid Registration: Once the initialization step was completed, region of interest was selected by adding 20 mm to the minimum and maximum extent of mid-brain structures. This step was followed by intensity based non-rigid registration. Proposed registration was run directly on image intensity values and used all available information content without previous elimination of data by the user. This computational cost of working on full image was reduced by using a multi-resolutional approach. Proposed non-rigid registration employs Cubic B-splines as transformation model, Normalized Cross Correlation as an image similarity criterion and GD as optimization technique (Holden *et al.*, 2000; Rueckert *et al.*, 1999; Flannery, 1992).

Cubic B-splines transform based registration scheme was used to cater for local warping and deformations. Such transformation assumed that corresponding points were marked in reference and target images, generally termed as nodes or control points (CPs). These CPs then aid in approximating the displacements using CBS based transformation model for mapping a particular CP in source image to corresponding CP in reference image. This produced a smooth transformation between control points as in (3)

$$T(p_i) = p'_i \qquad (3)$$

Where p_i and p'_i represented the coordinates of the CPs in target image and reference image respectively.

NCC was selected as the similarity criterion to check the status of alignment between reference image (M) and target image (N). Since both the images were acquired using the same imaging modality (MRI), so direct comparison of voxel intensities was possible. CBS transformation was determined/optimized iteratively to maximize the image similarity criterion. In the proposed programe, similarity measure was maximized using GD optimization technique.

To start with the multi-resolution non-rigid registration process, control points with lowest resolution of 20 mm were defined over the registration domain. Transformation achieved at this resolution was optimized iteratively, such that image similarity measure was maximized. Then was moved to the next higher resolution by defining control points with uniform spacing of 10 mm. These CPs were transformed using the transformation achieved at previous resolution i.e. $Transformation_1$. Optimization process using GD was repeated to maximize the similarity criterion. Consequently, transformation $Transformation_2$ for 2nd stage was achieved. Similar process was repeated once again for control points with uniform spacing of 5 mm to get the transformation for 3rd stage. The transformation reached at the end of stage-3 $Transformation_3$ which was the final transformation for the proposed registration. If M is considered as the reference image, N as the target image and D as the registration domain, then the optimization process is expressed by the transformation (4). ISM is the image similarity measure (NCC in this case)

$$Trans_n = \max[ISM(M(D), N(T_{CBS}(D)))] \qquad (4)$$

Mapping of segmented structures: Once the image registration process was completed, nine already segmented mid-brain structures of reference image ie left ventricle, right ventricle, 3rd ventricle, left putamen, right putamen, left caudate nucleus, right caudate nucleus, anterior commissure and posterior commissure were mapped (Ali and Khan, 2011) from the reference image to target images by applying the final transformation achieved, as a result of registration process. This provided the locations of the corresponding mid-brain structures in the target MRI and consequently automatic segmentation of the desired structures was achieved.

RESULTS AND DISCUSSION

Non-rigid registration of five target 3D MR images with reference to 3D MR image was carried out to segment the mid-brain structures. MATLAB was used for image registration and validation purposes. 2D slices of mid-brain region overlaid with CPs at three resolutions i.e. 20 mm, 10 mm and 5 mm Fig- 2 as a, b, c. 3D view of mid-brain region showing control points with 5 mm resolution and final location of these control points after applying the stage-3 transformation Fig- 2 as d, e.

Registration achieved using the proposed technique was evaluated qualitatively using checkerboard display of the reference and the registered target images (Fig. 3). Checkerboard display is a visualization technique for inspection of image registration that overlays the reference and registered target MR images showing alternate squares from the two images. Checkerboard slices of reference and target image after affine registration are shown (Fig. 4). Clear misalignment was visible after affine registration, especially at the edges of checkerboard slices. Affine registration acted as a good initialization step which was followed by three stage non-rigid registration to cater for the local deformations and warping. Fig. 5 depicts checkerboard slices of reference and target image after stage-3 of non-rigid registration. It could be easily noted that the misalignment decreased to huge extent after non-rigid registrations, and the intensities of both the images became similar.

The contours of automatically segmented structures using the proposed programe can be seen in Fig. 6 and Fig. 7. 2D axial slices and 3D view of reference image with overlaid pre-segmented mid-brain structures are depicted in Fig. 6. 2D axial slices and 3D view of registered target image with the overlaid contours of segmented mid-brain structures were achieved after reference to target structure mapping are shown in Fig. 7. It can be easily seen in Fig. 7 that the proposed scheme enabled satisfactory segmentation of desired structures. The misalignment of the posterior part of the right and left lateral ventricles (bottom row, center) is due to a significant lateral ventricle shape difference between the target and the reference image. Segmentation results of nine automatically segmented mid-brain structures were validated for five different target MR images.

In addition to the qualitative assessment, quantitative analysis was carried out using the truth model. For this purpose, manual segmentation of nine structures was carried out for each target MRI and was considered to be the ground truth. Results of automatic segmentation were compared with manual segmentation using Dice Coefficient (Zou *et al*., 2004), Positive Predictive Value (PPV) and sensitivity metrics (Table -1). Value of 0 indicated that there was no agreement between automatically segmented structures and the ground truth model, whereas value of 1 indicated maximum agreement between the two. It could be noted that the computed values of all the three metrics varied between 0.84-0.95, which means that more than 80% of the pixels matched the automatically and manually segmented structures. Mean value of DC, Sensitivity and PPV for five target MR images came out to be 0.89, 0.89 and 0.90 with standard deviation of 0.03, 0.03 and 0.02 respectively.

These results endorsed the findings of Tang *et al*. (2016) and Pallavaram *et al*. (2015) studies who proposed that the multi resolution non rigid registration can produce superior results. A coarse to fine multi resolution technique was used by (Tang *et al*. 2016) to increase the registration accuracy and convergence speed. Furthermore, this multi resolution technique prevented from falling into local extreme value. Experiments were conducted on checkboard test images similar to our study in Fig. 4 and Fig. 5 and other images including medical images and the results showed increase in accuracy of the proposed system by (Pallavaram *et al*. 2015) who showed a non-rigid image registration using the guided reference/atlas showing better results in terms of accuracy and precision as compared to popular manual methods for STN-DBS. Furthermore the present result have been endorsed by the studies carried out by Doshi *et al*. (2016) and Ji *et al*. (2014) who stated that atlas based guided approach using spatial relationship into consideration could produce better results as compared to pixel classification methods.

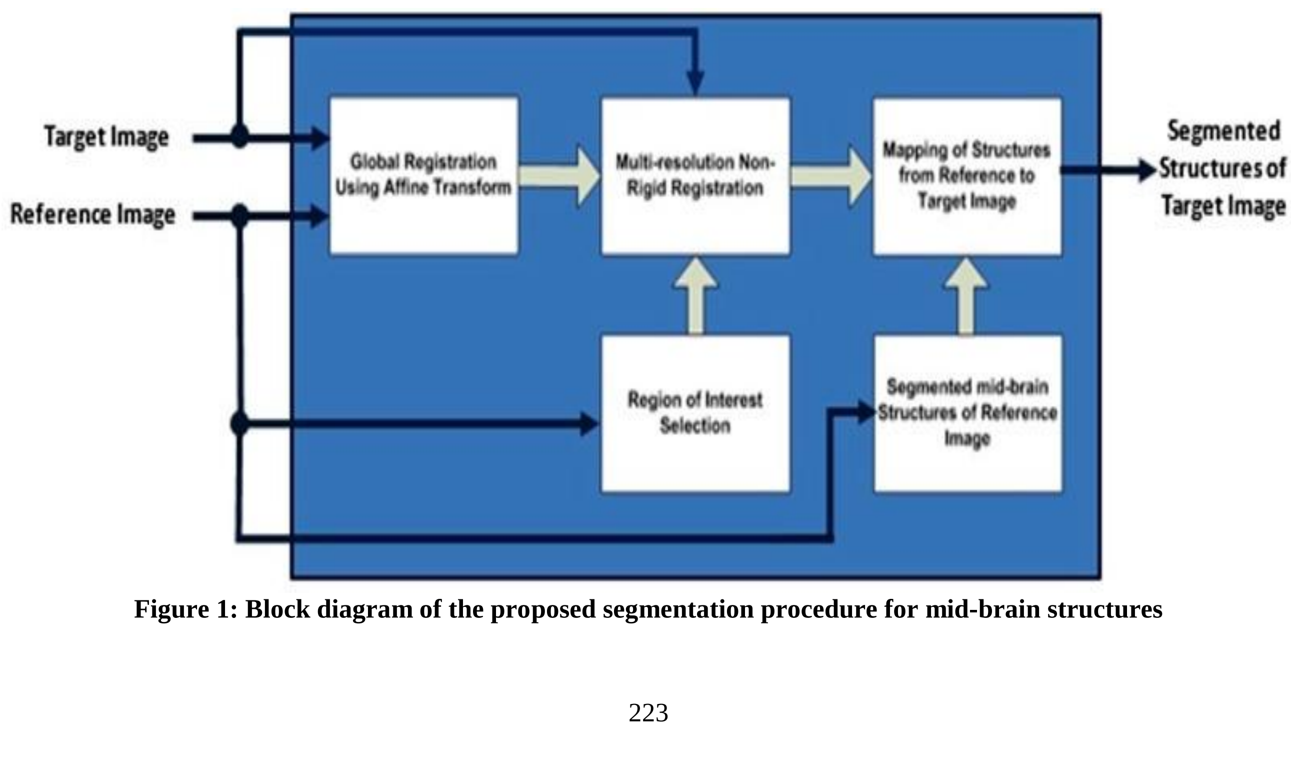


Figure 1: Block diagram of the proposed segmentation procedure for mid-brain structures

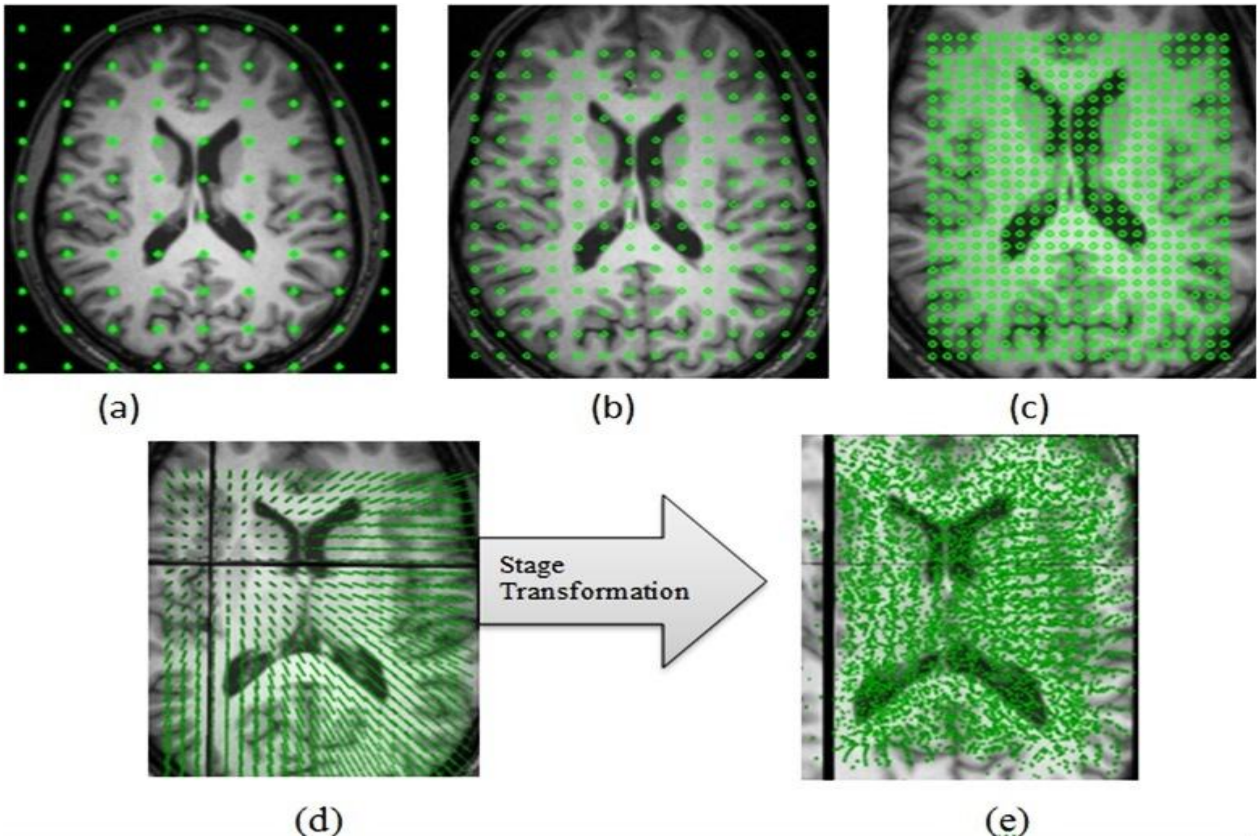


Figure 2: (a)-(c). Grid of control points showing 20mm, 10mm, 5mm spacing placed over 2D view of reference image. (d) 3D view of mid-brain region showing control points with 5mm resolution. (e) Final location of these control points after applying stage-3 transformation

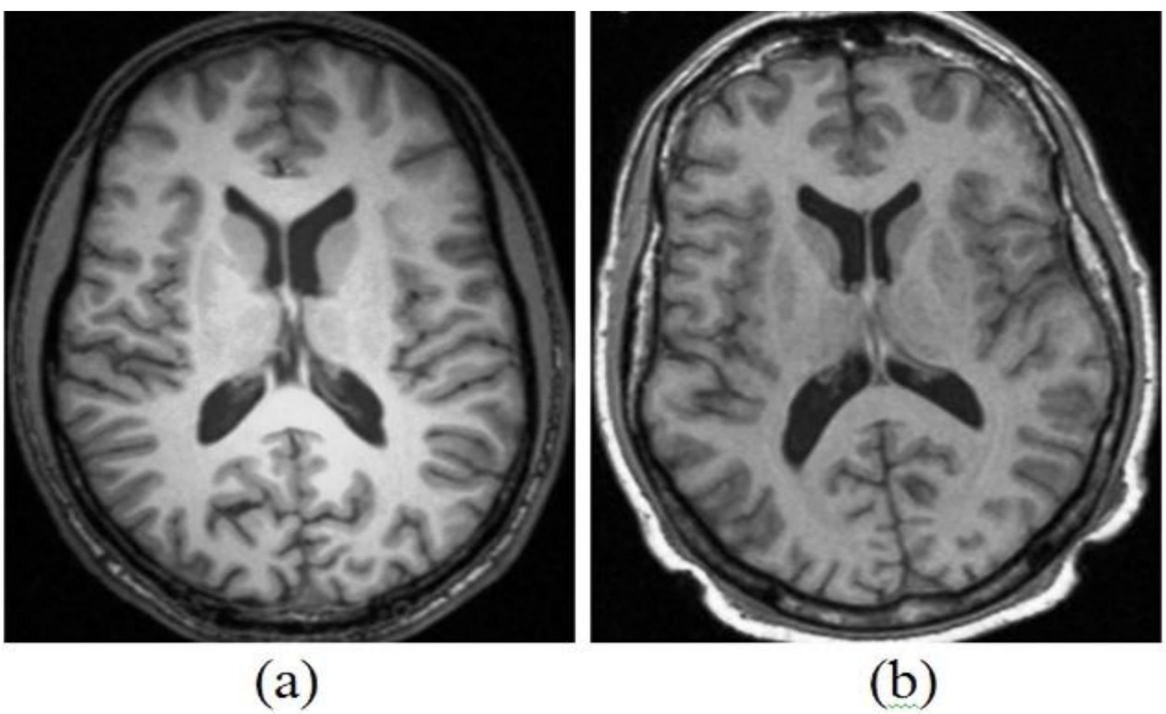


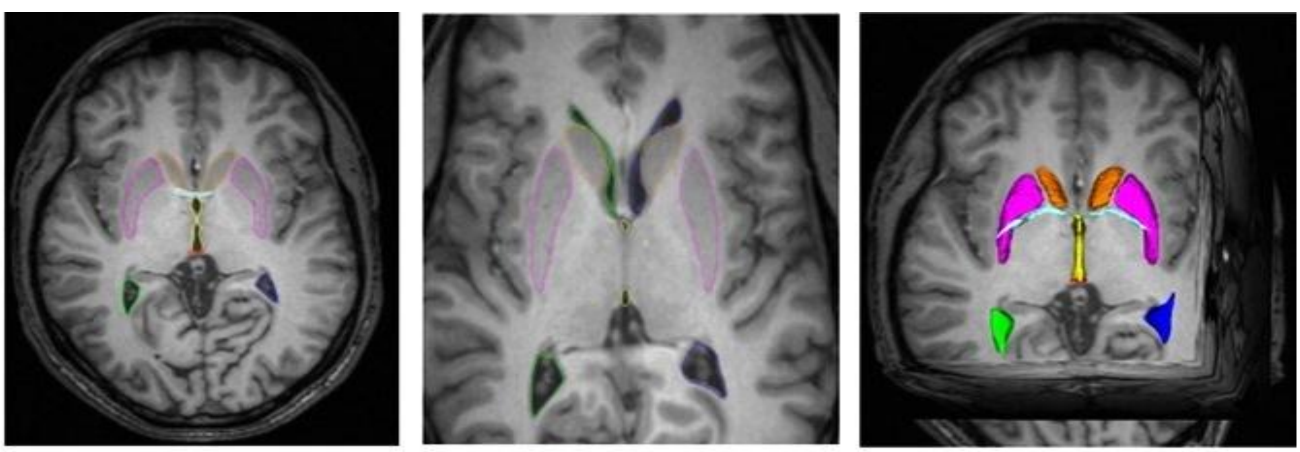
Figure 3: (a) Reference image (b) Target image

(a) (b)

Figure 4: Checkerboard slices of reference and target image after affine registration (a) Axial (b) Sagittal.

(a) (b)

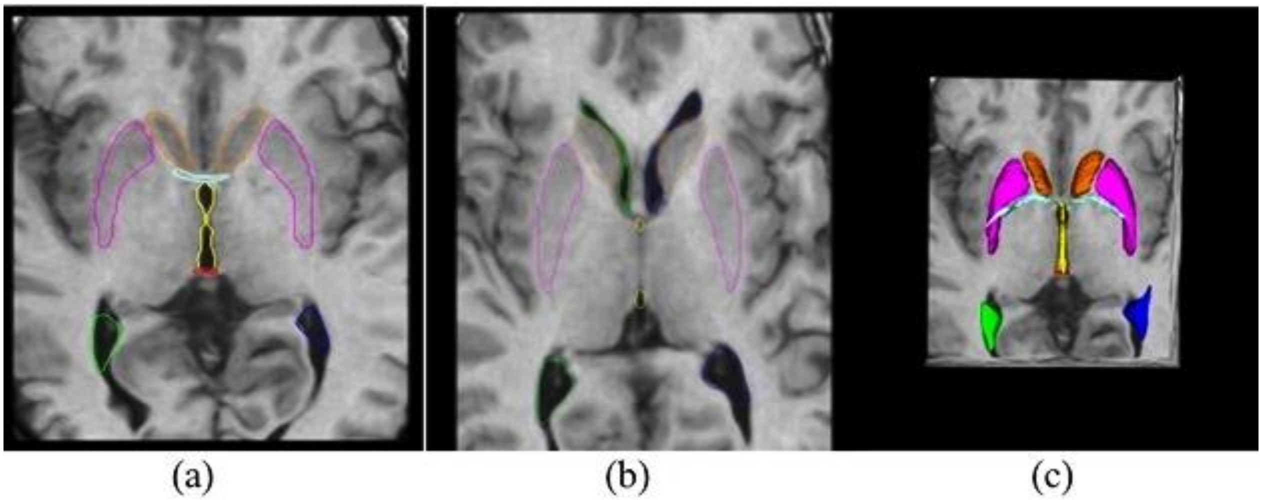
Figure 5: Checkerboard slices of reference and target image after stage-3 transformation (a) Axial (b) Sagittal



(a) (b) (c)

Left Right 3rd Caudate Putamen Anterior Posterior
Ventricle Ventricle Ventricle Nucleus Commissure

Figure 6: Reference image with overlaid pre-segmented mid-brain structures
(a) Axial slice (b) Zoomed axial slice (c) 3D view



Left Right 3rd Ventricle Ventricle Caudate Ventricle Putamen Nucleus Anterior Commissure Posterior

Figure 7: Registered target image with the overlaid contours of segmented mid-brain structures after reference to target mapping using stage-3 transformation

(a) Axial slice (b) Zoomed axial slice (c) 3D view

Table 1: Validation results for segmented mid-brain structures of five target images using Dice coefficient, Sensitivity and Positive Predictive Value

	Case No.	Left Ventricle	Right Ventricle	3rd Ventricle	Left Putamen	Right Putamen	Left Caudate Nucleus	Right Caudate Nucleus	Anterior Commissure	Posterior Commissure
Dice Coefficient (D)	1	0.8826	0.9240	0.8929	0.8711	0.9123	0.8441	0.9073	0.9161	0.9064
	2	0.9430	0.9325	0.9084	0.9152	0.8936	0.8409	0.8853	0.8820	0.8970
	3	0.9361	0.9443	0.8662	0.9204	0.9180	0.9226	0.8914	0.9343	0.9002
	4	0.9052	0.8711	0.9223	0.8404	0.9530	0.9175	0.9027	0.8972	0.9114
	5	0.8933	0.9028	0.9180	0.8620	0.9335	0.8914	0.9277	0.8852	0.9318
Sensitivity (S)	1	0.8931	0.9361	0.9015	0.8649	0.8847	0.9034	0.8959	0.8782	0.8617
	2	0.9217	0.9234	0.8810	0.9114	0.8719	0.9229	0.8808	0.9246	0.9082
	3	0.914 0	0.8812	0.8723	0.9071	0.8819	0.9259	0.9149	0.8774	0.8879
	4	0.9008	0.8583	0.8949	0.8832	0.9141	0.9144	0.9268	0.9190	0.8506
	5	0.9457	0.9093	0.9159	0.8741	0.9369	0.8947	0.9306	0.8767	0.8722
Positive Predictive Value (PP7 V)	1	0.912 0	0.9033	0.9228	0.8838	0.9007	0.8965	0.8637	0.9373	0.9270
	2	0.9045	0.9277	0.9190	0.8942	0.9167	0.9073	0.9170	0.8758	0.8848
	3	0.9438	0.8960	0.8914	0.9034	0.9243	0.9310	0.9076	0.8939	0.940
	4	0.9066	0.8819	0.8667	0.8746	0.8962	0.9102	0.8929	0.9087	0.8933
	5	0.893 0	0.9113	0.8708	0.9072	0.8860	0.8740	0.8846	0.9123	0.8765

Conclusion: The results indicate that the proposed scheme using multi-resolution non-rigid registration performed accurate segmentation of mid-brain structures in 3D magnetic resonance images.

REFERENCES

Ali, S.S. and M.F. Khan (2011). Atlas based segmentation of brain structures in 3D MR images. In 2011 4th Intl. Conf. Biomed Engg.

Info. (BMEI). IEEE, pp: 137–141.

Doshi, J., G. Erus, Y. Ou, S.M. Resnick, R.C. Gur, R.E. Gur, T.D. Satterthwaite, S. Furth and C. Davatzikos (2016). MUSE: Multi-atlas region segmentation utilizing ensembles of registration algorithms and parameters and locally optimal atlas selection. NeuroImage 127:186–195.

Press, W.H., S.A. Teukolsky, W.T. Vetterling and B.P. Flannery (1992). Numerical recipes in C. the art of scientific computing of Cambridge, 2nd edition (the art of scientific computing, Cambridge University Press, USA) pp. 137.

Hamid, N.A., R.D. Mitchell, P. Mocroft, G.W.M. Westby, J. Milner and H. Pall (2005). Targeting the subthalamic nucleus for deep brain stimulation: technical approach and fusion of pre and postoperative MR images to define accuracy of lead placement. J. Neurol. Neurosur. Psych. 76(3): 409–14.

Holden, M., D.L. Hill, E.R. Denton, J.M. Jarosz, T.C. Cox, T. Rohlfing, J. Goodey and D.J. Hawkes (2000). Voxel similarity measures for 3-D serial MR brain image registration. IEEE trans. med. imaging, 19(2): 94–102.

Iglesias, J.E. and M.R. Sabuncu (2015). Multi-atlas segmentation of biomedical images: A survey. Med. Img. Analysis 24(1): 205–219.

Jenkinson, M. and S. Smith (2001). A global optimisation method for robust affine registration of brain images. Med. Img. Analysis 5(2): 143-156.

Ji, Z., J. Liu, G. Cao, Q. Sun and Q. Chen (2014). Robust spatially constrained fuzzy c-means algorithm for brain MR image segmentation. Patt. Recog. 47(7): 2454–2466.

Ji, Z., Y. Xia, Q. Sun, Q. Chen, D. Xia and D.D. Feng (2012). Fuzzy local Gaussian mixture model for brain MR image segmentation. IEEE Trans. Info. Tech. Biomed. 16(3): 339–347.

Khan, M.F., K. Mewes, R.E. Gross and O. Škrinjar (2008). Assessment of brain shift related to deep brain stimulation surgery. Ster. Func. Neurosur. 86(1): 44–53.

Pallavaram, S., P.F. D’Haese, W. Lake, P.E. Konrad, B.M. Dawant and J.S. Neimat (2015). Fully automated targeting using nonrigid image registration matches accuracy and exceeds precision of best manual approaches to subthalamic deep brain stimulation targeting in Parkinson disease. Neurosurgery 76(6): 756–65.

Pham, D.L., C. Xu and J.L. Prince (2000). Current methods in medical image segmentation. Ann. Rev. Biomed. Engg. 2(1): 315–337.

Rueckert, D., L.I. Sonoda, C. Hayes, D.L. Hill, M.O. Leach and D.J. Hawkes (1999). Nonrigid registration using free-form deformations: application to breast MR images. IEEE Trans. Med. Imag. 18(8): 712–721.

Rueckert, D. and P. Aljabar (2010). Nonrigid Registration of Medical Images: Theory, Methods and Applications IEEE Sig. Proc.Mag. 27(4): 113–119.

Tsai, A., W.M. Wells, C. Tempany, E. Grimson and A.S. Willsky (2003). Coupled Multi-shape Model and Mutual Information for Medical Image Segmentation. In Biennial Intl. Conf. Info. Proc. Med. Imag. pp. 185–197.

Tang, X., D. Crocetti, K. Kutten, C. Ceritoglu, M.S. Albert, S. Mori, S.H. Mostofsky and M.I. Miller (2015). Segmentation of brain magnetic resonance images based on multi-atlas likelihood fusion: testing using data with a broad range of anatomical and photometric profiles. Front. Neurosci. 9: 61.

Tang, Z., P. Xue, P. Yang, D. Jia and E. Dong (2016). An Effective Non-rigid Image Registration Method Based on Active Demons Algorithm. IEEE 29th Intl. Symp. CBMS. IEEE, pp. 124–129.

Yousefi, S., N. Kehtarnavaz and A. Gholipour, (2010). Comparison of atlas-based segmentation of subcortical structures in magnetic resonance brain images. SSIAI, 2010 IEEE pp. 1-4.

Zou, K.H., S.K. Warfield, A. Bharatha, C.M. Tempany, M.R. Kaus, S.J. Haker, W.M. Wells, F.A. Jolesz and R. Kikinis (2004). Statistical validation of image segmentation quality based on a spatial overlap index. Acad. rad. 11(2): 178–89.