35th Annual International Conference of the IEEE EMBS
Osaka, Japan, 3 - 7 July, 2013

Fuzzy connectedness image segmentation for newborn brain extraction in MR images*

Syoji Kobashi, *Member*, *IEEE*, and Jayaram K. Udupa, *Fellow, IEEE*

Abstract— **Newborn's brain has a various shape, and easily changes with not only brain developing and cerebral diseases. Although the brain segmentation in MR images is an effective way to quantify the brain shape and size, there are few studies in neonatal brain MR image analysis. This paper introduces a novel method based on fuzzy connectedness (FC) with fuzzy object model (FOM). FOM is built from a training dataset, and gives fuzzy degree belonging to parenchyma with respect to location and intensity. FC is calculated from object affinity and homogeneous affinity, and the object affinity is given by the FOM. The method first segments the white matter, and then segments the surrounding cortex. The propose method has been applied to 10 newborn subjects whose revised age was between -1 month and +2 month. Leave-on-out cross-validation (LOOCV) was conducted, and the mean false-positive volume fraction was 1.33%, the mean false-negative volume fraction was 2.90%, and geometric-mean was 1.42%.**

I. Introduction

Newborn's brain fast changes by the brain development, and also by cerebral disorders. To investigate the newborn's brain, magnetic resonance imaging (MRI) is a promising way because it can acquire anatomical information non-invasively with high-contrast. Because MR images composed of over one hundred sectional images, we need visualization and quantification methods. For example, the cerebrum shape is visualized by volume rendering, and the size is quantified by measuring volume or surface area. Thus, automated cerebral segmentation is the fundamental and the crucial process.

As conventional analysis methods for newborn brain MR images, Weisenfeld *et al.* showed a method based on a probability density map [1], which is used to estimate probability function. Prastawa *et al.* showed a method using a registered probabilistic brain atlas [2]. They also utilize the probabilistic brain atlas to estimate the probability function. Leroy et al. proposed a method without an atlas model [3].

Scale-based fuzzy connectedness (FC) image segmentation [4] is an extension of FC image segmentation (FCIS) [5]. Scale-based and original FCIS frameworks have been applied to a variety of medical image segmentation problems; MR brain segmentation and tissue classification, artery extraction in MR angiography images [6], chest CT object identification, *etc*.

Fuzzy object model (FOM) is introduced for computerized automatic anatomy recognition (AAR), which aims to make quantitative radiology (QR) by Udupa *et al*. [7]. FOM presents anatomical knowledge by means of fuzzy approach. It assigns fuzzy degree belong to object for each point with respect to the position. To demonstrate the performance, FOM had been utilized to AAR of 25 organs in thoracic CT images.

Inspired by the FC and FOM, this paper presents a novel method for newborn brain MR image segmentation. The method extends FOM approach to model knowledge not only location but also intensity. And, we show AAR and delineation methods based on FC with FOM. Because the parenchyma is composed of the white matter (WM) and the surrounding cortex, we segment the WM inside the parenchyma and then segment the cortex. The proposed method is validated in 10 newborn brain MR images using leave-one-out cross validation (LOOCV) procedure.

II. Preliminaries

A. Newborn subjects and MR image acquisition

This study recruited 10 newborn subjects whose revised-age was between -1 and 2 months. The revised-age is an age revised by normal fetal age (*i.e.*, 40 weeks). These subjects had no significant cerebral disorders based on clinical diagnosis by radiologists and physicians. For each subject, a parental informed consent was obtained according to a guideline of local Ethics committee in Hyogo College of Medicine (Hyogo, JAPAN).

T2-weighted MR images were acquired using a 3.0 Tesla MRI scanner (Achieva 3.0T TX, Philips Medical Systems, USA) with a circularly polarized head coil as both the transmitter and receiver; TR = 2000 msec; TE = 106-165 msec. The slice thickness = 1.5 mm; space between slices = 0.75 mm; the number of sagittal slices depending on the width of the subjects' head, the matrix was 320 × 320 and pixel size was 0.75 mm by 0.75 mm.

B. Fuzzy connectedness image segmentation

FC is the maximum fuzzy affinity among all possible paths from seed voxels to a voxel of interest [4][5]. And, fuzzy affinity of a path is defined as the minimum fuzzy affinity between the neighboring voxels along the path. Fuzzy affinity between voxel *c* and voxel *d*, is defined by

*Resrach supported by Ishikawa Hospital, Japan, and Ministry of Education Science, Sports and Culture, Grant-in-Aid for Young Scientists (A), 2010-2012, Japan.

S. Kobashi is with University of Hyogo, Himeji, Hyogo 671-2280 Japan (corresponding author to provide e-mail: kobashi@eng.u-hyogo.ac.jp). He is also with IFReC WPI Osaka University, Suita, Osaka, 565-0871 Japan. And, he was the visiting scholar of Department of Radiology, University of Pennsylvania, Philadelphia, PA 19103-6021 USA.

J. K. Udupa is with Department of Radiology, University of Pennsylvania, Philadelphia, PA 19103-6021 USA.

978-1-4577-0216-7/13/$26.00 ©2013 IEEE

$$\mu_K(c,d) = \sqrt{\mu_\Psi(c,d)\mu_\Phi(c,d)}, \quad (1)$$

where $\mu_K(c,d)$ represents the scale-based FC, from voxel c to voxel d, $\mu_\Psi(c,d)$ estimates scale-based homogeneity affinity and $\mu_\Phi(c,d)$ estimates scale-based object affinity. The scale-based homogeneity affinity evaluates the intensity homogeneity between neighboring two voxels.

The scale-based object affinity estimates a similarity to seed voxels in terms of intensity. It is calculated by using a Gaussian function defined by a mean and a standard deviation intensity of the seed voxels. Scale means B-scale, $f_B(c)$, which is the radius of the largest ball centered at c within which image intensity is "homogeneous".

Absolute FCIS delineates a region whose fuzzy connectedness from seed voxels is higher than a threshold. It requires (1) a seed voxel extraction method, and (2) fuzzy affinity definition. The details are described in Ref. [4].

III. Extended fuzzy object model

This paper extends the concept of FOM [7] with respect to image intensity. For distinction, the former is called FSOM, and the latter is called FIOM. FIOM represents a fuzzy degree belonging to an object with respect to intensity at the position. They are built from training data sets in which experts delineate the cerebral parenchymal region. We built FSOM of foreground region (FG-FSOM) and, FSOM and FIOM of cerebral parenchymal region (CP-FSOM and CP-FIOM).

A. Definition

FSOM is a set of fuzzy degrees given for each voxel. Consider the aligned training dataset, and the parenchymal region is delineated by experts. First, it calculates signed distance from the boundary. For each voxel, the mean, μ, and standard deviation (SD), σ, of distance in the training dataset are transformed into fuzzy degree by a sigmoid function;

$$g(\mu,\sigma) = \begin{cases} 0 & if\ \mu \le -4\sigma \\ \frac{1}{2}\sin\left(\frac{\mu}{4\sigma}\pi\right) + \frac{1}{2} & if\ -4\sigma < \mu < 4\sigma \\ 1 & if\ \mu \ge 4\sigma \end{cases}, \quad (2)$$

It takes 0.5 on the surface voxels, the higher value inside the object, and the lower value outside the object.

FIOM is a set of fuzzy membership functions that are defined at each voxel. It represents a function of belonging to the parenchyma with respect to MR signal value at the position. We define the function as a Gaussian function whose mean and variance are those of the MR signal values in the aligned training datasets where the voxel belongs to parenchyma. The MR signal value is normalized by using cumulative MR signal histogram.

B. Building procedure

FOMs are built by the following steps.

Step 1. Automated foreground separation

Step 2. Manual delineation of parenchymal region

Step 3. Rough alignment of foreground region

Step 4. Distance transform, and mean and SD calculation for each voxel. Transformation of the mean distance into fuzzy degree of FG-FSOM.

Step 5. Fine alignment of FG-FSOM

Step 6. When the alignment is converged, go to the next step. Otherwise, return to step 3.

Step 7. Build CP-FSOM and CP-FIOM using the optimized alignment parameters.

Alignment is done by using only the FG region, and the optimized alignment parameters are applied to the parenchymal region.

To separate FG region, at first, thresholding is applied because the FG region has higher intensity than the background region such as air. The threshold used is a mean intensity of the whole image. Then, it applies opening operation and removes small regions. Next, it determines the most inferior boundary section, which contains the parenchyma. We determine the most inferior boundary section by counting FG voxels for each sagittal section and by using p-tile method.

Rough alignment is done by registering origins and by adjusting the diagonal length of bounding box. For each dataset, origin is set to center of mass of FG region. Linear interpolation is used for transformation. Fine alignment is done using the present FG-FSOM. It optimizes the alignment parameters by using the Nelder-Mead method. Each training dataset is aligned optimally with the present FG-FSOM. The objective function to be minimized is defined by

$$\mathbf{f}(\mathbf{X}) = \sum_{v \in \Omega} \left| \mu_{FG-FSOM}(\mathbf{F}(\mathbf{X}) \cdot v) - 0.5 \right|, \quad (4)$$

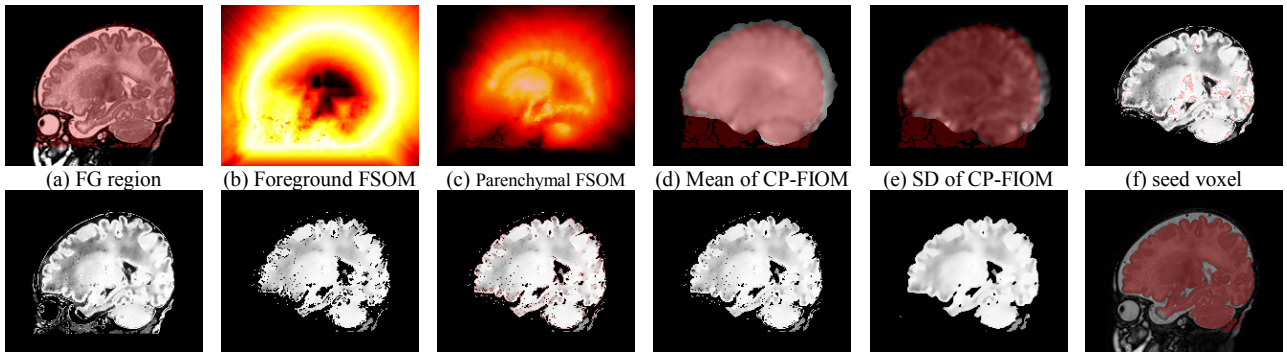
where Ω is the set of surface voxels of the object, $v = [x_v, y_v, z_v]^T$ is a voxel in Ω, $\mathbf{X} = \{x_o, y_o, z_o, s_x, s_y, s_z\}$, $\mathbf{F}(\mathbf{X}) \cdot v$ is the affine transform of v using a translation vector $[x_o, y_o, z_o]$ and a scaling factor $[\mathbf{s_x}, \mathbf{s_y}, \mathbf{s_z}]$, and $\mu_{FG-FSOM}(x)$ is the fuzzy degree at voxel x.

IV. Fully Automated Brain Segmentation method

Automated brain segmentation mainly consists of two players. The first player is AAR using FOMs. It roughly finds the cerebral parenchymal region by registering FOMs to the given MR image. The second player is automated delineation of the cerebral parenchymal region. It is performed with FCIS using FOMs. Because the parenchymal region consists of WM and the surrounding cortex which is gray matter (GM), homogeneity affinity between them takes a low value. Thus, we segment the inside WM, and then segment the surrounding cortex. The procedure is summarized below.

Step 1. Foreground separation, intensity normalization, and FOM alignment using the same procedure of building FOMs

Step 2. FOM based AAR



(a) FG region (b) Foreground FSOM (c) Parenchymal FSOM (d) Mean of CP-FIOM (e) SD of CP-FIOM (f) seed voxel

(g) updated affinity (h) WM fuzzy degree (i) cortex seeds. (j) FC results (k) PVE correction (l) results

Figure 1. Experimental results for subject 1. In (a), FG region (red shaded) is superimposed on raw MR image. In (b) and (c), black-red-yellow-white colors correspond to the low-to-high fuzzy degree. In (d) and (e), the red shaded area is foreground region. In (f) and (i) assigned seed voxels are red shaded area. In (f)-(k), the brighter intensity shows the higher fuzzy degree. In (o), red shaded area shows the segmented region superimposed on the raw MR image.

Step 3. WM segmentation using FOM based FCIS

Step 4. Cortex segmentation using FOM based FCIS

Step 5. PVE correction and defuzzification

A. *[Step 2] FOM based AAR*

We assign a fuzzy degree for each voxel by using FSOM. The fuzzy degree takes a value between 0 and 1, and the higher value means the higher degree of belonging to the object. By employing both CP-FSOM and CP-FIOM, we can assign fuzzy degrees with respect to shape, location, and intensity to the success of recognition. Consider a voxel v whose MR signal is $I(v)$. The fuzzy degree $\mu_{CP-FOM}(v)$ of belonging to the cerebral parenchyma is estimated by

$$\mu_{CP-FOM}(v) = \alpha(v)\mu_{CP-FIOM}(v)$$
$$\alpha(v) = \begin{cases} 1 & if\ \mu_{CP-FSOM}(v) > th_{CP-FSOM} \\ \dfrac{\mu_{CP-FSOM}(v)}{th_{CP-FSOM}} & otherwise \end{cases}, \quad (5)$$

where $\mu_{CP-FSOM}(v)$ is a fuzzy degree with respect to shape given by CP-FSOM, and $\mu_{CP-FIOM}(v)$ is a fuzzy degree given by CP-FIOM. $th_{CP-FSOM}$ is a parameter between 0 and 1, and 0.7 was chosen experimentally.

B. *[Step 3] WM segmentation using FOM based FCIS*

The proposed method extracts seed voxels by thresholding fuzzy degree belonging to the cerebral parenchyma, $\mu_{CP-FOM}(v)$. To assemble with FOM, we extend original fuzzy affinity shown in Eq. (1) as

$$\mu_K(c,d) = \alpha(d)\sqrt{\mu_\Psi(c,d)\mu_\Phi(c,d)}, \quad (6)$$

where $\mu_\Psi(c,d)$ is homogeneity affinity defined in Ref. [8]. $\mu_\Phi(c,d)$ is object affinity, and is defined by;

$$\mu_\Phi(c,d) = \min(\mu_O(c), \mu_O(d)). \quad (7)$$

$\mu_O(v)$ is object feature estimated by using both of seed objects and fuzzy object models, and is defined by

$$\mu_O(v) = \max\left(\mu_{seed}(I(v)), \mu_{CP-FSM}(v)\right), \quad (8)$$

where $\mu_{seed}(x)$ is a fuzzy membership function defined by Gaussian function whose mean and variance are those of seed voxels. It expresses how close MR signal x is to the MR signal of seed voxels. Use of Eq. (8) enables us to estimate affinity to the cerebral parenchyma based on two aspects, one from the given images, and the other from FOMs.

C. *[Step 4] Cortex segmentation using FOM based FCIS*

Because the homogeneity affinity between the inside WM and the surrounding cortex is small value, the previous step will stop at the boundary between them. This step again assigns seed voxels at voxels in the surrounding cortex neighboring the boundary.

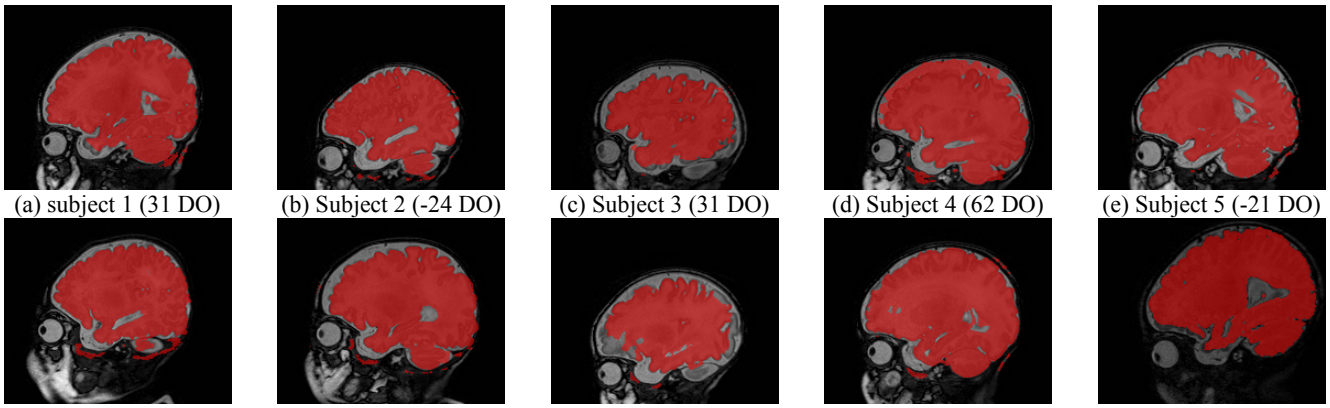
The method first segments voxels whose fuzzy connectedness is higher than or equal to a threshold, μ_{min}, and detects neighboring voxels in which the assigned fuzzy connectedness is less than μ_{min} and the object affinity is higher than or equal to μ_{min}. Then, FOM based FCIS described in B. is applied again using the reassigned seed voxels.

D. *[Step 5] PVE Correction and defuzzification*

To decrease pitfalls of fuzzy degree due to partial volume effect, median filter is applied to the resultant fuzzy degree map. Next, at the deffuzification step, we extract voxels whose fuzzy degree is higher than a threshold, μ_{min}, as the parenchymal region.

V. Experimental Results and Discussion

The proposed method was validated in 10 newborn subjects shown in Sec. II. Because the method needs training dataset, we conducted LOOCV test, which used one data as evaluation data, and used the remained data as training data. Figure 1 shows experimental results for Subject 1 at an axial section. The remained subjects were used for building FOMs. Figures (a)-(e) show FG region, and registered FOMs. They



(a) subject 1 (31 DO) (b) Subject 2 (-24 DO) (c) Subject 3 (31 DO) (d) Subject 4 (62 DO) (e) Subject 5 (-21 DO)

(f) Subject 6 (31 DO) (g) Subject 7 (31 DO) (h) Subject 8 (31 DO) (g) Subject 9 (31 DO) (g) Subject 10 (31 DO)

Figure 2. Experimental results by leave-one-out cross validation test.DO means days-old.

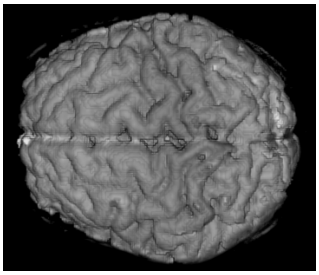


Figure 3. Volume rendering of the segmented region.

TABLE I. NUMERICAL RESLTS IN 10 SUBJECTS

	FPVF	***FNVF***	***G-means***
Subject 1	0.80%	1.69%	1.16%
Subject 2	0.81%	1.50%	1.10%
Subject 3	1.06%	5.32%	2.37%
Subject 4	1.89%	0.74%	1.18%
Subject 5	1.17%	1.10%	1.13%
Subject 6	1.02%	0.83%	0.92%
Subject 7	4.11%	0.37%	1.23%
Subject 8	1.09%	7.77%	2.91%
Subject 9	1.22%	1.12%	1.17%
Subject 10	0.12%	8.59%	1.02%
mean±SD	1.33±0.97%	2.90±2.81%	1.42±0.60%

show that the FOMs are well-registered to FG region. Figure (f) shows the results of AAR and seed voxels for FCIS. The higher degrees are assigned to the cerebral parenchyma. Figure (g) shows the updated affinity using that from seed voxels. Figure (h) shows the fuzzy degrees obtained by applying FOM based FCIS. Figure (i) shows the reassigned seed voxels on the cortex, (j) shows the obtained fuzzy degree map. Figure (k) is the PVE correction result; (l) shows the resultant image. And, Figure 2 shows the experimental results for every subject. Figure 3 shows volume rendering image of the segmented parenchymal region in Subject 1.

To evaluate the results quantitatively, they were compared with the ground truth data, which were binary images carefully delineated by experts. The validation indices used were false positive volume fraction (FPVF) and false negative volume fraction (FNVF). And, geometric-means (G-means) [8] is calculated. The lower values show the better segmentation accuracy. Table I shows the results. There are relatively some false-negative-voxels because of miss-alignment of FOM to the evaluating brain.

VI. CONCLUSION

We have introduced an FOM based FC approach to newborn brain MR image segmentation. The results showed the use of FOM is a promised way to segment the parenchymal region. However, there are still under-segmentation region because of miss alignment of FOMs. In the future, we will study FOM based AAR more, and evaluate the applicability of the method to the various age groups.

ACKNOWLEDGMENT

Syoji Kobashi is thankful to Doctors Y. Wakata, K. Ando, and R. Ishikura (Hyogo College of Medicine, Japan) for providing newborn brain MR images and instructing their anatomical knowledge, to Professors Y. Hata and K. Kuramoto (University of Hyogo, Japan) for supporting my research environment, and to Miss A. Hashioka (University of Hyogo, Japan) for her technical support to treat MR images.

REFERENCES

[1] N. I. Weisenfeld and S. K. Warfield, "Automatic segmentation of newborn Brain MRI," NeuroImage, vol. 47, no,. 2, pp. 564-572, 2009.

[2] M. Prastawa, J. H. Gilmore. W. Lin, and G. Gerig, "Automatic segmentation of MR images of the developing newborn brain," Medical image analysis, vol. 9, pp. 457-466, 2005.

[3] F. Leroy, J. F. Mangin, F. Rousseau, H. Glasel, L. Hertz-Pannier, J. Dubois, G. and Dehaene-Lambertz, "Atlas-free surface reconstruction of the cortical grey-white interface in infants," LoS One, vol. 6, no. 11, e27128 (online), 2011.

[4] P. K. Saha, J. K. Udupa, and D. Odhner, "Scale-based fuzzy connected image segmentation: theory, algorithm, and validation," Computer Vision and Image Understanding, vol. 77, pp. 145-174, 2000.

[5] J. K. Udupa and S. Samarasekera, "Fuzzy connectedness and object definition: theory, algorithms, and applications in image segmentaion," Graphical models and image processing, vol. 58, no. 3, pp. 246-264, 1996.

[6] B. L. Rice, Jr., and J. K. Udupa, "Clutter-free volume rendering for MR angiography using fuzzy connectedness," Int. J. of Imaging Systems and Technology, Vol. 11, no. 1, 2000.

[7] J. K. Udupa, D. Odhner, A. X. Falcao, K. C. Chiesielski, P. A. V. Miranda, P. Vaideeswaran, S. Mishra, G. J. Grevera, B. Saboury, and D. A. Torigian, "Fuzzy object modeling," Proc. of SPIE Medical Imaging, Vol. 7964, 2011.

[8] M. Kubat, R. Holte, and S. Matwin, "Learning when negative examples abound," Machine Learning: ECML-97, Lecture Notes in Computer Science, Vol. 1224, pp. 146-153, 1997