An automatic tumor segmentation framework of cervical cancer in T2-weighted and diffusion weighted magnetic resonance images

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ABSTRACT

Cervical cancer is one of the common malignant tumors and is a major health threat for women. The accurate segmentation of the cervical cancer is of important clinical significant for prevention, diagnosis and treatment of cervical cancer. Due to the complexity of the structure of human abdomen, the images in a single imaging modality T2-weighted MR images can not sufficiently show the precise information of the cervical cancer. In this paper, we present an automatic segmentation framework of cervical cancer, making use of the information provided by both T2-weighted magnetic resonance (MR) images and diffusion weighted magnetic resonance (DW-MR) images of cervical cancer. This framework consists of the following steps. Firstly, the DW-MR images are registered to T2-weighted MR images using mutual information method; then classification operation is executed in the registered DW-MR images to localize the tumor. Secondly, T2-weighted MR images are filtered by P-M nonlinear anisotropic diffusion filtering technique; and then bladder and rectum are segmented and excluded, so the Region of Interest (ROI) containing tumor is extracted. Finally, the tumor is accurately segmented by Confederative Maximum a Posterior (CMAP) algorithm combining with the results of T2-weighted MR images and DW-MR images. We tested this framework on 5 different cervical cancer patients. Compared with the results outlined manually by the experienced radiologists, it is demonstrated effectiveness of our proposed segmentation framework.

Keywords: cervical cancer, image segmentation, Confederative Maximum a Posterior, magnetic resonance image

1. INTRODUCTION

Cervical cancer is one of the most common cancers affecting women worldwide, especially in developing countries. Estimates of the worldwide burden of cervical cancer in 2008 suggest that 529,800 incident cases and 275,100 deaths due to cervical cancer occur annually [1],[2]. It can be cured in almost all patients, if detected and treated in time [3]. Magnetic resonance imaging (MRI) has advantages of high resolution and high soft tissue contrast, and is able to characterize deformable structure with superior visualization and differentiation of normal soft tissue as well as tumor-infiltrated soft tissue. In addition, advanced MR imaging such as diffusion imaging has the potential to better localize and understand the disease. Therefore, the accurate segmentation of cervical cancer in MR images is of important clinical significant for prevention, diagnosis and treatment of cervical cancer.

However, the automatic segmentation of cervical cancer in MR images is still a challenging problem [4],[5]. The structure of human abdomen is very complex, and there is noise and intensity overlapping, so the images in a single imaging modality T2-weighted MR images can not sufficiently show the precise information of the cervical cancer. Figure1 shows the abdomen anatomical structure of a cervical cancer patient in T2-weighted MR image (Figure 1 (a)) and DW-MR image (Figure 1 (b)) at the same location. From the two images, we can see that the cervix locates between the bladder and the rectum. From the figure 1 (a), we can see that the spatial resolution of T2-weighted MR image is higher than DW-MR image; in T2-weighted MR image, the tumor edge is clear; but it has intensity overlapping with the bladder wall and rectum. From the figure 1 (b), we can see that the tumor shows up with high signal intensity while the

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tumor edge is blurred in the DW-MR image which can be used to localize the tumor. So it is difficult to accurate segment the region of cervical cancer just from T2-weighted MR images or DW-MR images.

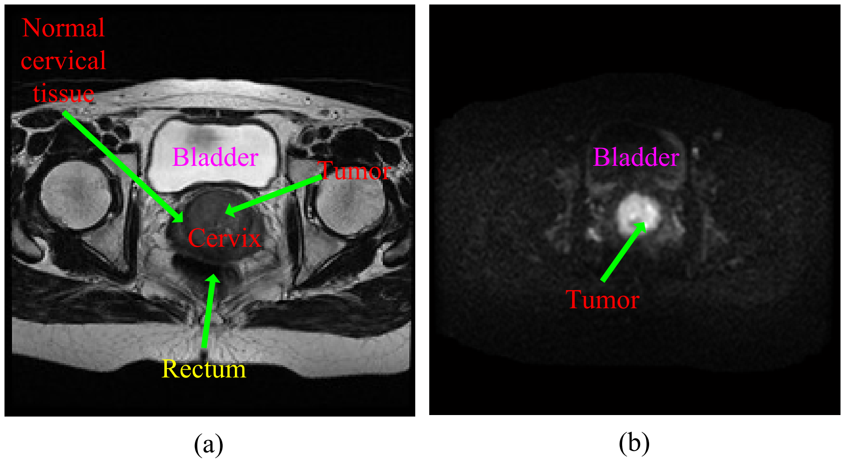


Figure 1. The abdomen anatomical structure of a cervical cancer patient. (a) T2-weighted MR image. (b) DW-MR image.

To the best of our knowledge, the study about solving the problem of segmentation of cervical cancer in MR images is very limited. So far only Lu *et al*. proposed a model in T2-weighed MR images [4],[5]. The model is based on a Maximum a Posteriori (MAP) framework which can achieve deformable segmentation, nonrigid registration and tumor detection simultaneously. But their method only used T2-weighed MR images, and is not automatic. In their method Gross Tumor Volume (GTV), bladder, and uterus were manually segmented for therapy planning of radiotherapy in the T2-weighed MR images of each patients at first phase [5].

In this paper, we present an automatic segmentation framework of cervical cancer, making use of the information provided by both T2-weighted MR images and DW-MR images of cervical cancer, and propose a CMAP algorithm for accurate segmentation of cervical cancer. This framework consists of the following steps. Firstly, the DW-MR images are registered to T2-weighted MR images using mutual information method; then classification operation is executed in the registered DW-MR images. Secondly, T2-weighted MR images are filtered by P-M nonlinear anisotropic diffusion filtering technique; and then bladder and rectum are segmented and excluded, so the ROI containing tumor is extracted. Finally, the tumor is accurately segmented by CMAP algorithm combining with the results of T2-weighted MR images and DW-MR images. Compared with the results outlined manually by the experienced radiologists, it is demonstrated that our proposed segmentation framework is effective.

2. METHODS

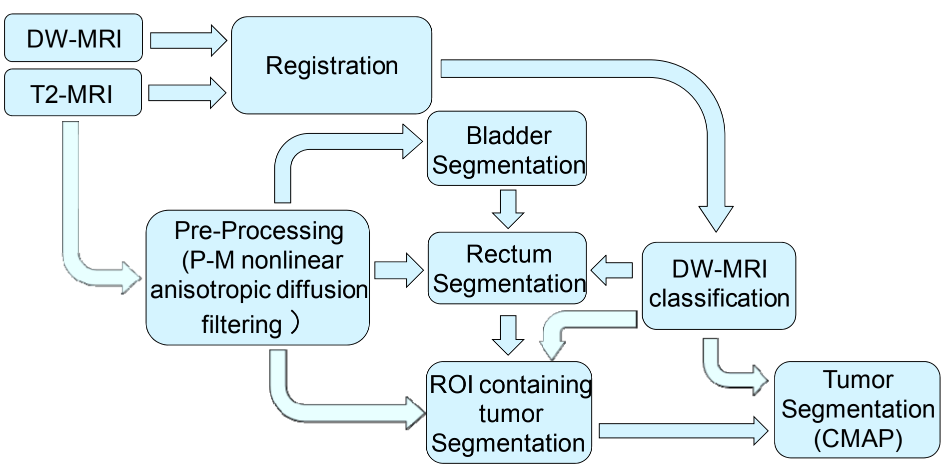


Figure 2. Diagram of the proposed method.

2.1 The segmentation framework

Figure 2 illustrates the workflow of our presented framework. This framework consists of the following steps. Firstly, the DW-MR images are registered to T2-weighted MR images using mutual information method; then classification operation is executed in the registered DW-MR images to localize the tumor. Secondly, T2-weighted MR images are filtered by P-M nonlinear anisotropic diffusion filtering technique; and then bladder and rectum are segmented and excluded, so the Region of Interest (ROI) containing tumor is extracted. Finally, the tumor is accurately segmented by Confederative Maximum a Posterior (CMAP) algorithm combining with the results of T2-weighted MR images and DW-MR images.

2.2 Registration and DW-MR images classification

Mutual Information method in the software package of SPM8 is used to register DW-MR images to T2-weighted MR images.

In the DW-MR images the tumor shows up with higher signal intensity than other tissues, while the tumor edge is blurred. So DW-MR images are used to localize the tumor. Classification operation is executed in the registered DW-MR images to get the tumor location.

2.3 Image Pre-Processing

Before the segmentation, the T2-weighted images are filtered by P-M nonlinear anisotropic diffusion filtering technique, which can smooth the image and reduce white noise while preserving edges. The P-M nonlinear anisotropic diffusion filtering technique is proposed by Perona and Malik in 1990 [6]. The nonlinear equation is

$$\begin{cases} \dfrac{\partial y(i,t)}{\partial t} = div(c(\nabla y(i,t))\nabla y(i,t)) \\ y(i,0) = y_0(i) \end{cases} \tag{1}$$

Where $y(i)$ stands for the image intensity on position i ; The variable t is the process ordering parameter, in the discrete implementation it is used to enumerate iteration steps. We indicate ∇ as the gradient， and div as the divergence operator; The diffusion function $c(\cdot)$ depends on the magnitude of the gradient of the image intensity, and it mainly diffuses within regions and does not affect region boundaries at locations of high gradients. They proposed two different diffusion functions:

$$c(\nabla y) = \exp(-\frac{\| \nabla y \|^2}{k^2}) \tag{2}$$

$$c(\nabla y) = \frac{1}{1+(\frac{\|\nabla y\|}{k})^2} \tag{3}$$

The parameter k is chosen according to the noise level and the edge strength.

2.4 Bladder segmentation

From the figure 1(a), in the T2-weighted MR images, we can see that tumor edge is clear, but it has intensity overlapping with the bladder wall and rectum. For the accurate segmentation of tumor, we decide to segment the bladder and rectum firstly. The intensity of bladders in T2-weighted MR images of human abdomen is higher than other tissues and homogeneous relatively. Based on this knowledge, CV model which is an active contour model defined by Chan and Vese [7] is used to segment the bladder.

2.5 Rectum segmentation and ROI containing tumor segmentation

The rectum segmentation is also needed. Rectum is below cervix generally in MR images. Its intensity is lower than other tissues and it overlaps with the intensity of cervix. According to these information and the classification results in DW-MR images, we use Fuzzy C-Means (FCM) clustering algorithm [8] to segment rectum in T2-weighted MR images excluded bladder.

To eliminate the influence of other organs, ROI containing tumor is extracted. From figure 2, after DW-MR images classification, bladder segmentation and rectum segmentation, FCM clustering algorithm is used to get ROI containing tumor in T2-weighted MR images excluded bladder and rectum.

2.6 CMAP algorithm

We propose a CMAP algorithm on the ROI containing tumor of both T2-weighted MR images and DW-MR images for accurate segmentation of cervical cancer. The CMAP algorithm is based on the traditional Maximum a Posterior (MAP) estimation [9],[10].

In this paper, let $y=\{y_i;i \in I\}$ be an image, y_i is the intensity of the image at site i .Suppose there are K different tissues (classes) in the image, and each of them is labeled by a number in $\Lambda = \{1,2,...,K\}$. Let $x_i=k,k \in \Lambda$ indicates that site I belongs to class k , then $x=\{x_i;i \in I\}$ denotes a segmentation of y . x can also be regarded as a realization of discrete random variables at I . The goal of image segmentation is to find an optimal or sub-optimal x under some principle.

The process of segmentation with MAP estimation is to find the optimal x that makes the $P(x|y)$ maximum:

$$\overset{\Lambda}{x}_{MAP} = \arg\max_{x \in X} P(x \mid y) \tag{4}$$

Here $P(x|y)$ is posterior density of the segmentation x given the image y .

From Bayesian theorem, the $P(x|y)$ is

$$P(x \mid y) = \frac{P(y \mid x)P(x)}{P(y)} \propto P(y \mid x)P(x) \tag{5}$$

Here $P(y|x)$ is the conditional probability density and is also the joint density function of $y=\{y_i;i \in I\}$ under segmentation x , $P(x)$ is probability density of x . So the problem is transferred to finding maximum product of $P(y|x)$ and $P(x)$.

We assume the noise of the MR images is additive, white, Gaussian, tissue dependent, and space variant. So if $x_i=k$, then the image model is

$$y_i = u_{ik} + n_{ik} \tag{6}$$

Where u_{ik} is the mean intensity of tissue k at site i , and n_{ik} is Gaussian noise of tissue k at site i , whose density function obeys $N(0,\sigma_{ik}^2)$. Since the noises in the image are conditionally independent, then $P(y|x)$ can be expressed as

$$\begin{aligned} P(y \mid x) &= \prod_{k=1}^{K} \prod_{i \in R_k} P_k(y_i \mid x) \\ &= \prod_{k=1}^{K} \prod_{i \in R_k} \frac{1}{2\pi\sigma_{ik}} \exp[-\frac{1}{2}\left(\frac{y_i - \mu_{ik}}{\sigma_{ik}}\right)^2] \\ &= \frac{1}{(2\pi)^{1/2}} \exp\left\{-\sum_{k=1}^{K}\sum_{i \in R_k}\left[\ln(\sigma_{ik}) + \frac{1}{2}\left(\frac{y_i - \mu_{ik}}{\sigma_{ik}}\right)^2\right]\right\} \end{aligned} \tag{7}$$

Here R_k is the set of sites that belong to class k .

The probability density of x is based on a Gibbs distribution [11],[12], so the form of $P(x)$ is

$$P(x) = \exp\left\{-\sum_{k=1}^{K}\sum_{i \in R_k}\sum_{j \in N_i} b \cdot V_k(x_i, x_j)\right\} \tag{8}$$

Where b is a normalizing constant, N_i is a set of points that are neighbors of the point at site i , and $V(x_i,x_j)$ is a function which is estimated by using the information of segmentation x .

By substituting the definition of $P(y|x)$ and $P(x)$ in Eq. (2), the posterior probability is

$$P(x \mid y) \propto \exp\{-U(x)\} \tag{9}$$

The MAP estimation is equivalent to minimizing the energy function

$$\hat{x}_{MAP} = \arg\min_{x \in X} U(x) \tag{10}$$

Where

$$U(x) = \sum_{k=1}^{K} \sum_{i \in R_k} \left[\frac{1}{2} \left(\frac{y_i - \mu_{ik}}{\sigma_{ik}} \right)^2 + \ln(\sigma_{ik}) \right] + \sum_{k=1}^{K} \sum_{i \in R_k} \sum_{j \in N_i} b \cdot V_k(x_i, x_j) \tag{11}$$

For the accurate segmentation of cervical cancer, we decide to utilize the effective information of T2-weighted MR images and DW-MR images. Traditional MAP algorithm is only implemented to one image at a time, so we presented a CMAP algorithm which can be performed in the ROI containing tumor of a T2-weighted MR image and a registered DW-MR image simultaneously.

Because the posterior density of T2-weighted MR image $P_{T2}(x \mid y_{T2})$ is independent of the posterior density of DW-MR image $P_{DW}(x \mid y_{DW})$, the process of segmentation with CMAP estimation is to find x that makes the confederative posterior density maximum:

$$\hat{x}_{CMAP} = \arg\max_{x \in X} (P_{T2}(x \mid y_{T2}) P_{DW}(x | y_{DW})) \tag{12}$$

According to the Eq. (5) and Eq. (9), where

$$P_{T2}(x \mid y_{T2}) P_{DW}(x | y_{DW}) \propto \exp\left\{ -\left(U_{T2}(x) + \beta U_{DW}(x) \right) \right\} \tag{13}$$

Here β is a constant and used to balance the influence of T2-weighted MR image and DW-MR image. If $\beta = 0$, CMAP algorithm will become MAP algorithm in T2-weighted MR images. The problem of finding the CMAP estimate of the segmentation is the minimization problem of the energy function

$$\hat{x} = \arg\min_{x \in X} (U_{T2}(x) + \beta U_{DW}(x)) \tag{14}$$

Then by substituting the Eq. (11) in Eq. (14), the segmentation $\hat{x}$ can be got.

However, it is hard to decide the value of constant β , and the segmentation result may be not the best one. In addition, even if the value of β is befitting, there are also registration error in the process of registration. To solve this problem, we define a strip between the tumor and normal tissues based on the edges of segmentation $\hat{x}$ result and reclassified the pixels in the strip [13]. There are two steps in this reclassification modul. The first step is to search the pixels that have the similar features with tumor by detecting the tumor edges and the range of tumor intensity from inside of the strip to outside; the second step is to reclassify the pixels again in its small neighborhood on the first step results. In this way, we get the final segmentation.

The pseudocode for CMAP algorithm is as follows:

Begin

Input the ROI containing tumor of T2-weighted MR images and DW-MR images, and classification results of DW-MR images

Initialize segmentation with FCM clustering algorithm

Set $k = 0$

While ($k < \max$)

Calculate energy function of T2-weighted MR image $U_{T2}(x)$

Calculate energy function of DW-MR image $U_{DW}(x)$

Calculate confederative energy function of the two images $U_k(x) = U_{T2}(x) + \beta U_{DW}(x)$

$k = k + 1$

If $|U_k \text{-} U_{k\text{-}1}| < threshold$

End while

End while

Find segmentation $\hat{x}$ based the $U(x)$

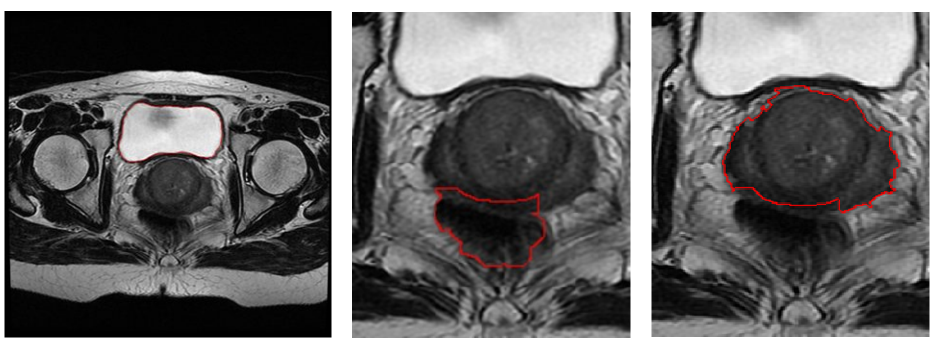
Reclassify the pixels near edges of segmentation $\hat{x}$ result to get the final segmentation $\hat{x}_{CMAP}$

End

3. RESULTS

This implemented framework was tested on T2-weighted MR images and DW-MR images of 5 different cervical cancer patients from Peking Union Medical College Hospital. All programming was conducted in MATLAB R2008a.

From figure 2, in our proposed segmentation framework, after image pre-processing, the bladder and rectum are segmented firstly, then ROI containing tumor is segmented. Figure 3 shows the results of segmented bladder, rectum and ROI containing tumor of a patient in axial view.



(a) (b) (c)

Figure 3. The results of segmented bladder, rectum and ROI containing tumor of a patient in axial view. (a) The contour of bladder in red. (b) The contour of rectum in red. (c) The contour of ROI containing tumor in red.

The results of segmented cervical cancer of two patients in axial view are shown in figure 4. From column (c) and (d) in figure 4, we can see that the segmentation result for cervical cancer by MAP on T2-weighted MRI only ($\beta = 0$, in Eq. (7)) is rough and is influenced by its surrounding tissue with overlapping intensity, while the segmentation result for cervical cancer by CMAP on both T2-weighted MRI and DW-MRI ($\beta = 1$, in Eq. (7)) is much better. From column (d) in figure 4, we can see that the segmentation result for cervical cancer by CMAP is influenced by the registration result of DW-MR images. Column (e) in Figure 4 shows the segmentation result for cervical cancer by CMAP after reclassification which is more accurate.

To validate the segmentation results, we compared our results with Tumor Regions outlined manually by the experienced radiologists. The results were quantified by the similarity index derived from a reliability measurement known as kappa statistic described by Atkins and Mackiewich [14] and Zijdenbos *et al.*[15]. The similarity indexes between the final segmentation results in figure 4 and expert's manual segmentation results were 0.9441 and 0.9545 respectively. Our proposed approach was applied on 5 different cervical cancer patients. For most images of the five patients, the similarity indexes between the final segmentation results and expert's manual segmentation results was over 0.9, and the segmented results demonstrated that our proposed approach is effective for cervical cancer segmentation.

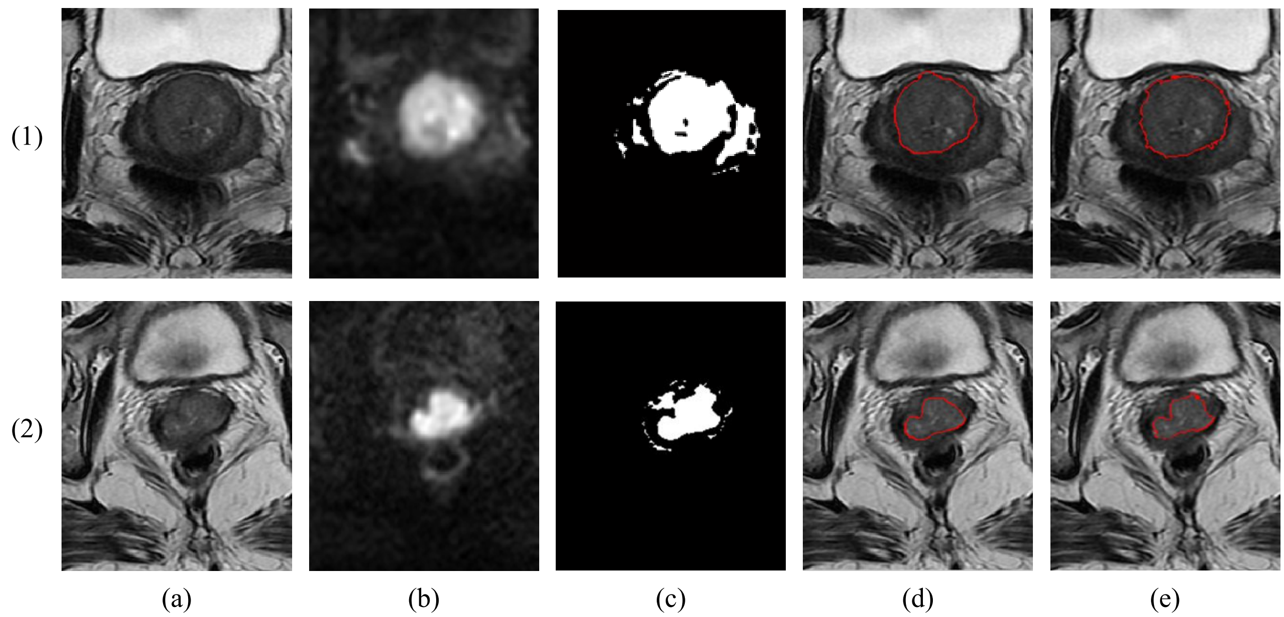


Figure 4. Illustration of segmentation results of cervical cancer on two patients in axial view. Rows (1) and (2) show the results of segmented cervical cancer of each patient in axial view respectively. Column (a) shows the original T2-weighted MR images. Column (b) shows registered DW-MR image to T2-weighted MRI. Column (c) shows segmentation result for cervical cancer by MAP on T2-weighted MRI only ($\beta = 0$, in Eq. (14)). Column (d) shows the contour of segmentation result for cervical cancer by CMAP on both T2-weighted MRI and DW-MRI before reclassification ($\beta = 1$, in Eq. (14)). Column (e) shows the contour of final segmentation result for cervical cancer by CMAP on both T2-weighted MRI and DW-MRI after reclassification ($\beta = 1$, in Eq. (14)).

4. DISCUSSIONS

T2-weighted MR images have high spatial resolution and high soft tissue contrast, it can provide the details of tumor information, but there is intensity overlapping between tumor and other tissues; for DW-MR images, intensity of tumor is higher than any other tissues apparently, but DW-MR images suffer from low resolution and low soft tissue contrast. So DW-MR images can provide the information of tumor localization, while T2-weighted MR images can be used to segment tumor accurately. In this paper, both T2-weighted images and DW-MR images are used for cervical cancer segmentation.

In our proposed tumor segmentation framework, to make the accurate tumor segmentation, the bladder, rectum and ROI containing tumor are segmented firstly. Bladder and rectum has intensity overlapping with tumor. They can influence the segmentation of tumor. After exclude the region of bladder and rectum, the ROI containing tumor can be acquired, and accurate tumor region can be segmented.

CMAP algorithm is proposed for accurate segmentation of cervical cancer. By incorporating the information of DW-MR images, the CMAP model is influenced by both the T2-MR images and DW-MR images, so the misclassification caused by T2-weighted MR images could be reduced. In addition, in the end of CMAP algorithm, the reclassification process is performed, so the misclassification caused by registration could also be reduced.

Although an effective experimental result has been achieved, there are still some limitations. In the future, we will make some improvement in the framework and CMAP algorithm, more subjects will be tested, and the segmentation result will be combined with clinical analysis.

5. CONCLUSIONS

We have implemented an automatic tumor segmentation framework combining T2-weighted MR images with DW-MR images and proposed a CMAP algorithm on both T2-weighted MR images and DW-MR images for automatic cervical cancer segmentation. The experimental results demonstrated that the CMAP algorithm could segment the cervical cancer effectively.

6. ACKNOWLEDGMENTS

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REFERENCES

[1] Jemal, A., Bray, F., Center, M. M., Ferlay, J., Ward, E. and Forman, D., "Global cancer statistics," CA-Cancer J. Clin., 61(2), 69-90 (2011).

[2] Shi, J. F., Canfell, K., Lew, J. B. and Qiao, Y. L., "The burden of cervical cancer in China: Synthesis of the evidence," Int. J. Cancer, 130(3), 641-652 (2012).

[3] Amir, A., Hayit, G. and Jacob, G., "Automated and Interactive Lesion Detection and Segmentation in Uterine Cervix Images," IEEE Trans. Med. Imaging, 29(2), 488-501 (2010).

[4] Lu, C., Chelikani, S., Jaffray, D. A., Milosevic, M. F., Staib, L.H. and Duncan, J. S., "Simultaneous Nonrigid Registration, Segmentation and Tumor Detection in MRI Guided Cervical Cancer Radiation Therapy," IEEE Trans. Med. Imaging, 31(6), 1213-1227 (2012).

[5] Lu, C., Chelikani, S., and Duncan, J. S., "A unified framework for joint segmentation, nonrigid registration and tumor detection: Application to MR-guided radiotherapy," Proc. IPMI2011, 6801, 525-537 (2011).

[6] Perona, P. and Malik, J., "Scale-Space and Edge Detection Using Anisotropic Diffusion," IEEE Trans. Pattern Anal. Mach. Intell., 28(7), 629-639 (1990).

[7] Chan, T. F. and Vese, L. A., "Active contours without edges," IEEE Trans. Imag. Process., 10(2), 266-277 (2001).

[8] Cannon, R., Dave, J. V., and Bezdek, J. C., "Efficient Implementation of the Fuzzy c-Means Clustering Algorithms," IEEE Trans. Pattern Anal. Mach. Intell., 8(2), 248-255 (1986).

[9] Zhang, Y. Y., Brady, M., and Smith, S., "Segmentation of Brain MR Images through a Hidden Markov Random Field Model and the Expectation-Maximization Algorithm," IEEE Trans. Med. Imaging, 20(1), 45-57 (2001).

[10] Liu, F., Gao, S. and Gao, X., "Segmentation of MR image based on maximum a posterior," Proc. IEEE EMBS, 3,2861-2864 (2001).

[11] German, S. and Geman, D., "Stochastic relaxation, Gibbs distribution, and the Bayesian restoration of images," IEEE Trans. Pattern Anal. Mach. Intell., 6(6), 721-741 (1984).

[12] Pappas, T. N., "An adaptive clustering algorithm for image segmentation," IEEE Trans. Signal Process., 40(4), 901-914 (1992).

[13] Li, W., Tian, J., Li, E. Z. and Dai J. P., "Robust unsupervised segmentation of infarct lesion from diffusion tensor MR images using multiscale statistical classification and partial volume voxel reclassification," Neuroimage, 23(4), 1507-1518 (2004).

[14] Atkins, M. S. and Mackiewich, B., "Fully automatic segmentation of the brain in MRI," IEEE Trans. Med. Imaging, 17(1), 98-107 (1998).

[15] Zijdenbos, A. P., Dawant, B. M., Margolin, R. A. and Palmer, A. C., "Morphometric analysis of white matter lesions in MR images: method and validation," IEEE Trans. Med. Imaging, 13(4), 716-724 (1994).