International Journal of Information Technology
Vol. 8, No. 2 September 2002

MRI Tumor Segmentation for Nasopharyngeal Carcinoma Using Knowledge-based Fuzzy Clustering

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Abstract: Tumor segmentation is one of the important steps for volume measurement of nasopharyngeal carcinoma (NPC) tumor by imaging diagnostics. A knowledge-based fuzzy clustering (KBFC) MRI segmentation algorithm was proposed to obtain accurate NPC tumor segmentation. An initial segmentation was performed on T1 and contrast enhanced T1 MR images using a semi-supervised fuzzy c-means (SFCM) algorithm. Then, three types of anatomic and space knowledge--symmetry, connectivity and cluster center were used for image analysis which contributed to the final tumor segmentation. Visual evaluation on MR images of NPC patients showed that KBFC achieved better tumor segmentation results than seeds growing (SG) and maximal likelihood method (MLM), compared with ground truth (GT). KBFC could provide high quality of MRI tumor segmentation for further tumor volume measurement, 3D visualization and treatment planning.

Keywords: MRI, tumor segmentation, fuzzy clustering, image processing

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1. INTRODUCTION

Nasopharyngeal carcinoma (NPC), a type of cancer located in the skull base, has a high frequency in Southeast Asia and South China. Recent findings indicated that tumor volume is an important diagnostic and prognostic indicator in the diagnostics and treatment of NPC[1,2,3]. Therefore, tumor volume analysis using magnetic resonance imaging (MRI) can be a useful tool in these researches[4]. However, NPC tumor shows an aggressive and infiltrative growth pattern and often has a high degree of regional spread at presentation with propensity to spread into the parapharyngeal spaces as well as to the skull base foramina[1]. In addition, there are complex anatomic structures of normal tissue around the tumor tissue[2]. As a result, tumor volume of NPC cannot be easily assessed clinically, and even with the help of imaging, the often irregular shaped tumor would make crude measurement difficult and of limited accuracy. Accurate and reproducible assessment of tumor volume in NPC therefore required detailed analysis of tumor extent from imaging, calculation of tumor volume from a 3D perspective and the most important, accurate tumor segmentation.

Pattern recognition methods using multi-spectral image data such as k-nearest neighbor (kNN), fuzzy c means (FCM), semi-supervised fuzzy c-means (SFCM), adaptive fuzzy c-means (AFCM), artificial neural network (ANN) and knowledge-based technique have been proposed for image segmentation in MRI, and have shown promising results. But all these algorithms were performed on brain and abdomen tumors that their image contents is relatively simple. Up to now, the quantitative method for tumor volume analysis of NPC using imaging studies is still not well established and there is no specially developed algorithm for NPC tumor segmentation. In this work, a knowledge-based fuzzy clustering (KBFC) method was proposed for MRI segmentation of NPC tumor. Evaluations were performed in visual format by comparing the results using KBFC, seeds growing (SG) and maximal likelihood method (MLM) with ground truth (GT), which was manually mouse-traced by an experienced radiologist and labeled by computer.

2. MATERIALS AND METHODS

2.1 MRI data

MR images of NPC patients (before therapy) were acquired at Singapore National Cancer Centre. The patients were imaged on a 1.5T MR scanner (GE Medical System) using a standard clinical imaging protocol. Fast spin echo or spin gradient sequence was used to obtain T1-weighted (T1) and contrast enhanced T1-weighted (CET1, gadolinium enhanced) images. The 512×512 pixel images of the head in the axial plane were acquired with a 256 (8 bits) grayscale after window/level adjustment, field of views of 200-230 mm, slice thickness of 3-5 mm and slice gaps of 0-2.2 mm.

2.2 Knowledge-based fuzzy clustering segmentation method

2.2.1 Multispectral histogram analysis

Figures 1.a and 1.b show the T1 and CET1 images of a typical slice respectively. Although in most previous brain tumor analysis, T1, T2 and PD images were needed for multispectral segmentation, the T1 and CET1 images currently used in this study can also provide the feature space for tumor-represented areas. Fig. 2 shows the average joint histogram (after logarithm processing) of 12 pairs of tumor-represented MRI slices. There are six primary tissue types: Tumor (sometimes includes edema and necrosis), bone marrow, fat, lymph node, air and other normal soft tissues. Each MR voxel of interest has a (T1, CET1) location in R^2, forming a feature space distribution. Based on the knowledge in Fig. 2 and the fact that pixels belonging to the same tissue type will exhibit similar relaxation behaviors (T1 and CET1), they will then also have approximately the same location in feature space[5]. In addition, there is some overlap between classes because of the "partial-averaging" where different tissue types are quantized into the same voxel and also due to the artifact and the adhesion of different tissues. In Fig. 1.b, the tumor tissue shows adhesion to the normal soft tissue in the soft palate and because of the contrast agent, the soft palate shows similar signal intensity features in feature space with tumor.

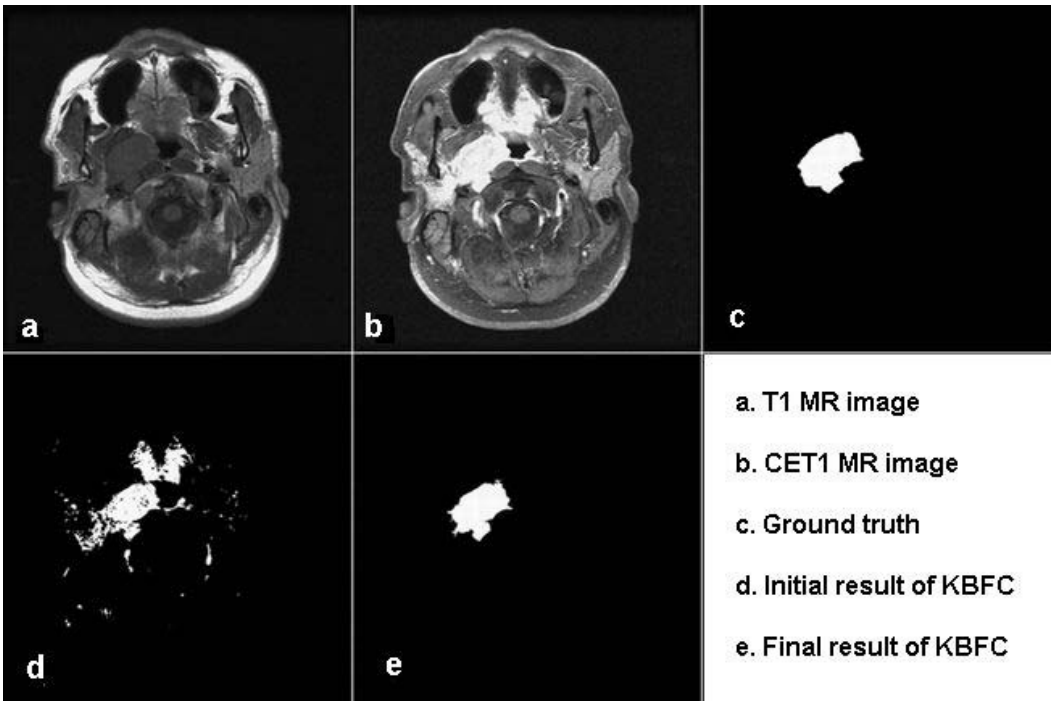

Fig. 1: MR images and segmentation results.

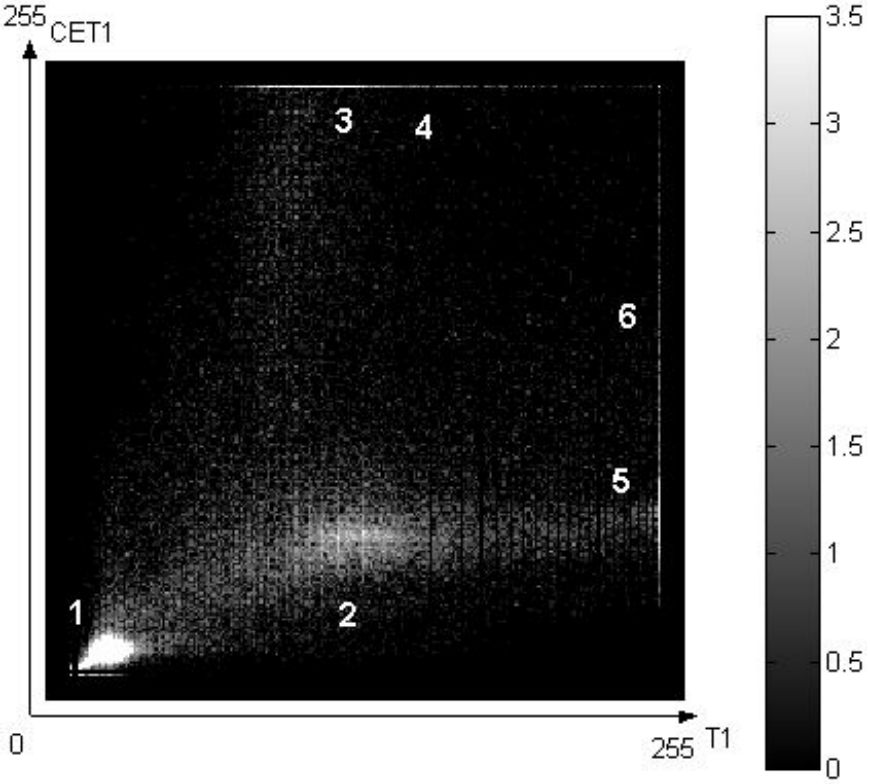

Fig. 2: Average joint histogram of 12 pairs of tumor-represented MRI slices. The six primary tissue types shown here are: 1. Air; 2. Other normal softe tissue; 3. Tumor; 4. Lymph node; 5. Fat; 6. Bone marrow.

2.2.2 Initial segmentation using SFCM

SFCM is a hybrid, modified version of the fully unsupervised FCM clustering method, by helping to minimize or eliminate the errors introduced in FCM clustering[6]. In SFCM, the training set selected by operator is used to initialize and guide the segmentation algorithm. The principle of SFCM is described below.

The MR image data consisting of n (n=512×512) pixels from each of the two features (T1, CET1) form a set of pixel vectors $\mathbf{X}=\{\mathbf{X_1}, \mathbf{X_2}, \mathbf{X_3}, \ldots \mathbf{X_n}\}$ where $\mathbf{X_k}=(X_{T1}, X_{CET1})$, $1 \le k \le n$. Each **X** vector is labeled with a fuzzy membership having a value between 0 and 1. **X** is partitioned into c subsets of u where $\{u_i: \mathbf{X} \rightarrow [0,1]\}$; $u_i(\mathbf{X_k})$ is the membership of pattern $\mathbf{X_k}$ in class i, $1 \le i \le c$. The fuzzy membership grades form a **U** matrix consisting of $c \times n$ elements, i.e., $\mathbf{U}=[u_{ik}]=[u_i(\mathbf{X_k})]$, $1 \le i \le c$ and $1 \le k \le n$, with the following constraints: 1) For all i and k, $0 \le u_{ik} \le 1$; 2) For all k, $\sum_{i=1}^{c} u_{ik} = 1$. The initial U matrix is formed with n_l columns (n_l is the number of elements in the training set for class i, l means "labeled") of labeled pixel vectors having crisp membership grade of 1 or 0, and the remaining n_u ($n_u = n - n_l$, u means "unlabeled") elements from the unlabeled pixel vectors of the image to be classified. The values of the unlabeled columns of the **U** matrix are found by minimizing the objective function:

$$J_2(U, V; X) = \sum_{i=1}^{c} \sum_{k=1}^{n} (u_{ik})^2 \left\| X_k - V_i \right\|^2 \quad (1)$$

where $\mathbf{V_i}=\{\mathbf{V_1}, \mathbf{V_2}, \ldots \mathbf{V_c}\}$ are the cluster centers that we are seeking and $\left\| X_k - V_i \right\| = \sqrt{(X_k - V_{i)}{}^T (X_k - V_i)}$. This objective function is really $\mathbf{J_m}$ as in FCM with m=2 which is used to approximate the minimum of a sum-of-weighted-distance function. In other words, it leads to the minimal square errors of the estimated membership matrix. An iteration[6] with the target of limiting the difference of Euclidean distance between the new and old unlabeled columns of the U matrices (i.e., $\left\| U^u_{new} - U^u_{old} \right\|$) in a threshold value, is used to minimize the function $\mathbf{J_2}$. After the iteration ends, tumor tissue is labeled according to the final **U** matrix.

2.2.3 Knowledge-based image analysis

The initial tumor segmentation using fuzzy clustering is a coarse procedure. After this procedure, many pixels that do not represent tumor are classified as tumor tissue because these non-tumor pixels also have the similar MRI feature vectors with tumor pixels, due to RF nonuniformity, partial volume effect and other reasons we mentioned in 2.2.1. Figures 1.d and 1.c show the initial tumor segmentation result and the GT of Figures 1.a and 1.b, respectively. The initial segmentation shows that in addition to the soft palate that is adhesive to the tumor, a number of spatially disjoint small areas (scatter points) are also regarded as tumor. Moreover, there are some small "holes" which may represent small edema and necrosis in the true tumor area. Therefore, a knowledge-based analysis is introduced to refine the initial segmentation and the corresponding result is shown in Fig. 1.e. In this study, three types of anatomic and space knowledge—symmetry, connectivity and class center contribute the refinement of tumor segmentation.

1) **Symmetry**: In normal condition the nasopharynx is morphologically bilaterally symmetric while in NPC condition, the tumor always shows a unilateral growing pattern, which causes the unilateral disappearance of pharyngeal recess[7]. Therefore in image space, most normal tissues are roughly symmetrical along the vertical axis, while tumors often have poor symmetry. In image analysis, a fuzzy symmetric measure[8] was introduced and those areas with certain grade of symmetry along the previous determined vertical axis (Y Axis) will be removed. (Before the initial segmentation, the center of the head is calculated via the first moment of the binary image and then a Cartesian coordinate system is set up in the center of the head[8], according to the slant of head position.) The resultant image of this step is named as image I.

2) **Connectivity and class center**: After the symmetry refinement, the tumor mass accounts for a large part of the pixels, always more than 80%. In addition, in most cases the tumor tissues appear as a morphologically continuous region in the MR image. Therefore the geometric class center of tumor in image I is similar with the actual class center of tumor. In contrast those non-tumor areas which are classified as tumor, are always disconnected and the pixel number in those areas is relatively small, some areas containing only a few pixels. Therefore, those areas which are spatially disjoint to class center and contain low pixel number will be removed. For implementation, the first moment of image I is calculated as class center and an eight-wise connected components operation is applied from the class center. The resultant image of this step is named as image II.

3) **Mathematical morphology refinement**: For these small "holes" which represent small edema and necrosis (regarded as a part of tumor in most cases) inside the tumor area, a mathematical morphology refinement is performed to fill these holes and get the complete presentation of the tumor. First a dilation operator is applied to image II to fill these small holes and then an erosion operator is applied to eliminate the newly grown tumor outline created by the dilation operator.

2.3 Tumor segmentation by SG and MLM

Seeds growing (SG) is a single grayscale, hard threshold decision method that combines with connectivity constraint. It requires an operator to select a seed and threshold in contrast enhanced T1 image. Pixels in the 8-neiborhood of the seed are examined and included in the region if they are within the threshold. Each added pixel then becomes the new seed whose neighbors are also inspected for inclusion in the region and therefore, the region grows[9]. The maximal likelihood method (MLM), a type of multi-spectral s method, is based on the Bayes decision rule which maximizes a posteriori probability. This rule can be written as:

$$X \text{ is in class 2 if } P_1 p_1(X) < P_2 p_2(X) \tag{2}$$

where X is a feature vector, in this case a vector with as elements the intensities for a pixel in each of the MR images. Here, capital P stands for a prior probability for a class and the low case p is the conditional probability of X given that it is in that class. The conditional probabilities are given by the multivariate normal density function[10].

3. RESULTS

Representative visual results of the three segmentation methods and GTs are shown in Figures 3 and 4. It is obvious that KBFC can achieve fine segmentation results, compared with GT. SG method is poor for primary tumor segmentation, but few false positives are included in its results because of its connectivity constrain. Although MLM can obtain better primary tumor segmentation than SG, but more false positives are included because of its global searching and the lack of anatomic and structural analysis.

Fig. 3: MRI segmentation result 1. a. T1 image; b. CET1 image; c. GT; d. KBFC; e. SG; f. MLM.

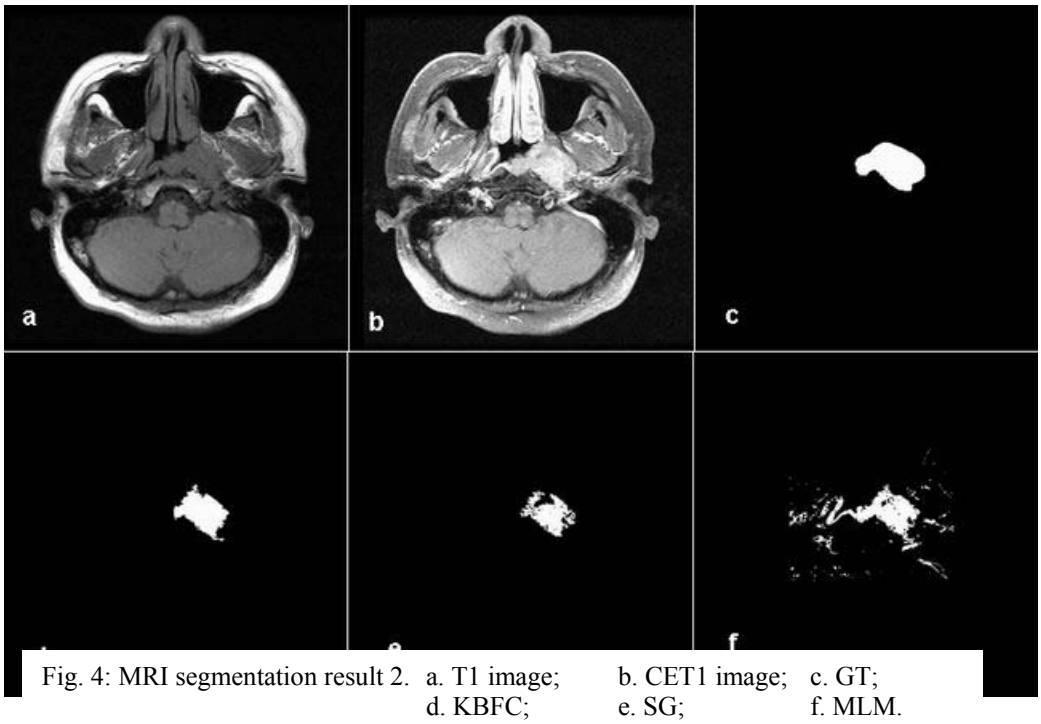

Fig. 4: MRI segmentation result 2. a. T1 image; b. CET1 image; c. GT; d. KBFC; e. SG; f. MLM.

4. DISCUSSION AND CONCLUSION

It is well recognized that tumor segmentation is one of the most important steps in tumor volume measurement, visualization and treatment planning using medical imaging. In this study, a knowledge-based fuzzy clustering method which only requires two image modalities (T1 and CET1 images), was developed for NPC tumor segmentation. The guidance of knowledge base gives this method additional power and flexibility by allowing semi-supervised segmentation and classification decisions to be made through iterative and successive refinement. It is different from most other multi-spectral methods such as MLM and KNN, which attempt to segment tumor from the entire image in one step regardless of the complex anatomic and spatial structures. The intervention of supervision is another important factor in tumor segmentation. In previous automatic knowledge-based tumor segmentation studies, unsupervised FCM was used for initial segmentation and training data sets were used for the provision of initial class information[5, 11]. In previous research, FCM was shown to depend on subtleties in MRI performance characteristics and does not appear to be suitable for robust segmentation, although its reproducibility is good. In addition, initialization is very important for FCM to get meaningful clustering results and reduce computation times[9]. Enabling operator input to guide structure detection in the underlying data, SFCM utilizes operator's experience to achieve more meaningful clustering results than unsupervised clustering and at the same time, reduce the operator dependency compared to supervised clustering such as kNN. MR contrast enhancement for tumor boundary detection and definition in SE T1-weighted sequence is commonly used, although it has some inherent problems. However, MR contrast may not be optimal for the quantitative differentiation of active tumor tissue, scar tissue, necrosis or edema, or for recurrent tumor. This is why SG method cannot obtain fine segmentation results. Although further quantitative investigation for segmentation quality is needed, initial visual evaluation shows that KBFC achieves more successful tumor segmentation result than SG and MLM, as compared with GT. It indicates that the proposed method may be a useful tool for further tumor volume measurement, 3D visualization and treatment planning.

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