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Molecular Biological Characteristics based Hierarchical Mumford-Shah Vector-Model for the Delineation of Biological Target Volumes Corresponding to Head and Neck Tumors*

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Abstract—**To more accurately and precisely delineate a biologic target volume (BTV) for the positron emission tomography (PET)-guided radiotherapy treatment planning, we proposed a novel Hierarchical Mumford-Shah Vector Model (HMSMv), where the image-vector was composed of the molecular biological characteristics such as contrast, busyness and the standard uptake value (SUV) of tumors. The BTV was delineated via the propagation of the level set flow of the proposed HMSMv. The propagation took place inside a ring-volume of interest (VOI) which was defined by an adaptive volume-growing algorithm based on the PET SUV, contrast and busyness of a tumor. Four patient studies were assessed and visually inspected by two radiation oncologists (Suyu Zhu and Zaijie Huang). Compared the resulting BTV with the gross target volume (GTV) of one patient study, the sensitivity, specificity and similarity were 92.28%, 87.29%, 79.28% respectively. Moreover, all of four BTVs were between the corresponding GTV and planning target volume (PTV). Most of the BTVs were between the GTV and the clinical target volume (CTV). The results demonstrated that the proposed method can delineate the BTVs of nasopharyngeal carcinomas more accurately and precisely than the manual delineation and also the threshold segmentation method with SUV of 2.5 as the threshold. The GTV, CTV, and PTV were manually delineated by the two radiation oncologists based on PET, CT and MRI images for the intensity modulated radiotherapy (IMRT) planning of the four patients.**

I. Introduction

The biologic target volume (BTV) delineation of a tumor plays a vital role in the intensity modulated radiotherapy (IMRT) planning of tumors, especially with the radiotherapy strategy of dose painting by contours or dose painting by numbers. The accurate and precise delineation of biologic target volumes has an important clinical significance to improve the quality of treatment and subsequent life of patients and to alleviate the suffering of patients [1]. As a molecular functional image, PET provides more accurate information about malignant tumors, compared to CT. PET can display tumor volumes that are invisible in CT images, and can provide functional information of tumors, such as metabolism, proliferation and hypoxic information while CT or MRI, in most cases, only provide anatomical information. Currently, PET is widely used in various radiation treatment stages for head and neck cancer, especially for target volume delineation. The PET standard uptake value (SUV) is a normalized activity uptake by the injected dose and the body weight. It is a semi quantitative indicator of the malignancy of a lesion. PET SUV-guided delineations via level set methods have been proposed [2-3]. However, it is not possible to accurately and precisely delineate the BTV of a tumor only based on PET SUV. It is very difficult to discriminate between tumors and normal tissues or organs if the normal tissues with a high SUV such as brain stem and other brain tissues that are close to the tumors, or if the sub-clinical tumor volumes with a low SUV are enclosed by normal tissues also with a low SUV. PET image textures can offer helpful information to discriminate between tumors and normal tissues. Yu et al. [4] analyzed some textures such as coarseness, busyness, contrast, etc. which were extracted from PET and CT of tumors. They also demonstrated that corresponding decision tree-based KNN (K nearest neighbors) classifiers can better determine tumors and can get higher sensitivity and specificity [4].

We observed that the molecular biological busyness and contrast extracted from PET of nasopharyngeal carcinomas can more accurately and precisely define the corresponding BTV. Therefore, we proposed a novel Hierarchical Mumford-Shah Vector Model (HMSMv) by combining the SUV, contrast and busyness of tumors from PET images, and delineated the corresponding BTV via the propagation of the level set flow of the proposed HMSMv. The propagation took place only inside a ring-volume of interest (VOI) which was defined by an adaptive volume-growing algorithm based on PET SUV, contrast and busyness of a tumor.

II. Method

A. Hierarchical Mumford-Shah Vector Model

Hierarchical Mumford-Shah Vector-Model (HMSMv) is a formulation of the real world image [5-6]. Its 'hierarchical' level is the formulation of complexity of a real image. The boundary of a tumor at the hierarchical level of h and n is obtained by minimizing the novel Mumford-Shah equation (1a), where $u_{i,0}$ is the i^{th} cell of the image vector , namely $\boldsymbol{u}$,

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of a tumor, which is composed of PET SUV and the molecular biological contrast, busyness of PET of tumors (1b). The contrast and busyness were calculated according to reference [7]. N is the number of cells of image vector. h denotes the hierarchy of HMSMv, and n is the series number of connected volumes in the h^{th} hierarchy image. c^{hn} denotes the closed surface of sub-tumor volume that partitions Ω^{hn} into Ω_1^{hn} and Ω_2^{hn} as seen in (1c), and A^{hn} denotes the area of surface c^{hn}. Ω^{hn} is a sub-VOI (volume of interest), and Ω is an initial VOI which encloses a tumor. $c_{i,1}^{hn}$ and $c_{i,2}^{hn}$ are the mean values of $u_{i,0}$ in Ω_1^{hn} and Ω_2^{hn} respectively. μ^{hn}, λ_i^{hn} are the weight values.

$$\inf_{c_{i,1}^{hn}, c_{i,2}^{hn}, c^{hn}} \{F_{hn}^{HMS}(c_{i,1}^{hn}, c_{i,2}^{hn}, c^{hn}) = \mu^{hn} \cdot A^{hn} + \int_{\Omega_1^{hn}} \frac{1}{N} \sum_{i=1}^{N} \lambda_i^{hn} \cdot |u_{i,0} - c_{i,1}^{hn}|^2 \, dx \quad (1a)$$

$$+ \int_{\Omega_2^{hn}} \frac{1}{N} \sum_{i=1}^{N} \lambda_i^{hn} \cdot |u_{i,0} - c_{i,2}^{hn}|^2 \, dx\}$$

$$\boldsymbol{u} = [PET\_SUV, PET\_contrast, PET\_busyness] \quad (1b)$$

$$\Omega^{11} = \Omega, \ \Omega^{hn} = \Omega_1^{hn} \cup \Omega_2^{hn} \cup C^{hn}, \bigcup_n \Omega^{hn} = \Omega, \quad \Omega^{hn} \bigcap_{n \neq m} \Omega^{hm} = \varnothing, \quad \Omega^{(h+1)(2n-1)} = \Omega_1^{hn}, \Omega^{(h+1)(2n)} = \Omega_2^{hn} \quad (1c)$$

B. Ring-VOI Definition

To get a more accurate and precise BTV of a tumor, we first constructed an initial ring VOI, namely Ω, which was composed of the partial tumor tissues and a few normal tissues or organs adjacent to the tumor.

Second, we determined the partial tumor volume with a high SUV by the adaptive 3D volume growing method [8] based on the PET SUV, and denoted the resulting volume as V1 whose outer surface acted as the inner surface of Ω.

Third, we took V_1 as the seed volume, and used the adaptive 3D volume growing method [8] again based on SUV and busyness with the growing criterion(2), or based on the PET contrast with the growing criterion(3). Denote the resulting volumes as V_2 and V_3 respectively. The outer surface of the union volume of V_2 and V_3 acted as the outer surface of Ω. The two growing criteria can be expressed as following:

$$\begin{cases} CON(x,y,z) < t_2 \bullet CONmean(sx,sy,sz) \\ SUV(x,y,z) <= SUV(sx,sy,sz) \end{cases} \quad (2)$$

$$\begin{cases} BUS(x,y,z) < t_3 \bullet BUSmean(sx,sy,sz) \\ SUV(x,y,z) <= SUV(sx,sy,sz) \end{cases} \quad (3)$$

where *BUS(x, y, z)* and *CON (x, y, z)* were the values of the busyness and contrast. *BUSmean* and *CONmean* were their mean values of the busynesss and contrast, respectively. *(x, y, z)* was the current appended voxel, and *(sx, sy, sz)* was the previous one. t_2 and t_3 were the thresholds of contrast and busyness respectively.

III. RESULTS

We have applied the proposed method to studies of four patients with nasopharyngeal carcinomas. The processing flow of the proposed method was illustrated in Fig.1. Fig.2 and Fig.3 showed the results on one clinical PET image of a patient who had a recurrent nasopharyngeal carcinoma with lesions in the right retropharyngeal space and cranial base which was close to brainstem. The patient was injected with 181 MBq ^{18}F-fluorodesoxyglucose (FDG) and scanned with the uptake time of 94.2 minutes, and the frame duration of 3 minutes in a GE Discovery ST PET/CT scanner. The PET Data were reconstructed iteratively after the 3D Fourier rebinning. The PET image size was 128×128×131, with a pixel size of 2.34×2.34mm^2, and slice thickness of 3.27 mm.

The resulting BTV was deemed more accurate and more precise than the manually delineating gross target volumes (GTV) and also the threshold segmentation result with SUV of 2.5 as the threshold (BTV_SUV2.5) through visual inspection by two head-and-neck radiation oncologists (Suyu Zhu and Zaijie Huang). To quantify the quality of the resulting BTV, we used the GTV as a surrogate of the ground truth. The resulting sensitivity, specificity and similarity were 92.28%, 87.29%, and 79.28% respectively. Compared the BTV with the clinical target volume (CTV) and planning target volume (PTV), the sensitivity were 55.96% , and 46.75% respectively, the specificity were 98.53%, and 99.38% respectively, and the similarity were 71.22%, and 63.58% respectively. Moreover, all of four BTVs were between the corresponding GTV and the corresponding PTV. Most of BTVs were between the corresponding GTV and the corresponding CTV as seen in Fig.2. The GTV, CTV, and PTV were manually delineated by the two radiation oncologists based on PET, CT and MRI images via a commercial software, Oncentra MasterPlan v3.2, from Nucletron B.V., Veenendaal, The Netherlands for the intensity modulated radiotherapy (IMRT) planning of the patient.

We have also compared the threshold segmentation with SUV of 2.5 as the threshold (BTV_SUV2.5) with the GTV, the sensitivity, specificity and similarity were 97.96%, 55.97%, and 55.72% respectively. The similarity between the resulting BTV and BTV_SUV2.5 was 71.04%.

The 3D Surfaces of the BTV, BTV_SUV_2.5 and GTV were also shown in Fig.3. We noted that the threshold method (BTV_SUV2.5) does not take into account the correlation between voxels. As a result, there are many disconnected sub-volumes inside the BTV_SUV2.5 in Fig.3f.

To delineate the sub-BTV with different biological characteristics for IMRT plan with the radiotherapy strategy of dose painting by contours or dose painting by numbers, we took the resulting BTV as the initial VOI in HMSMv. The resulting sub-BTVs and the reconstruction images from HMSMv with h=2 were shown in Fig.4.

IV. CONCLUSION

We have proposed an HMSMv segmentation framework based on SUV, contrast and busyness in PET images of

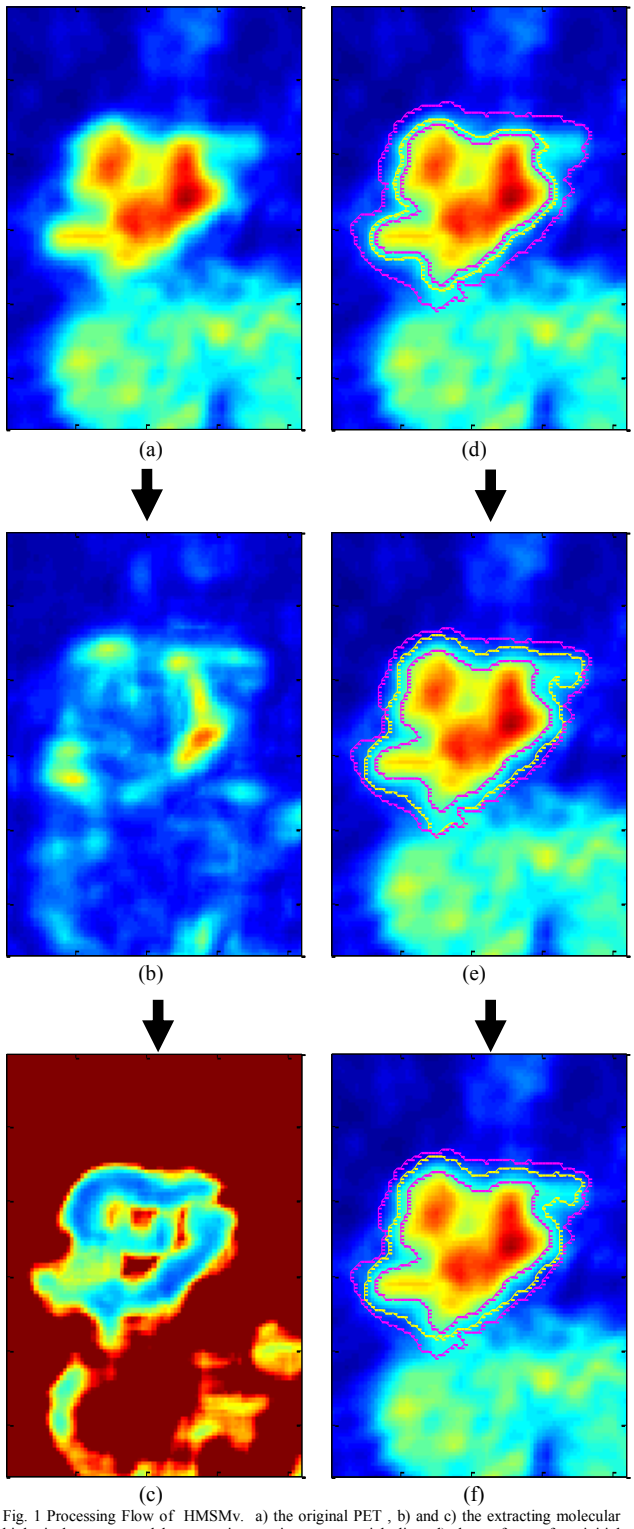

Fig. 1 Processing Flow of HMSMv. a) the original PET , b) and c) the extracting molecular biological contrast and busyness images in a same axial slice. d) the surfaces of an initial ring-VOI(red) and the initial zero-level set (yellow), e) the propagating zero-level set (yellow), f) the final zero-level set corresponding to the surface of the resulting BTV (yellow), which were overlaid on the PET SUV images in a same axial slice.

tumors. We found that SUV, contrast and busyness can offer complementary information to BTV delineation. Nevertheless, we need more clinical experiments to validate the proposed method of HMSMv because manual GTVs were not accurate due to the invisibility of some tumor volumes in CT or MRI images. In addition, partial key organs were enclosed in PET-guided BTV, because PET images cannot offer anatomical information of some normal key organs or tissues close to tumors. Hence, incorporating information of molecular biological characteristics of PET and CT or MRI can be useful for BTV delineation.

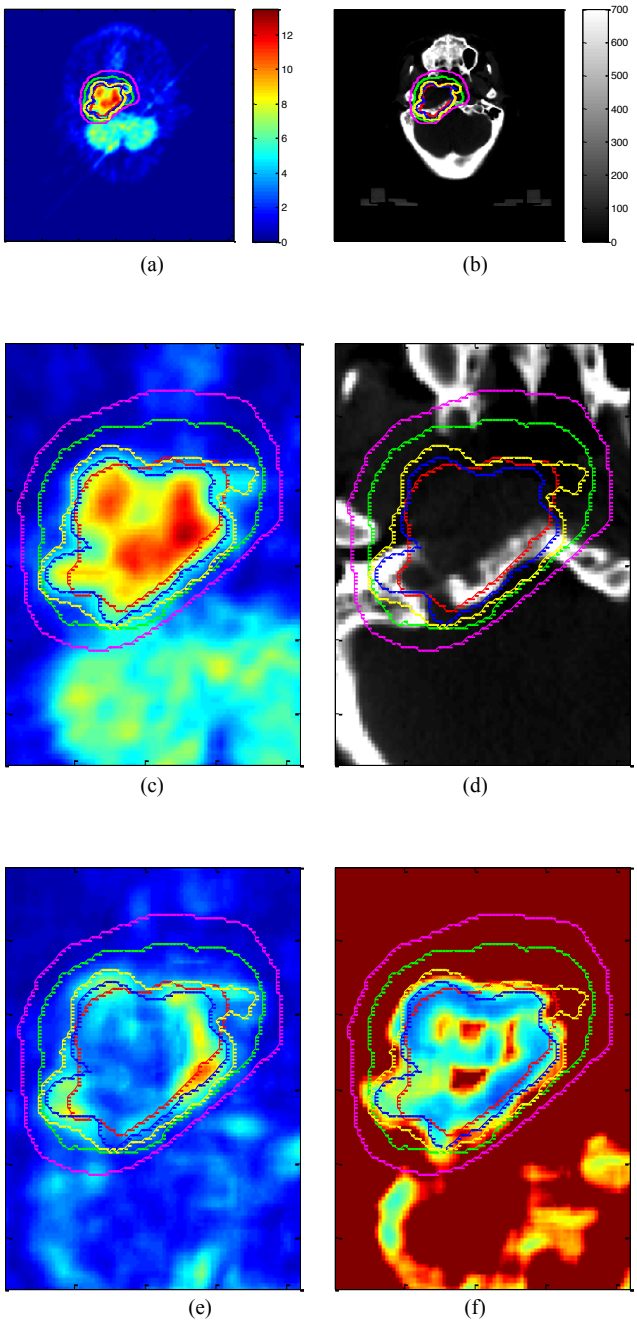

Fig.2 The resulting BTV compared with GTV, CTV and PTV delineated by radiation oncologists for IMRT planning. a) and b) the resulting BTV, GTV, CTV and PTV respectively overlaid on whole PET SUV and CT images in a same axial slice. c), d), e), and f) the resulting BTV, GTV, CTV and PTV respectively overlaid on partial PET SUV, CT, PET-contrast, and PET-busyness images in same axial slice, where the resulting BTV (enclosed by yellow surface), GTV(red, internal), CTV(green), PTV(red , external), and high SUV volume (blue).

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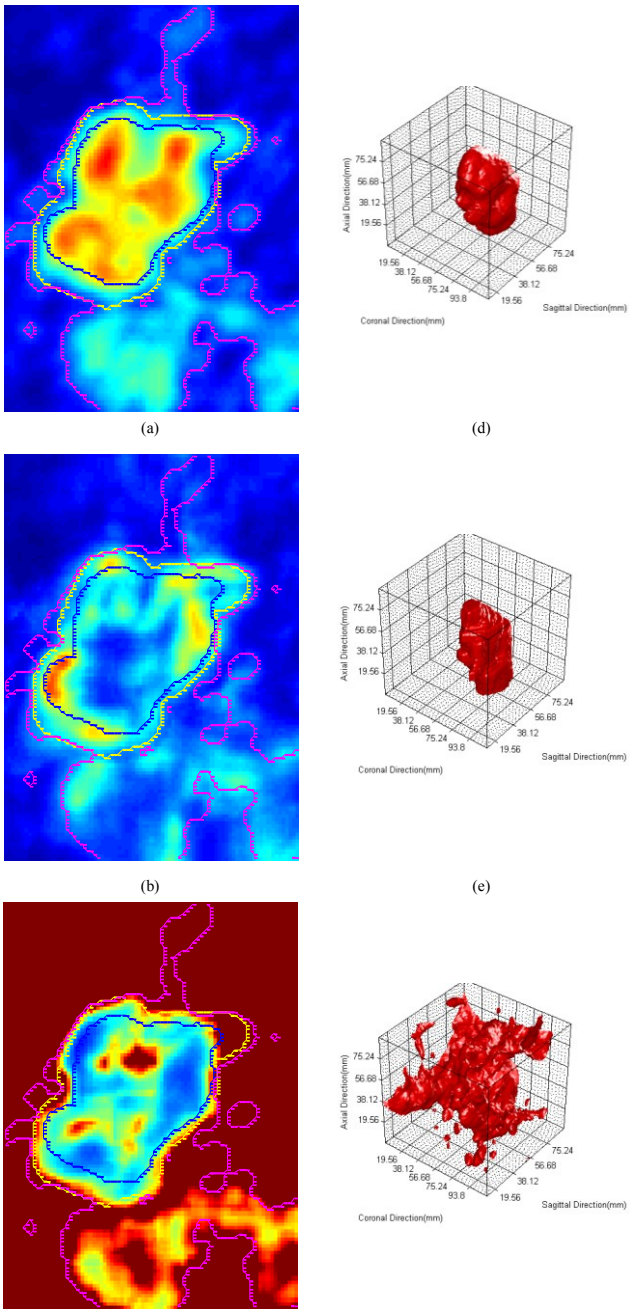

Fig.3 The resulting BTV compared with BTV_SUV_2.5 and GTV. a) the surfaces are overlaid on SUV, b) on contrast, c) on busyness image in a same axial slice, where yellow for BTV, red for BTV_SUV2.5, and blue for GTV. d) the 3D surface of BTV, e) GTV, f) BTV_SUV_2.5.

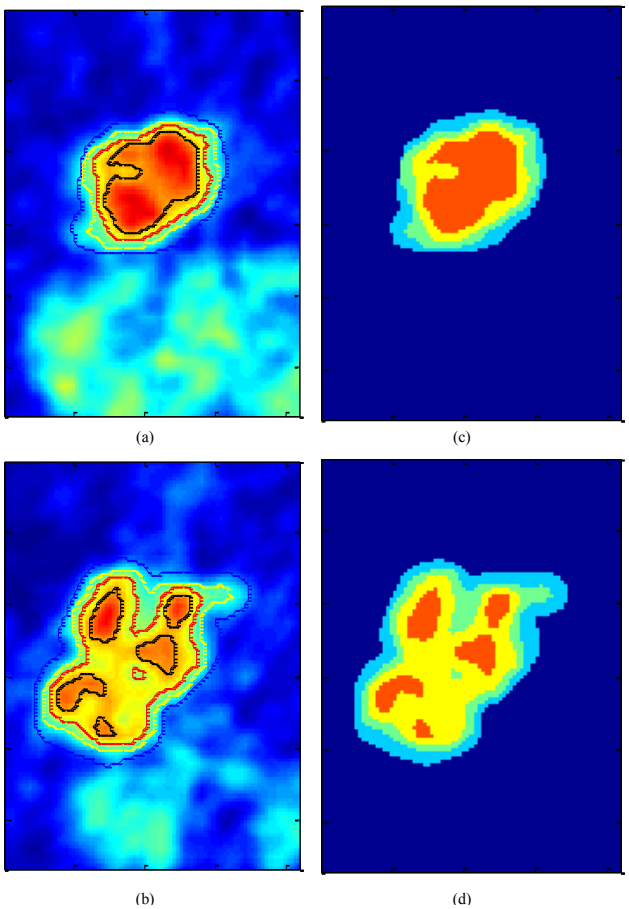

Fig.4 The resulting sub-BTVs of BTV from HMSMv with h=2 based on PET SUV. a) and b) the surfaces of sub-BTVs overlaid on PET SUV images in two different axial slices, where BTV (enclosed by the blue surface, Ω^{11}); sub-BTV (enclosed by the red surface, $\Omega_1^{11} = \Omega^{21}$) and sub-BTV (red and blue, $\Omega_2^{11} = \Omega^{22}$) from HMSMv with h=1 and n=1; sub-BTV (black, $\Omega_1^{21} = \Omega^{31}$, with SUVmean= 10.58) and sub-BTV (black and red, $\Omega_2^{21} = \Omega^{32}$, with SUVmean= 8.43) from HMSMv with h=2 and n=1; sub-BTV (yellow and red, $\Omega_1^{22} = \Omega^{33}$, with SUVmean= 6.40) and sub-BTV (yellow and blue, $\Omega_2^{22} = \Omega^{34}$, with SUVmean= 4.30) from HMSMv with h=2 and n=2. c) and d) The reconstruction images of the corresponding PET SUV images, which the SUVs are the SUVmeans of sub-BTVs respectively, where red for Ω^{31}, yellow for Ω^{32} , light green for Ω^{33} , light blue for Ω^{34} .

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