Automatic segmentation of glioblastoma for radiation therapy treatment planning

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Abstract

During the radiation therapy (RT) process, the treatment is planned and simulated with a treatment planning system (TPS): the organs at risk (OAR) and the tumor target are identified and contoured, and the RT dose, delivered by the planned photon beams, is obtained for optimization of the resulting plan. The contouring work-up of tumor target identifies the Planning Treatment Volume (PTV), i.e. the physical RT treatment volume. PTV of glioblastomas (GB) includes, after expansion, Gross Tumor Volume (GTV, the tumor) and Clinical Target Volume (CTV, tumor plus edema). Usually, GTV contouring is performed manually. In this work, we used GlioCAD, a Computer-Assisted Detection software for automatic contouring of gliomas in MRI/DTI, to delineate GTV. The dataset included the images of 21 patients undergoing RT for GB. For each patient, we co-registered CT-planning images and diagnostic MRI (16 T1-gad, 6 T2 Flair, 13 Flair Fat Sat), which were used for GlioCAD training and validation. CAD outlined the tumor with good accuracy, after ruling out some false positives in post-processing. We identified GTVs, suitable for RT requirements. An evolution of GlioCAD will take into account edema for outlining CTV. The method seems promising. A further automatic system for the delineation of sites at risk in the brain is under development, which may be helpful for standardization of RT-treatment planning.

Introduction

The gold standard treatment for malignant gliomas consists of surgical intervention followed by radiotherapy and chemotherapy [1]. The contouring process in radiotherapy (RT) of malignant gliomas consists in the identification of two volumes: the macroscopically appreciable tumor (GTV, *Gross Tumor Volume*) and a region (edema) of likely infiltration (CTV, *Clinical Target Volume*), Fig. 1. A further margin is added to CTV to create the PTV (*Planning Target Volume*), which takes into account the possible positioning errors during treatment. The CTV can be targeted with a boost irradiation, with respect to the reference RT dose delivered to CTV/PTV.

Both planning CT and diagnostic MR images are used to improve contouring reliability.

The definition of treatment volumes in GB differs in subsequent, various cooperative group trials by EORTC (Organization for Research and Treatment of Cancer) and RTOG (Radiation Therapy Oncology Group), with some differences in margins (regarding, e.g.: GTV, inclusion of peritumoral edema, etc. [1,2,3]), and a definitive consensus has not yet been reached. Moreover, heterogeneity between operators may occur, due to experience and image interpretation [4]. In this perspective, a reproducible and efficient method for delineating the tumor volumes for RT is advisable.

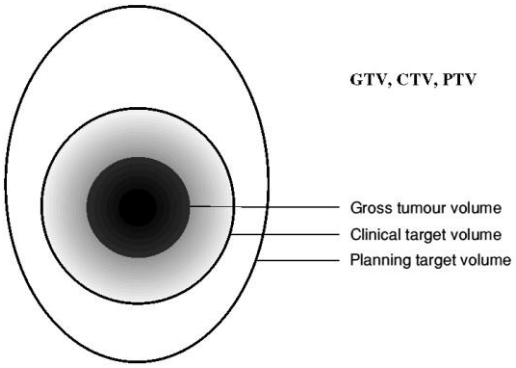

Figure 1. Diagram of the main irradiation volumes (from ICRU 50).

It has been demonstrated that MRI is more sensitive than CT in lesion detection and glioma margin delineation [5], which makes MRI more appropriate for (semi)automatic GB contouring and GTV/CTV delineation.

In this preliminary work, GlioCAD [6], a CAD (Computer-Assisted Detection) software system for cerebral glioma segmentation in MRI/DTI, was used to delineate the GTV treatment volumes in GB patients, in order to get operator-independent semi-automatic contouring. GlioCAD application was preceded and followed by data processing steps whose purpose was to match the data with the software, and to make the automatically-contoured volumes compliant with the radiotherapy requirements.

Materials and methods

The dataset consisted of the images of 21 patients treated for GB at the Radiotherapy Unit of Siena (Italy). For each patient we obtained planning CT images and diagnostic MRI. MR images (16 T1-gad, 6 T2 Flair, 13 Flair Fat Sat scans) were achieved for a better identification of the macroscopic tumor region (GTV) and the surrounding edema (CTV). The images, after the manual contouring of the treatment volumes and organs at risk (OAR), were used to train GlioCAD, a CAD system for automatic segmentation of cerebral gliomas in MRI and DTI (Diffusion-Tensor Imaging).

The manual contouring procedure included the following steps:

1. Manual segmentation and contouring of T1-gad images identifying the macroscopic tumor volume (GTV), that is, the area of contrast enhancement; or, in post-surgical patients, the surgical cavity including any contrast-enhanced surrounding area.
2. A margin of at least 2 cm was added isotropically to the GTV to obtain the CTV, extended if necessary to include perilesional edema as evident in FLAIR images, with manual adjustments. Manual correction was also performed if the expansion resulted in a volume extending beyond natural anatomical barriers (e.g. bone structures, falx, ventricular system).
3. A further 0.5-cm margin was added to CTV to create PTV.

The application of GlioCAD to the automatic GTV contouring (Figs. 2 and 3) is described hereafter, and is based on the combined use of T1-gad images and FLAIR images, all of them co-registered with the CT scans.

GlioCAD [6] is a supervised system, thus it requires an initial set of images where the desired GTV has already been delineated by the physicians. GlioCAD is based on the calculation of texture features (derived from

gray-level histograms, cooccurrence matrices, and run-length matrices) with a sliding-window approach, and on the Fisher Linear Discriminant Analysis classifier.

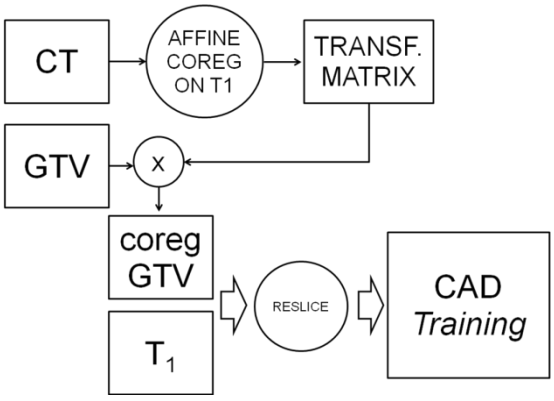

Figure 2. Semiautomatic GTV delineation: preprocessing and CAD training.

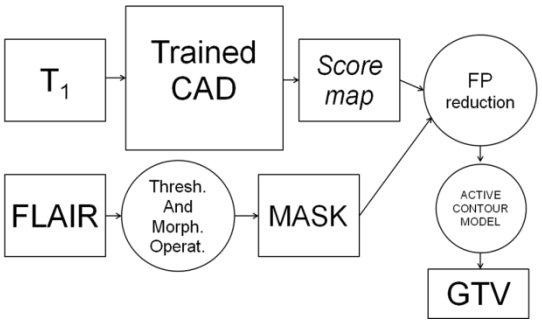

Figure 3. Semiautomatic GTV delineation: Segmentation and post-processing.

After training, the ability to locate and contour the lesions in a new (validation) set of images is verified. Hence, a preprocessing step followed by a training step is needed. In first place (Fig. 2), the CT images are affine co-registered to the corresponding T1-gad, then the transformation matrices are used to project the GTV drawn by the radiation oncologist onto the T1-gad images. Co-registrations were performed by elastix (http://elastix.isi.uu.nl) [7,8]. After co-registration, the T1-gad series with the co-registered GTV was resliced to have homogeneous voxel size in the data set, and was then used to train GlioCAD to recognize and segment the tumor regions in T1-gad.

During the segmentation and post-processing phases (Fig. 3), the trained CAD detects possible neoplastic regions in the T1-gad images of the validation set, reducing false positives through a mask obtained from the FLAIR image by thresholding and morphological operations. An active contour model merges the found regions into a single ROI, smoothing borders and solving inhomogeneity problems. The final identified ROI is used as the (computer-calculated) GTV. Accuracy quantification is given by the Jaccard coefficient, which compares the result with the manually defined GTV.

The extension to the CTV will be performed by using again the mask obtained from the FLAIR image, and by considering a 2-cm border added to the GTV by morphological dilation. Finally, a descalping mask automatically obtained from the T1-gad images will be applied to further reduce false positives.

Results

Segmentation and accuracy assessment were carried out with Leave One Patient Out (LOPO) Cross Validation: the CAD system was applied in turn to each patient scan (Fig. 3), after training on the remaining patients (Fig. 2). In all cases, the CAD outlined the tumor structure with good accuracy. A post-processing step was needed to reject some false positives and to make the identified volumes compliant with radiotherapy treatment requirements, with an acceptable hypothesis for the final GTV estimation (Fig. 4). Most of post-processing is automatic, with some manual interventions for verification and refinement. The mean Jaccard coefficient with its standard deviation was J=0.73±0.08, while the Dice coefficient was 0.83±0.09.

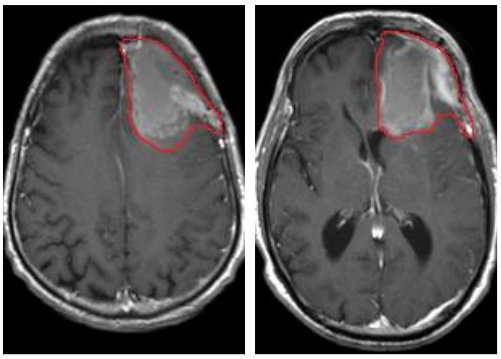

Figure 4. CAD GTV segmentation examples.

Discussion

(Semi)automatic segmentation out of glioma imaging has been the subject of a large number of papers [9–13], while less contributions specifically address RT applications and GTV contouring [14–20]. Among the latter, only few papers ([14,16] report quantitative accuracy data, which we can compare with our results.

In [14] the effectiveness of knowledge-guided (KG) and supervised k-Nearest Neighbors (kNN) segmentation for delineating the GTV from glioma MR images are compared. The average accuracy of the kNN approach was 56%±6% for 11 cases, whereas that of the KG was 52%±7% for 7 of the 11 cases, compared with the manual contouring. The kNN method lead to more robust segmentation results in all patients. The ground truth for accuracy assessment was obtained by multiple contours drawn by three physicians, and the probability that a given pixel is properly classified as part of the tumor (its "weight") was determined by the number of times that this pixel was included in the outlines prepared by the physicians. Accuracy for the computer segmentation is the ratio of the total sum of weights contained within the computer segmentation volume to the total weights generated from the volumes produced by the physicians. This measure is a kind of probabilistic true-positive rate (i.e. sensitivity). Observing that by definition the Jaccard coefficient is always lower than or equal to sensitivity, our method clearly outperforms their results.

Ref. [16] proposed a method for semi-automated GTV segmentation of GB out of MR images for RT planning. Three-dimensional (3D) MR images of 28 GB cases were used. First, a spherical volume of interest (VOI) including the GB was interactively defined. Then, the VOI was transformed to a two-dimensional (2D) image by a spiral-scanning technique. Active contour models were used to delineate an optimal outline of the GB in the transformed 2D image. After inverse transform to the 3D space, a morphological filter was applied to smooth the shape of the 3D segmented region. The computer output was compared with the manually segmented regions by the Jaccard similarity coefficient (JSC) and the True Segmentation Coefficient (TSC), giving on average 74.2±9.8% and 84.1±7.1%, respectively. This paper is written in Japanese, making difficult a detailed comparison, but our results are similar in terms of Jaccard coefficient.

Conclusions

Although the proposed method is still under development and not fully automatic, nonetheless it is promising. It is currently under test on larger sets of images, and our aim is to increase accuracy while making the procedure as automatic as possible. The following step will be the complete CTV/PTV automatic delineation process. Together with the use of automatic or semiautomatic systems for OAR delineation [21–23], the procedure may be helpful in optimizing RT planning in patients affected by GB, in order to achieve standardization in contouring, thus reducing the operator-dependent variability.

Acknowledgements

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