A graph-based method for biological target volume segmentation.

A.Stefano[1,2], S.Vitabile[3], G. Russo[2], M. Ippolito[4], D. Sardina[5], M.G. Sabini[5], F.Gallivanone[6], I. Castiglioni[6] and M.C. Gilardi[6,7].

(1) DICGIM, University of Palermo, Palermo (2) IBFM CNR - LATO, Cefalù (PA) (3) Di.Bi.MEF, University of Palermo, Palermo (4) Nuclear Medicine Department, Cannizzaro Hospital, Catania (5) Medical Physics Unit, Cannizzaro Hospital, Catania (6) IBFM CNR, Segrate (MI) (7) University of Milano-Bicocca, Milano

Purpose: Computerized tomography (CT) is considered to be the gold standard for target tumor delineation and dose calculation in head and neck cancer (HNC) radiotherapy (RT) treatments. CT imaging is based on the variation of tissue density and provides high resolution morphological information. Nevertheless, CT imaging may not show the viable extension of tumors and it does not localize isolated positive lymph nodes. Vice versa, Positron Emission Tomography (PET) imaging provides molecular-functional information of lesions with a low spatial resolution. The 18F-fluoro-2-deoxy-D-glucose (FDG), an analogue of glucose, is the radiotracer commonly used in PET studies. FDG PET is able to characterize lesions that remain equivocal on CT and to detect CT invisible lesions, offering the opportunity to radically change the patient treatment. In RT, within or without the CT gross tumor volume (GTV), it is possible to define the PET biological target volume (BTV) and to apply a specific deliver radiation strategy to these regions. BTV delineation is challenging because of the low spatial resolution and high noise level in PET images. In addition, BTV varies substantially depending on the algorithm used. Visual delineation is widely-used, but it is strongly operator-dependent.
The aim of this work is the development of a robust, fast, accurate, and scanner independent segmentation method of the BTV. The method has been tested on phantom images in order to assess the accuracy respect to region growing (RG) standard approach. To assess the applicability in a clinical environment, a pilot patient study was also considered.
Materials and Methods: The NEMA IEC body phantom including six spheres of different diameters (10,13,17,22, and 37mm) was used to estimate the BTV segmentation accuracy. Spheres and background were filled with FDG with a ratio between measured sphere radioactivity concentration and measured background radioactivity concentration (S/B) that ranged from 1.5 to 11 for 7 experiments at 2 different matrix sizes (256x256 voxels of 2.73x2.73x3.27 mm^3 voxel size and 512x512 voxels of 1.36x1.36x3.75 mm^3 voxel size).
The patient study was selected to evaluate clinical applicability of the PET segmentation algorithm: a 80 years old male with HNC fasted for 12 hours before PET exam and was intravenous injected with FDG. PET/CT scan began 60 minutes after the injection and was performed in diagnostic position with the patient on a flat carbon bed similar to the RT treatment couch. A thermoplastic mask was used for the immobilization of the head.
In phantom studies, the sphere sizes were known and a manual segmentation was not required. In patient study, the GTV was manually outlined by the radiation oncologist. The BTV was manually defined by the radiation oncologist in consensus with the nuclear medicine physician. The semi-automatic BTV segmentation was obtained using a graph-based approach in which the seeds (foreground and background) were specified by the user inputs.
An undirected graph G can be represented as a pair $G = (V,E)$ with nodes $v \in V$ and edges $e \in E \subseteq VxV$. A node v_i is a neighbor of another node v_j if they are connected by an edge e_{ij} with a weight w_{ij} ($w_{ij}=w_{ji}$ being an undirected graph). This approach represent an image as a graph in which the voxels are its nodes and the edges are defined by a cost function which maps a change in image intensity to edge weights. The image is then converted into a lattice where some pixels are known (nodes with label specified by user input) and some pixels are not known. The delineation problem is to assign a label to unknown nodes. This is done by trying to find the minimum cost/energy among all possible scenarios in the graph to provide an optimal segmentation. In our study, the random walks (RW) method proposed by Grady [1] was used.
The RW problem is to determine the highest probabilities for each pixel to reach the target node and has the same

solution as the combinatorial Dirichlet problem: $D[x]= (X^TLx)/2$ where L indicates the graph's Laplacian matrix and x the vector of the probabilities that each voxel is included in target region.
The Gaussian weighting function for PET image was defined as: $w_{ij} = \exp(-B(SUV_i-SUV_j)^2)$ where SUV is the Standardized Uptake Value, the widely used PET semi-quantitative parameter. In our experiments, the B weighting factor was set to 50. Hence the image is converted into a lattice where SUV of each voxel is mapped to wij.
To obtain the BTV delineation, the operator chooses the best slice containing the target lesion in order to identify the target seed with a single mouse click and RW algorithm partitions the nodes into two disjoint subsets (lesion and background).

The effectiveness of the proposed method has been evaluated comparing to well-known and commonly used RG method, calculating the difference between actual sphere sizes and semi-automatic PET segmentations. For each sphere of the phantoms, the percentage difference (E%) was calculated at different S/B. In a phantom study the morphological regions must match with metabolic regions. This is not true in patient studies: the patient study was mainly used to assess the applicability in a clinical environment of the RW algorithm.
At last, the average of the time for delineating BTV in phantom and patient studies was recorded to assess algorithm performances. RWg and RG algorithms were implemented on the Matlab R2012b simulation environment, running on a general purpose PC with a 3.00GHz Intel R CoreTM i5-2320 processor, 4 GB memory, and 64-bit Windows 7 Professional.
Results: Table 1 shows the percentage segmentation accuracy results as 100-E% averaged on different spheres in each phantom experiment: phantoms (a-e) with a sampling matrix of 256x256 voxels and a S/B of 1.5-2 (a), 2-3 (b), 3-5 (c), 5-6 (d), and 6-7 (e), and phantoms (f-g) with a sampling matrix of 128x128 voxels and a S/B range of 3.5-9 (f), and 9-11 (g).

Table 1. Segmentation accuracy % in NEMA experiments

	(a)	(b)	(c)	(d)	(e)	(f)	(g)
RW	92.2±6.6	94.5±3.2	94.5±4.4	95.5±4.1	95.3±2.7	93.4±6.6	94.5±1.4
RG	82.8	87.7±15	83.8±7.4	87.7±16	91.9±3.8	87.1±12	90.3±1.4

The E% range of RW algorithm between segmented and real sizes was found to be from 0.5% up to 16.8% without any restriction in diameter and in S/B. The range reduced from 0.5% up to 5.4% for the spheres with a diameter >1.7cm. The minimum error was obtained in the sphere with a diameter of 3.7 cm and with a S/B of 5 (c). For the spheres with a diameter <1.7cm, the range was found to be from 4.5% up to 16.8%. The maximum error was obtained in the smaller sphere with a S/B of 3.5 (g). RW algorithm failed in the smaller sphere segmentation at very low S/B ((a) and (b)) where the percentage segmentation accuracy was obtained by considering the five spheres with a diameter > 1 cm. The average of the time for 1 slice segmentation was around 0.1 seconds in 128x128 images and around 0.2 seconds in 256x256 images.
The E% range of PET delineation using RG algorithm was found to be from 9.3% up to 36.3% for the sphere < 17 mm diameter and from 0.7% up to 20.4% for the sphere > 17 mm diameter, respectively. RG algorithm failed to delineate spheres with a diameter of 1 cm. In the experiment with a S/B<2 (a) only the sphere with a diameter of 3.7 cm was segmented. The average of the time for 1 slice delineation was around 0.11 seconds in both 128x128 and 256x256 images.
In the clinical case, BTV radically changed the treatment volume because uptake was found outside the GTV in a involved lymph node not CT visible. The volume (13 slices) was segmented in around 1.4 seconds.

Conclusion: The aim of this work was to validate a FDG-PET image segmentation algorithm based on RW and to assess its applicability in a clinical environment. The RW algorithm segments PET images from SUV and it is very fast if compared against the time needed for a manual segmentation.
In the NEMA IEC body phantom experiments, the accuracy of RW segmentation was higher than RG segmentation. This was evident for the spheres with a diameter of 1 cm, despite a drop in the RW accuracy for the smaller spheres at low S/B. This was compatible with the severe errors in the volume estimation produced by partial volume effect (PVE), one of the most important physical factors that impacts the quality and the quantitative accuracy in PET images [2]. Several corrective techniques have been developed and a PVE correction method could be included in the algorithm, such as that described in [3]. Increasing the target size, RW time performance and accuracy remain steady, while RG accuracy increases and time performance decreases. Moreover, RW method provided resolution independent results considering the two set of images tested. In the clinical case, FDG-PET has been proved to modify size, location, and shape of RT treatment planning, leading to the opportunity to prevent potential disease progression. In many cases, such as the one presented in the paper, qualitative interpretation and manual contouring are sufficient to obtain fundamental information for patient care, including invisible metastases using traditional radiologic techniques. However, the implementation of automatic algorithms to estimate BTV for RT treatment is mandatory and the RW meets the requirements in a clinical environment.

References:

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