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SPEQTACLE: a Hilbertian norm generalization of the Fuzzy C-Means algorithm for tumor delineation in PET/CT images

Jerôme Lapuyade-Lahorgue[1], Dimitris Visvikis[1], Mathieu Hatt[1*]

[1]LaTIM, INSERM UMR 1101, Brest, France.
[*]Corresponding author, hatt@univ-brest.fr

Abstract — Accurate and robust tumor delineation in PET/CT images is crucial in oncology and radiotherapy and is still challenging for tumors with complex shapes, low signal-to-noise ratio and high uptake heterogeneity. We have developed a method called SPEQTACLE, based on a generalization of the Fuzzy C-Means (FCM) algorithm using a Hilbertian norm, estimated for each modality through an automatic scheme on each image. Robustness of the algorithm was assessed on multiple phantom acquisitions. Accuracy was evaluated on simulated and clinical images. On PET images, SPEQTACLE demonstrated high performance with significant improvement over the state-of-the-art for the most complex cases. For PET/CT cases, SPEQTACLE provided results in high agreement with manual delineations, outperforming other FCM implementation.

Index terms - Image Processing, Nuclear imaging, Radiotherapy.

I. INTRODUCTION

Positron Emission Tomography / Computed Tomography (PET/CT) is established as a powerful tool in oncology, *e.g.* for target definition in radiotherapy (RT) planning and for therapy monitoring, for which tumor delineation is an important step. Within this context, automatic segmentation offers several advantages compared to manual delineation which is tedious, time-consuming and suffers from low reproducibility. The existing variability in scanner models and associated reconstruction algorithms also leads to images with varying properties of noise, contrast and resolution in clinical practice, an important issue in multi-centric clinical trials.

On the one hand, regarding the determination of metabolically active tumor volumes (MATV) in PET images, there is still room for improvement, especially regarding the delineation of tumors with complex shapes, high uptake heterogeneity, low contrast and/or signal-to-noise ratio (SNR) [1].

Regarding PET/CT multimodal segmentation, although some recent developments have paved the way, automatic, repeatable, accurate, and robust delineation remains an open research topic [1].

Our goal was to generalize the Fuzzy C-Means (FCM) clustering for tumor delineation in PET/CT images.

II. MATERIALS AND METHODS

SPEQTACLE stands for *Spatial Positron Emission tomography / computed tomography Quantification of Tumor with AutomatiC Lp-norm Estimation*.

II.1. Generalized Fuzzy C-Means

We replaced the Euclidian norm with a Hilbertian l^p-norm in FCM and developed an associated automatic estimation scheme for optimal delineation on a case-by-case basis. SPEQTACLE aims at minimizing Eq. 1:

$$\sum_{u\in V}\sum_{i=1}^{C} p_{u,i}^{m}\sum_{n=1}^{N} q_n\left|y_u^{(n)}-\mu_i^{(n)}\right|^{\alpha_i^{(n)}} \tag{1}$$

C is the number of classes in the resulting segmentation map, V is the image(s) volume, N is the number of modalities, $y_u^{(n)}$ is the intensity value for the voxel u and the modality n, m is the fuzzy parameter (set as m=2), q_n are the weights of each modality and $p_{u,i}$, $\mu_i^{(n)}$ and $\alpha_i^{(n)}$ are the unknown parameters: $p_{u,i}$ is a probability depending on the voxel u and the class i, $\mu_i^{(n)}$ is the mean of class i in modality n and $\alpha_i^{(n)}$ is the generalized Hilbertian norm that depends on both class i and modality n. Eq. 1 is minimized through a variational method:

1. Let $P_{u,i}^{(0)}$, $\mu_i^{(n)(0)}$ and $\alpha_i^{(n)(0)}$ the initial values.
2. From $P_{u,i}^{(k)}$, $\alpha_i^{(n)(k)}$, compute $\mu_i^{(n)(k+1)}$ using *Eq. 2*:

$$\sum_{u\in V} p_{u,i}^{m}(k)\sum_{n=1}^{N} q_n \operatorname{sgn}(y_u^{(n)}-\mu_i^{(n)}(k+1))\left|y_u^{(n)}-\mu_i^{(n)}(k+1)\right|^{\alpha_i^{(n)}(k)-1}=0 \tag{2}$$

3. From $P_{u,i}^{(k)}$, $\mu_i^{(n)(k+1)}$, compute $\alpha_i^{(n)(k+1)}$ using *Eq. 3*:

$$\sum_{u\in V} p_{u,i}^{m}(k)\sum_{n=1}^{N} q_n \log(\left|y_u^{(n)}-\mu_i^{(n)}(k+1)\right|)\left|y_u^{(n)}-\mu_i^{(n)}(k+1)\right|^{\alpha_i^{(n)}(k+1)}=0 \tag{3}$$

4. From $\mu_i^{(n)(k+1)}$, $\alpha_i^{(n)(k+1)}$, compute $p_{u,i}^{(k+1)}$ using *Eq. 4*:

$$p_{u,j}(k+1)=\sum_{i=1}^{C}\left(\frac{\sum_{n=1}^{N} q_n\left|y_u^{(n)}-\mu_j^{(n)}(k+1)\right|^{\alpha_j^{(n)}(k+1)}}{\sum_{n=1}^{N} q_n\left|y_u^{(n)}-\mu_i^{(n)}(k+1)\right|^{\alpha_i^{(n)}(k+1)}}\right)^{\frac{1}{m-1}} \tag{4}$$

Eq. 2-4 are solved with Newton-Raphson algorithm [2].

II.2. Performance evaluation

All compared methods were used with the same number of classes (2 or 3 depending on tumors heterogeneity). For PET/CT segmentation, weights were 0.45 and 0.55 for q_{CT}

and q_{PET} respectively to model the increased relevance of PET data for radiation oncologists in clinical practice.

The robustness of SPEQTACLE for monomodal PET segmentation was evaluated using a phantom containing homogeneous spheres acquired in 3 PET/CT scanners, used previously for the evaluation of our Fuzzy Locally Adaptive Bayesian (FLAB) method [3]. The 4 largest spheres (37, 28, 22 and 17mm in diameter) were segmented and the standard deviation (SD) of the volumes for a given sphere across the dataset was reported. Accuracy was evaluated on 34 simulated PET images of tumors generated with a wide range of image characteristics using a previously described workflow [4]. Classifications errors (CE) [5] were calculated relatively to the known ground truth. Accuracy of multimodal PET/CT segmentation was evaluated using 15 clinical lung cancer cases, CE being calculated relatively to a surrogate of truth defined as a statistical consensus of 3 experts' manual delineations defined with STAPLE [6]. SPEQTACLE was also applied to PET/CT datasets using a single norm value, in order to quantify the added value of estimating a different norm for each modality. On PET, SPEQTACLE was compared to the state-of-the-art FLAB method [5], [7] whereas on PET/CT it was compared to the Fuzzy Local Information C-means (FLICM), a FCM implementation with a weighted norm taking into account noise outliers [8]. The Wilcoxon rank sum test was used to compare the results between methods. P-values below 0.05 were considered significant.

III. RESULTS

The robustness of SPEQTACLE was high and not statistically different from FLAB with SDs of 5%, 17%, 13% and 27% *vs.* 5%, 12%, 20%, and 19% ($p=0.15$) for the 37, 28, 22 and 17mm spheres, respectively.

In terms of accuracy, SPEQTACLE provided lower CE than FLAB (14±11% *vs.* 22±20%, $p=0.004$).

SPEQTACLE most significantly outperformed FLAB (17±11% *vs.* 28±22%, $p<0.0001$) on the 19 more challenging cases with the norm estimated ≥3. In the 15 simpler cases (estimated norm <3), SPEQTACLE still led to the most accurate results although without significant improvement (11±9% *vs.* 15±14%, $p=0.22$).

SPEQTACLE provided accurate delineations in PET/CT images compared to the statistical consensus of manual delineations. When using a single norm value for PET and CT, CE were 36±14%, and significantly decreased to 25±8% ($p<0.01$) when using a norm value for each, also outperforming FLICM (25±8% *vs.* 43±12%, $p<0.0001$).

IV. DISCUSSION – CONCLUSION

FCM, with or without improvements, has been considered for delineation of PET tumors before, with limited accuracy and robustness [1]. Here we generalized FCM to improve its accuracy in challenging PET and PET/CT cases, by implementing a fully automated and repeatable estimation of the Hilbertian norm on a case-by-case basis. Our results suggest that the norm parameter can indeed vary substantially across PET and PET/CT images, from ~2 to ~18. Regarding PET/CT multimodal segmentation, several methods have been recently developed and have shown promising results [1]. A future study comparing these algorithms including SPEQTACLE would be of interest for the community but was out of the scope of the present work.

We want to emphasize that SPEQTACLE did not undergo any parameter empirical pre-optimization as it is often the case in PET image evaluation frameworks. The advantage of SPEQTACLE compared to other methods lies in its ability to estimate reliably the norm parameter value on a case-by-case basis. The norm estimation scheme is also deterministic and convergent, with perfect repeatability, which is an important point to ensure clinical acceptance.

The present work has a few limitations. SPEQTACLE aims at the accurate delineation of a single object, and was thus not evaluated within the context of multiple or diffuse/multifocal uptakes. We do not have realistic simulated CTs available, which prevented us to evaluate the multimodal version of SPEQTACLE on simulated data with known ground-truth. Instead we used clinical data with a surrogate of truth obtained with a statistical consensus of manual delineations by experts.

In this paper, we have presented a fully automatic and perfectly repeatable scheme for estimating the Hilbertian norm parameter in a generalized fuzzy C-means. The proposed approach SPEQTACLE was demonstrated to be accurate and robust in PET and PET/CT datasets.

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