Target volume segmentation of PET images by an iterative method based on threshold value

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ARTICLE INFO

Article history:
Received 5 December 2013
Accepted 26 February 2014

Keywords:
PET
Target volume delineation
Segmentation
Thresholding
Iterative method

ABSTRACT

Objectives: An automatic segmentation method is presented for PET images based on an iterative approximation by threshold value that includes the influence of both lesion size and background present during the acquisition.

Material and methods: Optimal threshold values that represent a correct segmentation of volumes were determined based on a PET phantom study that contained different sizes of spheres and different known radiation environments. These optimal values were normalized to background and adjusted by regression techniques to a two-variable function: lesion volume and signal-to-background ratio (SBR). This adjustment function was used to build an iterative segmentation method. Based on this method, a procedure of automatic delineation was proposed. This procedure was validated on phantom images and its viability was confirmed by retrospectively applying it on two oncology patients.

Results: The resulting adjustment function obtained had a linear dependence with the SBR and was inversely proportional and negative with the volume. During the validation of the proposed method, it was found that the volume deviations with respect to its real value and CT volume were below 10% and 9%, respectively, except for lesions with a volume below 0.6 ml.

Conclusions: The automatic segmentation method proposed can be applied in clinical practice to tumor radiotherapy treatment planning in a simple and reliable way with a precision close to the resolution of PET images.

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Segmentación de volúmenes tumorales en imágenes PET mediante un método iterativo basado en valor umbral

RESUMEN

Objetivos: Se presenta un método de segmentación automático para imágenes de tomografía por emisión de positrones (PET) basado en una aproximación iterativa mediante valor umbral, que incluye la influencia tanto del tamaño de la lesión como del fondo presente durante la adquisición.

Material y métodos: A partir de un estudio de imagen PET de un maniquí que contiene esferas de diversos tamaños y en diferentes entornos radiactivos conocidos, se determinan los valores umbral óptimos que suponen una correcta segmentación de volúmenes. Estos valores óptimos son normalizados al fondo y ajustados, mediante técnicas de regresión, a una función de 2 variables: volumen de la lesión y relación señal-fondo (RSF). Esta función de ajuste es usada para construir un método de segmentación iterativo, y, basándose en él, se propone un procedimiento de contorneo automático. Se valida dicho procedimiento sobre estudios en maniquí y se comprueba su viabilidad aplicándose, de manera retrospectiva, sobre 2 pacientes oncológicos.

Resultados: La función de ajuste obtenida presenta una dependencia lineal con la RSF e inversamente proporcional y negativa con el volumen. Durante la validación del método iterativo propuesto se encuentra que las desviaciones de volumen respecto al valor real y al volumen CT están por debajo del 10% y del 9%, respectivamente, excepto para lesiones con un volumen por debajo de 0,6 ml.


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Introduction

In addition to providing the necessary support to calculate the radiation-matter interaction the use of computed tomography (CT) in the setting of radiotherapy provides images with anatomical information with good spatial resolution. One of its limitations is that it does not give information about the functional properties of the tissues visualized. On the other hand, positron emission tomography (PET) provides molecular and metabolic images with information of the biological behavior of the tumor. Several studies have reported a greater sensitivity and specificity of PET versus CT in the diagnosis and staging of certain types of tumors. Nonetheless, the images obtained present poor spatial resolution. The technological development of systems integrating both techniques, PET/CT, allow joint acquisition of data which overcome the limitations of the two techniques used alone, providing functional images of PET together with the anatomical information of CT as an anatomical reference of the tracer.

The use of hybrid PET/CT equipment is therefore becoming a very useful tool in the radiotherapy planning. The uses of this equipment include the localization and the staging of the lesion. Many studies have shown that the use of PET modified tumor staging and allowed the diagnosis of distant metastasis in a significant percentage of patients, thereby representing a change in the radiotherapy procedure and even in the clinical treatment approach. On the other hand, the PET signal indicates the concentration of tracer present in the tumor. This information may be used for better delimitation of target tumor volume for treatment, which has the advantage of reducing inter-observer variability. Indeed, it is possible to differentiate areas with different tracer concentrations, allowing different doses to be applied in each. The joint use of PET/CT images may lead to a change in the surrounding volumes in radiotherapy planning when compared with images obtained from delineation based exclusively on CT.

Nevertheless, the integration of PET images in the delineation process in radiotherapy is a challenge since, compared with CT images, the low spatial resolution and elevated noise lead to poor definition of the edges of the lesions and the organs involved. In addition, both the visualization parameters (selection of window, color scale, etc.) and the contrast relationship between the lesion and the background may significantly modify the apparent size of the tumor volume.

Visual interpretation of the images is usually performed by the nuclear physician together with the radiotherapy oncologist in order to delineate volumes. However, automated or semi-automated procedures are being increasingly used to help in the determination of the edges of the lesion. One of the most popular methods is segmentation by threshold value, which has been reported in studies comparing segmental volumes with surgical samples to support the results.

The method of segmentation by threshold value is based on considering the tumor area as the pixels with an intensity greater than the cutoff or threshold value. Its application in volume delineation consists in choosing the appropriate threshold value of signal intensity to achieve an outline of the lesion which is closest to reality. However, the use of a single threshold value for all the possible situations does not necessarily provide correct delineation because it depends on many things; one being the lesion size. This is especially critical due to the small volumes used since the partial volume effect (PVE) must be taken into account. This has been described in several studies as one of the causes for the lack of reproducibility of the tumor uptake value in PET studies. One of the origins of this effect is the finite spatial resolution of the detectors that produces blurring of the images. A second cause is the sampling carried out for the image formation in which the signal presented by a voxel is an average of the signals of the adjacent tissues. The PVE makes small sized objects appear smaller or cannot even be seen due to the loss of signal.

This dependence of the threshold value on size also means that it is necessary to previously know the volume of the lesion, which implies previous knowledge of the quantity to be measured. This study presents the implementation of an iterative method which allows the delineation of volumes without knowledge a priori of their size.

Another factor to take into account when defining the threshold value is the uptake of the adjacent tissues with respect to the tumor mass which is usually quantified by the signal-to-background ratio (SBR). The optimum cutoff values vary with the equipment (type of detector, efficiency and sensitivity, spatial resolution), the reconstruction algorithm and the radionuclide used.

The present study analyzed the dependence of the optimum threshold value on the size of the lesion and the SBR using phantom images, presenting an adjustment curve with both parameters. With this curve and using an iterative approach we developed a semi-automated procedure for segmentation of PET images. In order to validate the method proposed this procedure was applied on phantom which contains hot spheres. Lastly, the utility of the procedure was demonstrated with clinical images.

Material and methods

PET/CT scanners

The acquisitions were performed in a hybrid PET/CT scanner Discovery LS from General Electric (General Electric Medical Systems, Milwaukee, USA). This hybrid equipment combines the multi-slice LightSpeed CT with the PET Advance NXi with 18 rings (14.5 cm) and block detector of bismuth germanate oxide (BGO).

Phantom and patients acquisition

The acquisition technique was similar to daily clinical practice but the phantom images were obtained in a single bed position. CT scan acquisition consisted in a spiral whole body scan at 140 kVp, 80 mA, and 0.8 s per rotation. The field of view (FOV) used was 50 cm in diameter and images were reconstructed with 5 mm slice thickness. 2D PET was performed with the same FOV and with an acquisition time per bed position of 4 min. Reconstruction was carried out applying an iterative Ordered-Subset Expectation Maximization (OSEM) method with an axial Gaussian filter and a full-width at half-maximum (FWHM) of 8 mm, using the CT images to correct attenuation. The PET images were reconstructed with a slice thickness of 4.25 mm. The reconstructed matrix size was 128 × 128, with a pixel size of 3.906 × 3.906 mm.
**Phantom and concentration of activity**

The IEC Body Phantom 2001 from NEMA was used for the study. This phantom is specific for controlling the quality of PET. It is a metacrylate phantom simulating the human thorax and has an internal length of 194 mm. This phantom contains 6 spheres with internal diameters of 10, 13, 17, 22, 28 and 37 mm (volumes of 0.52, 1.15, 2.57, 5.57, 11.49 and 26.52 ml, respectively). The wall thickness of the spheres is 1 mm and it has a cold cylindrical shaped central area of 180 mm in length and 51 mm in diameter. The volume of the thoracic cavity without spheres is 9.7 l. The interior of both the spheres and the cavity can be filled with a radionuclide solution to simulate different sized lesions or simulate the surrounding radioactive background.

The initial concentration of $^{18}$F-fluorodeoxyglucose ($^{18}$F-FDG) activity for the spheres was set at approximately 250 kBq/ml, being high enough to have acceptable statistics of events throughout the whole data acquisition period (several hours) without increasing the acquisition time. The phantom was filled with water and the $^{18}$F-FDG was gradually added. Different SBR values were obtained taking into account the exponential decay in activity produced between acquisitions and the progressive increase in the background: infinite (acquisition 1, no radioactive background), 25.0 (acquisition 2, with radioactive background of 5.5 kBq/ml), 10.9 (acquisition 3, with radioactive background of 11.6 kBq/ml) and 5.4 (acquisition 4, with radioactive background of 20.4 kBq/ml).

**Patients and administered activity**

The method used was retrospectively verified in 2 patients with a head and neck tumor. In both cases this was done according to the requirements of radiotherapy treatment for use in treatment planning: immobilization with thermoplastic mask and tongue separation with a oral cavity device, lowering of the shoulders by traction and neck hyperextension.

The first patient (A) was a 70-year-old male presenting oropharyngeal epidermoid carcinoma. The second case (B) was a 65-year-old male with moderately differentiated supraglottic epidermoid carcinoma.

Image acquisition was done 60 min after the administration of 300 MBq (10 mCi) of $^{18}$F-FDG.

The clinical target volume (CTV) is delimited according to the image obtained with PET/CT. This volume is included in the radiotherapy treatment and, in addition to the information from the multimodal image, it provides a margin to include the subclinical dispersion of the tumor which is not visualized.

**Determination of optimal threshold values**

Image analysis was performed with ImageJ. This software is free, with many plugins having been made by different authors for the analysis and treatment of images.

The segmentation method based on the threshold value consists in separating the image into 2 parts from its histogram: a region made up of pixels which present radiotracer concentrations above a certain value, denominated the cutoff value or threshold ($U$), and another region consisting of pixels with concentrations below this value. The volume of each sphere ($V$) is determined for each series of images acquired from the region with pixels above the threshold value, varying at intervals of 1% according to the formula:

$$U = \frac{\text{CU}_{\text{max}}(\text{MBq/ml})}{\text{Background}(\text{MBq/ml})} \cdot P \quad \text{with} \quad 0 \leq P \leq 1 \quad \text{each} \quad 0.01$$

In which $\text{CU}_{\text{max}}$ is the concentration of maximum activity within the sphere. The value of Background represents the concentration of uptake associated with the surroundings of the sphere and is measured from the mean value obtained in 4 regions of interest (ROI) defined in 2 central slices of the sphere to be analyzed. Two ROI are used for each circular section slice with a diameter of 2 cm. They are situated around the sphere to be analyzed, being far enough away from the adjacent sphere to avoid their uptake zone.

Fig. 1 shows a reconstructed image of the acquisition with SNR 25.0 depicting the ROI selected in this slice to determine the radioactive background.

The real volumes of the spheres ($V_{\text{real}}$) are known from the radius specified by the manufacturer ($V_{\text{real}} = 4/3 \pi \text{ radius}^3$). Thus, the optimal threshold value ($U_{\text{optimal}}$) is defined as that which achieves segmented volumes closest to reality or, in other words, when the difference in the volumes, $V_{\text{measured}} - V_{\text{real}}$, is minimum.

Once the $U_{\text{optimal}}$ values have been obtained these are adjusted to the function of the independent SBR variables and volume. Analysis of each variable is done separately using regression techniques to determine the expression best describing the relationship between the variables. The $R^2$ regression coefficient is proportionate for each of the adjustments.

**Recovery coefficient**

The SBR can be estimated from the concentrations measured in the images. The concentration of activity associated with the background, $B$, is measured by ROI as explained above, while the signal, $S$, is estimated from the maximum value within each sphere.

It should be taken into account that for small volumes the uptake signal is decayed by the PVE so that the value of SBR is decreased compared to its real value and, consequently, does not coincide with this value or, in other words, with that obtained in a larger volume not affected by the PVE. Contrary to studies with phantoms in which the real SBR can be estimated by the concentrations of activity measured or from those measured in the large volume images, the true SBR value for clinical studies is not known.

Thus, in the present study the SBR measured in the image was corrected by a factor denominated the recovery coefficient (RC) which varies based on the estimated volume of each iteration. The RC is determined by the phantom measures as the quotient between the concentration of activity measured in the sphere to be analyzed and the concentration measured in the sphere over that having

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very little influence on the PVE. In our case we chose the sphere with a diameter of 37 mm:

\[ RC = \frac{CU_{sphere}(MBq/ml)}{CU_{sphere37\,mm}(MBq/ml)} \]  

(2)

The corrected SBR is the result obtained by dividing the SBR measured by the RC \((SBR_{corr} = SBR/RC)\).

**Iterative method**

To apply the iterative method it is first necessary to determine the SBR value from the concentration of signal activity and the background defined in the images as explained above. The starting value \(V_0\) is then assigned. This initial value should be reasonable to allow the method to converge in a result. In our case \(V_0\) was a value of 30 ml (volume large enough to not be significantly affected by the PVE). The RC is calculated from this \(V_0\) and this, in turn, determines the \(SBR_{corr}\). Using the \(SBR_{corr}\) and \(V_0\) values in the previously mentioned adjustment formula (shown later as formula (6)), we obtain the optimal threshold value \(U_1\). The segmentation method is then applied to the image with this threshold value, obtaining a volume \(V_1\) which is used to generate a new \(SBR_{corr1}\). Threshold \(U_2\) is obtained from \(V_1\) and \(SBR_{corr1}\), which, in turn, determines a second volume \(V_2\). An associated volume \(V_n\) is generated in the iteration \(n\) on applying a threshold \(U_n\). Fig. 2 shows a scheme of the iterative process for 3 iterations. The iterative process does not stop until the convergence criteria is fulfilled, for which the difference of volumes between successive iterations should be less than a determined value \(\Delta\), that is:

\[ V_n - V_{n-1} \leq \Delta \]  

(3)

In this way it is presumed that the method always achieves convergence even when the result might not make physical sense. Despite this, the convergence led to reasonable values in all the cases analyzed except the smallest sphere which was close to the detection limits of the equipment.

**Semi-automated volume delineation method**

Once the optimal value curves are known the following segmentation method can be applied to any type of clinical image acquired with the same scanner and in the same conditions. The proposed methodology involves the following steps:

- Localization of the lesion in PET images.
- Definition of a volume of interest drawing the lesion with a certain margin. From this we obtain the maximum value of concentration of activity that determines the signal (5).
- Definition of the ROI necessary to determine the concentration of background (B) activity surrounding the lesion.
- Obtain the S/B quotient to determine the SBR.
- Determination of the RC from the \(V_0\), and obtain the \(SBR_{corr0}\).
- Obtain the starting threshold value \(U_1\) of the iterative method from the \(V_0\) and \(SBR_{corr0}\).
- Application of the iterative method until the convergence criteria are fulfilled and obtain the resulting volume \(V_n\).

**Analysis in phantom: validation of the delineation method**

To validate the method proposed the procedure was applied on the same phantom after having changed the localization of the spheres and selecting a different SBR; that is, the nominal SBR was equal to 12.6 with a radioactive background of 7.4 kBq/ml (comparable to the average concentration of a 70 kg patient receiving 300 MBq of \(^{18}\)F-FDG, 4.3 kBq/g). The method was applied on the PET images of the different spheres. The resulting volume was...
Analysis in patients: application of the delineation method

The procedure described was applied in the PET images of both patients to determine the tumoral lesions.

Results

Determination of the optimal threshold values

Fig. 3 shows the optimal threshold value required to correctly delineate the 2 largest spheres in the PET images, with little influence by the PVE in different radioactive SBR regions. The graph does not include the SBR with infinite value due to differences in the scale, but it is shown in the adjustment. In addition, the limits of each sphere were delineated in the CT image, being easily identifiable.

Optimal threshold value normalized to the background based on the signal-to-background ratio (SBR) obtained for the largest spheres together with the corresponding adjustment obtained in formula (4). The bars of uncertainty are included for the adjustment calculated using the value of the mean error squared.

$$U_{\text{optimal}}(\text{SBR}) = 0.3532 \cdot \text{SBR} + 0.4209$$  \hspace{1cm} (4)

The regression coefficient $R^2$ for the adjustment is 0.999.

Fig. 4 shows the ratio between the optimal threshold normalized to the background and the volume. The infinite SBR value is not included due to scale differences. The error squared value is again included as bars of error as an estimator of adjustment uncertainty. The dependence found is more complex than in the case of SBR. There is a more or less constant and stable optimal value for volumes above approximately 2.5 ml, which significantly falls at volumes below this value.

To adjust the data to the dependence of the volume, the stable value in each series of data with a determined SBR was normalized by dividing each series by the corresponding value obtained in (4). Then, the data were adjusted by minimum squared from the average of the normalized series. With $V$ as the volume in ml, the adjustment function in each case is:

$$U_{\text{optimal}}(V) = -0.186/V + 0.9856$$  \hspace{1cm} (5)

in which an inversely proportional negative ratio was chosen as the adjustment function.

The regression coefficient $R^2$ obtained is 0.8936. The adjustment functions were defined so that the resulting formula to obtain the optimal threshold in the conditions of the present study was the product of both:

$$U_{\text{optimal}}(\text{SBR}, V) = (0.3532 \cdot \text{SBR} + 0.4209) \times (-0.186/V + 0.9856)$$  \hspace{1cm} (6)

This adjustment formula relates the optimal threshold value with the SBR and the volume, with deviations associated with values of less than 5 voxels (0.325 ml).
also shows the volume determined in both PET and as the first SBR value. shows the volumes (7) and denote the most representative axial slices of ), denominated PET-VOL2 with an depiction the most representative axial slices of ), denominated PET- ) was adjusted to the function: 

\[ \text{SBR} = \frac{V_{\text{PET}}}{V_{\text{CT}}} \] 

(6) 331–339

Patients

Figs. 6 and 7 depict the most representative axial slices of patients A and B, respectively. The images show the CTV drawn by the radiotherapy oncologist with the cooperation of the nuclear physician (especially in case A) as well as the volume segmented by the method proposed. According to criteria of microscopic risk, these volumes were not comparable because the CTV extended beyond the visual volume. That is, the automated volume is smaller and should be included in the volume defined manually if the automated system and the manual delineation are correct.

The data applied in lesion segmentation are: patient A presented 2 lesions which were independently segmented. With regard to the lesion in the amygdala, denominated PET-VOL1 which had an SBRcorr of 21, we applied a threshold value of 7.7 over the background value (Fig. 6a and b), obtaining a volume of 14.4 ml; the delineated CTV1 volume was 37.1 ml. The lymph node lesion (Fig. 6b and c), denominated PET-VOL2 with an SBRcorr of 8.3, was segmented with a threshold value of 3.2 over the background value, obtaining a volume of 5.7 ml; the delineated CTV2 volume was 23.9 ml.

In the supraglottic lesion of patient B (Fig. 7), denominated PET-VOL3, with an SBRcorr of 7, we applied a threshold value of 2.8 over the background value, obtaining a volume of 7.0 ml; the delineated CTV3 volume was 11.1 ml. Less than 4 iterations were required in all the cases and the corrections by size, RC values, were approximately factor 1; the largest correction was applied to the PET-VOL2, being of about 5% of the SBR value measured.

Discussion

Automatic segmentation algorithms using threshold value are being increasingly used for the delineation of the target volume.

Table 1

<table>
<thead>
<tr>
<th>Vreal (ml)</th>
<th>VPET (ml)</th>
<th>VCT (ml)</th>
<th>Absolute difference VPET − Vreal (ml)</th>
<th>Relative difference (VPET − Vreal) × 100/Vreal (%)</th>
<th>Absolute difference VPET − VCT (ml)</th>
<th>Relative difference (VPET − VCT) × 100/VCT (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>26.52</td>
<td>27.04</td>
<td>26.65</td>
<td>−0.52 (8)</td>
<td>2.0</td>
<td>0.39</td>
<td>1.5</td>
</tr>
<tr>
<td>11.49</td>
<td>11.61</td>
<td>11.37</td>
<td>−0.11 (2)</td>
<td>1.0</td>
<td>0.24</td>
<td>2.1</td>
</tr>
<tr>
<td>5.58</td>
<td>5.19</td>
<td>5.53</td>
<td>0.39 (6)</td>
<td>−6.9</td>
<td>−0.34</td>
<td>−6.2</td>
</tr>
<tr>
<td>2.57</td>
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<td>2.56</td>
<td>0.24 (4)</td>
<td>−9.2</td>
<td>−0.23</td>
<td>−9.0</td>
</tr>
<tr>
<td>1.15</td>
<td>1.10</td>
<td>1.11</td>
<td>0.05 (1)</td>
<td>−4.2</td>
<td>−0.01</td>
<td>−0.9</td>
</tr>
<tr>
<td>0.52</td>
<td>1.10</td>
<td>0.54</td>
<td>−0.58 (9)</td>
<td>110.6</td>
<td>0.56</td>
<td>103.7</td>
</tr>
</tbody>
</table>

* The number of voxels in PET resolution is shown in parenthesis, representing the difference found.

Fig. 5. Recovery coefficient for the different values of the signal-to-background ratio (SBR) together with the corresponding adjustment according to formula (7). The bars of uncertainty are included for the adjustment, calculated using the value of the mean error squared.

In formula (6), the dependence of the optimal threshold with the SBR was obtained with the data of the largest spheres not decayed by the PVE. However, as explained previously, the real SBR is not known when the iterative method is applied and it is necessary to correct the SBR value measured by the PVE before being introduced in (6). The correction factor or RC determined from the data of the phantom (Fig. 5) was adjusted to the function:

\[ RC = -0.249 \cdot (V)^{-1.043} + 0.995 \] 

(7) with a regression coefficient \( R^2 \) of 0.9212. Thus, the correct SBR, \( \text{SBRcorr} \), is the coefficient of the SBR measured between the RC in order to correct the decay in activity due to size. The \( \text{SBRcorr} \) value is introduced into formula (6) as the first SBR value.

Analysis in phantom: validation of the delineation method

The iterative delineation method proposed (see Section “Semi-automated volume delineation method”) was applied in PET images in the phantom, changing the localization of the spheres and introducing a nominal SBR of 12.6. Table 1 shows the volumes obtained using the iterative method proposed compared to the real volumes and the discrepancies found in absolute and relative terms and in number of voxels.

The percentage differences were not greater than 10%, except for the smallest sphere in which the method did not converge to an adequate value. This is mainly because such small volumes are close to those of scanner resolution thereby making correction by PVE difficult. If we exclude the sphere of 10 mm in diameter from the analysis the difference in voxels is not greater than 8. The number of iterations needed for convergence was 3 or 4 in all the spheres.

Table 1 also shows the volume determined in both PET and CT and the discordances. From the results it can be seen that the iterative segmentation method proposed provides reliable results, presenting an accuracy matching the intrinsic resolution of PET.

Table 1 shows the volumes determined in both PET and CT and the discordances. From the results it can be seen that the iterative segmentation method proposed provides reliable results, presenting an accuracy matching the intrinsic resolution of PET.
However, several precautions should be taken into account when they are used. Thus, the influence of the volume and the SBR over the optimal threshold value must be included which means that a single threshold value is not valid for all the possible situations and values adapted to each specific situation are necessary.

The reduction of contrast between the object and its surroundings, whether due to an increase in the radioactive background or PVE, makes it necessary to reduce the threshold value of the concentration of activity normalized to the background to adequately segment and obtain an object volume as close to the real volume as possible. Indeed, in certain conditions this may not even be possible due to the limits of detectability of the equipment. In our case, formula (6) expresses the optimal threshold value with tumor size and with the uptake quotient of the lesion with respect to the background. In general this curve should be determined for each equipment, reconstruction algorithm and radionuclide used.

The iterative method proposed is similar to that described by other authors, albeit with significant differences. We preferred to express the optimal segmentation threshold in relation to the background value instead of the maximum uptake value. We did this for 2 reasons. First, the maximum uptake is influenced by the volume which is considered a dependent variable in our adjustment. The use of the maximum uptake may produce “unnecessary complications” in the adjustment procedure. Moreover, we believe it may be more intuitive to express a lesion as having an uptake $n$ times greater than the background.

Another feature of our algorithm compared to that by Jentzen et al. is that we introduce a correction of the SBR during the iterative process according to the volume measured so that we work with a surface rather than a curve. This may explain the slightly lower deviations we found on comparing the results for validation of the algorithm in the phantom, if we omit the smallest sphere of 0.52 ml. Compared to the real volume the error in our case was not greater than 10%, with an average difference of 4% (the differences regarding CT volume vary from $+2$ to $-9\%$, Table 1). Jentzen et al. obtained an average difference of 8%. Other authors also describe iterative methods to determine the correct area of each slice instead of volume. The algorithm is applied in 3 orthogonal directions to thereafter identify the elements (pixels) making up the volume to segment. The results are similar to ours when the object is a sphere. The study by areas could, a priori, provide better adaptation to irregular geometries, but would be much more complex.

One of the strengths of the method proposed here is its simplicity. Once the optimal threshold curve has been adjusted to the volume and the SBR, we only have to measure the concentrations of maximum activity within and surrounding the lesion.

Image analysis was performed using a software application (Image). However, we performed tests with this software application associated with the PET equipment used to assess its viability and the time consumed and determined that its implementation is feasible in PET work stations provided that these include tools for delineation using the threshold value, as occurs with most of the commercial applications currently available. With respect to the radiotherapy planning systems, many of these do not have tools for concentration quantification, making the segmentation process unfeasible, although these applications seem to be increasingly included in the new versions.

The resolution of the PET images may induce uncertainty, albeit limited, with respect to the results obtained. The voxel size of the PET image ($3.906 \times 3.906 \times 4.25$ mm, in this case) makes the convergence of the iterative method of the experimentally measured volumes and the real or segmented volumes between 2 successive iterations present certain differences inherent to this low resolution. This inaccuracy increases as the lesion size

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**Fig. 6.** Images of patient A with segmented PET volumes using the iterative method proposed and the CTV volumes determined manually for different axial slices.

**Fig. 7.** Images of patient B with segmented PET volumes using the iterative method proposed and the CTV volumes determined manually for different axial slices.
approaches that of the resolution. For example, the smallest sphere with a diameter of 10 mm is ideally constituted by 8 voxels. The addition or subtraction of a voxel changes the volume size 12.5%.

The experimental approach with a phantom simulates a realistic situation in terms of photon scatter and correction of attenuation. However, the volumes studied represent lesions which are regular in shape and homogeneous in concentration while the shapes and concentrations of lesions in clinical practice may be irregular and/or non-homogeneous. In this latter case the methodology proposed may be the first approach for volume delineation and may later be modified manually.

The physiological uptakes adjacent to the volume of interest are especially complex and require the collaboration of nuclear physicians who determine the criteria of normal uptake. In patient A the tumor was shown to be close to a zone of parapharyngeal uptake which was symmetric with the contralateral. Definition of the limits of the tumor region is a challenge in both automated segmentation and manual delineation. In this case the definition of the zone corresponding to normal uptake was achieved among the specialists involved. However, on determining the volumes extended to cover microscopic risk and geometric uncertainty, the region of physiological uptake was only partially included.

The algorithm presented may be applied in lesions without movement during image acquisition. For example, lesions involving respiratory movement may lead to errors in the quantification of the concentration of the tumor since the acquisitions are made during an interval of time including several respiratory cycles. On the other hand, PET images may be used to measure 3D extension of tumor uptake and provide the edge of internal tumor movement. It should be noted that scattering of the activity in solution of the PET images.

Rapid accurate knowledge of this minimum volume can be used to assess dosimetry; for example, to avoid minimum doses, or on the other hand, it could be a volume in which the maximum doses are achieved if doses are to be scaled. The method proposed can automatically segment most of the cases of blank volumes with an accuracy close to that of the resolution of the PET images.

Conclusions

The use of molecular imaging has introduced an additional dimension to the management of patients with cancer. With respect to local treatment with radiotherapy, it helps to define the tumor volume and the lymph nodes affected. Modifications in the delineation of the target volume are reflected as differences in the distribution of doses when compared with planes based only on CT.

Today in radiotherapy and especially in head–neck cancer such as in the cases presented here, anatomical changes may occur which require re-planning. The value of an automated segmentation method will therefore facilitate evaluation and comparison of the target volume. This method is fundamental in two senses; the first, is for defining a minimum volume of tumor involvement to which a margin is added for microscopic risk or to contribute to the anatomical image, and the second is to be able to make this definition quickly.

Rapid accurate knowledge of this minimum volume can be used to assess dosimetry; for example, to avoid minimum doses, or on the other hand, it could be a volume in which the maximum doses are achieved if doses are to be scaled. The method proposed can automatically segment most of the cases of blank volumes with an accuracy close to that of the resolution of the PET images.

Conflict of interest

The authors declare no conflict of interest.

References


