Three-dimensional ROIs in Brain PET

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Abstract

A semi-automatic system for determining volumes of interest (VOI) from positron emission tomography (PET) scans of brain is described. The VOIs surface extraction is based on user selectable threshold and three-dimensional target flood-fill. Contrast to anatomical volume detection approaches, volumes are determined from functional PET images and the obtained objects are checked against anatomical images. The developed VOI program was evaluated with brain FDOPA-PET studies where the striatum was the object. The results were comparable to entirely manual method and the target extraction time is reduced to about one third of manual method.

Keywords: volume of interest, region of interest, positron emission tomography

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1 Introduction

An analysis method used in positron emission tomography (PET) imaging is to determine interesting areas from an image and calculate results by using these areas. The areas are called region of interest (ROI). A set of ROIs describing the same object in a volume space constructs a volume of interest (VOI). This can be used to calculate average radioactivity concentration in a homogeneous functional or anatomic structure.

A region of interest can be determined by manually drawing areas point by point and plane by plane on the image. Points are connected (in order) by lines to obtain a closed region. With PET images, this manual approach has been reasonable because of the irregularity of target objects, noisy data and relatively low resolution. The number of transaxial planes of new PET-imaging devices has been increased, for example, from the range of 8 to 15 to the range of 35 to 63. Consequently, the same functional object definition can now take seven planes instead of three, because of thinner slices. The anatomic accuracy of a manually drawn region is likely to decrease when the number of subjects and planes grows. Results are also sensitive to the individual analyzer's personal style to draw. Relatively more time is spent to the laborious manual drawing task instead of analyzing results and making judgments.

Image processing techniques can offer tools for automating parts of this demanding process of outlining objects from medical images. In literature, there are some papers concerning the subject on the radiation treatment planning. These studies are based on the anatomical computed tomography (CT) and magnetic resonance (MR) images. In [7, 8], a three-dimensional shape model using prior knowledge of anatomical structures is used for interactive segmentation. In [4, 9, 5], a system for radiation treatment planning is described. It is used for outlining a target volume and organs at risk in order to plan radiation treatment. Image processing techniques were applied and practical testing was carried out by clinicians. The study having same aims is also reported in [10]. With all these studies, the time used for target extraction is reduced significantly and the reproducibility of results is superior compared to the results of manual segmentation. Hours of manual drawing work can be reduced to a few minutes interaction.

In the work described here, the volumes of interest are determined from PET images with minor user interaction. The user checks out results, modifies (if required) and accepts found objects. The functional structures can be shown on the corresponding MR image in order to ensure results. The obtained VOIs can be stored to a conventional ROI file format. This semi-automatic approach can improve the quality and shorten the time of the analysis compared to traditional manual object determination techniques.

2 Concept to determine volume of interest

The spatial distribution of tissue radioactivity concentration is registered by a PET-scanner and the acquired data is stored to a sinogram. Images are reconstructed from the sinogram. The program determines a volume of interest from the image with the aid of user. The volume of interest is written out to a file. Average radioactive concentration of a target object is determined from the image by using the obtained volume of interest. Figure 1 shows the schema of the whole analysis process including data acquisition.

2.1 Preprocessing

The original image is a three-dimensional stack of planes representing spatial distribution of radioactive concentration. The threshold image represents the original image in binary form and it is split to left and right thresholds. The threshold values are set by user. Surface extraction of the functional structure will be done by referring to the threshold image. The user selects a start pixel inside of the functional structure.

2.2 Algorithms

Flood-fill (region growing) [3] algorithm is used from the start pixel to generate marked image for extracting the surface of object. The surface is described by a set of boundaries on the three-dimensional image. A boundary is extracted from flood-filled image by following the edge on plane. Boundary pixels are added to the list. All distinguishable boundaries are seeked, extracted and stored. The algorithm 1, find-voi, describes the whole process.

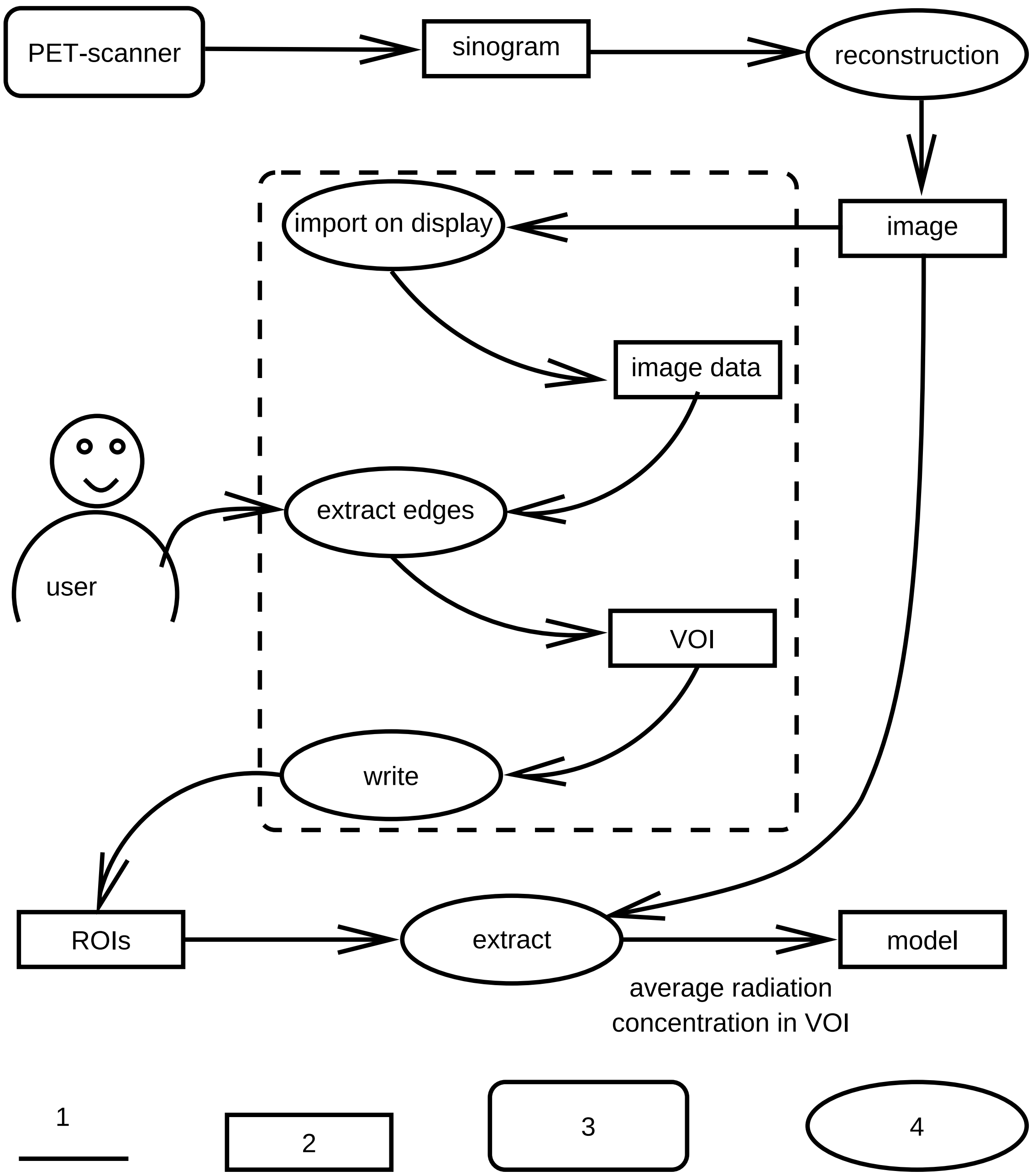

Figure 1: Schema of the analysis process and the data flow. Symbols: 1 data flow and direction, 2 data, 3 active process producing data and 4 action. The dotted box outlines the developed program duties in the whole analysis process.

Set thresholds.
Select start pixel.
Flood-fill object starting from start pixel
for all (marked) planes **do**
  scan all pixels from the marked image to find coordinates projected VOI in the original image space.
  if pixel is marked **then**
    Trace boundary by algorithm 2 from the marked pixel with direction left.
    Mark traced boundary by two-dimensional version of the flood-fill algorithm to prevent tracing the same boundary again.
  end if
end for
Determine volume of obtained VOI.
Store obtained projections of VOI.

Algorithm 1: Find projections of VOI on planes

Get direction and pixel.
Set last direction $\neq$ direction.
repeat
  if direction $\neq$ last direction and pixel not included to the boundary **then**
    add pixel to the boundary,
    update pixel according to current direction,
    update direction according to neighbourhood pixels.
    Boundary tracing is done counter-clockwise by keeping in pixels on the left-hand side.
  else
    update pixel according to current direction
  end if
until back on the start pixel or maximum number of pixels exceed

Algorithm 2: Trace boundary

Get pixel
Increase x-coordinate until out of the thresholded area. {It is the start pixel of boundary candidate}
Perform boundary following algorithm 2
from the start pixel with direction up
if the pixel is inside of obtained boundary **then**
  accept the boundary
  add it to a list
end if

Algorithm 3: Trace single boundary

3 Implementation

The user interface is shown in the figure 2. The program window is split to three main parts, menu bar, the data display area and status bar. The data display area includes name of an image file, plane view to an image, vertical scale to select a plane, a plane view to a threshold image, two horizontal scales to select the threshold values and selected information about the currently defined VOI. Optionally, it is possible to show a second image and its name on the left-hand side. For example, with this study anatomical MR images were shown.

The PET and optional MR image can be loaded by using a file browser. The first plane from a three-dimensional image package is shown. The plane on display can be selected with scale. Both images have their own colour map.

The program offers a set of actions for manipulating VOIs: Retrieve VOIs, and show projection of VOI on various planes, rename VOI, remove VOI, set new thresholds, and set new position between left and right thresholds. If there is an anatomic image available, the VOIs are automatically projected on it. The current VOI information is shown on the lower right part of the window. The projection volume and the total volume of the selected VOI is shown below the name. The name of VOI can be changed by selecting VOI and replacing the old name.

To obtain a VOI, user selects a plane near by the centre of a desired target object. A plane is selected by dragging the scale on the left. The current plane number is shown by the scale. Because of the physiological differences between left and right sides of the brain, the images can be split to the left

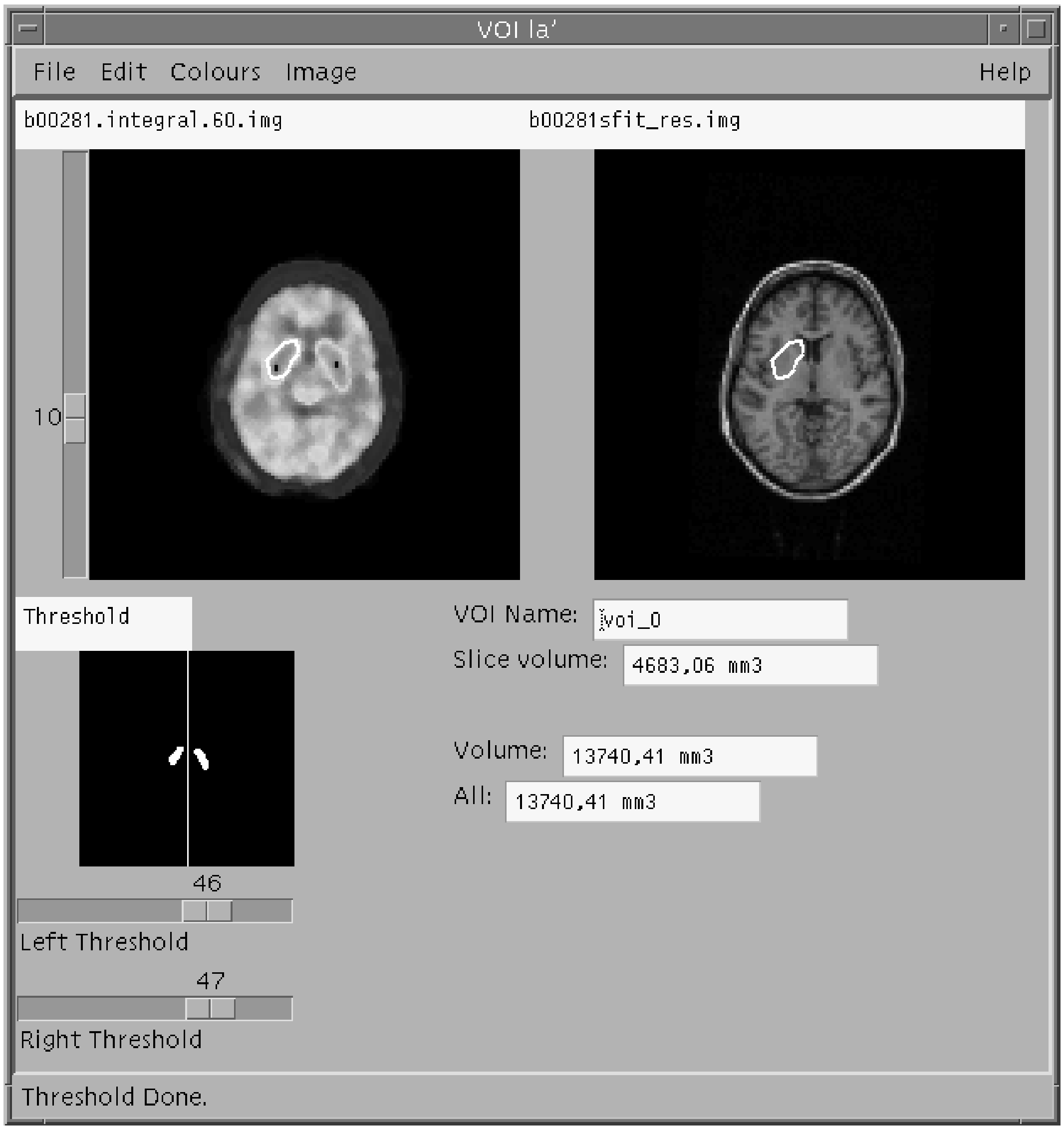

Figure 2: User interface. The upper left image is a user selected slice from a 3D image. A vertical scale on the left hand side is used for slice selection. The scale also shows the number of the current plane. The lower image shows the corresponding thresholded version of the current slice. User may select some other slice to view by dragging the scale. The horizontal scales at bottom are used to adjust threshold levels. The upper right image is optional and is used for verifying results by displaying corresponding ROIs on it. On the lower right part, the current VOI information is shown with a user editable name.

and the right sides having separate user selectable threshold levels. The left and the right sides threshold levels are set to one by default. The user has to adjust both values to correspond to a particular volume of interest. The levels can be set by dragging the horizontal scales below the threshold image. The result of thresholding can be seen in real time in the threshold image.

After setting thresholds, the start pixels must be selected near by the centre of the target objects by clicking a mouse button for each separate object. The left mouse button triggers algorithm 3 to find an area. The middle button triggers algorithm 1 to find a volume. If boundary seeking succeeds in finding a closed boundary and number of pixels is not exceeding pixels in image, a new VOI is created. User can set a name for it by writing a desired name in the VOI name field. By default, VOIs are named 'voi_x', where x is the order number of the obtained VOI. The image coordinates of obtained volumes can be written in a ROI file for further analysis.

The program was implemented by using Sun's Workshop, X11 (Release 5), Motif libraries and C-compiler. The hardware used for development is Sun Ultra 2 workstation with Solaris 2.x operating system. At the present implementation, 8-bit pseudo colour visual is supported for displaying. The PET scans were made with ECAT 931/08-12 (CTI/Siemens, Knoxville, US-A) scanner. It produces fifteen planes per scan. Transaxial slice width is $6.75mm$, pixel size with the applied reconstruction zoom, and matrix size of 128 x 128 is $2.76mm$ x $2.76mm$. Magnetic resonance images were obtained with 1.5 T Magneton (Siemens, Erlangen, Germany) PET and MR scans were coregistered by using AMIR [2] method. The phantom PET scan was made with GE Advance (GE, Milwaukee, USA) scanner, which produces 35 planes per scan. Transaxial slice width is $4.5mm$.

4 Experiments

Brain PET studies offers an interesting target for applying image processing techniques. With specific tracer, FDOPA (Fluoro dopa) study has high contrast against background and the visible functional structures can be seen clearly. For example, the striatum consisting of caudatus and putamen is such target and it was studied. The total volume of striatum is about $20cm^3$ [6].

4.1 Test arrangement

Experiments of the described concept was carried out in the Turku PET-Centre, Finland. The program was applied to five FDOPA PET studies and one phantom study. The images, except phantom, were reconstructed with a new iterative median root prior (MRP) [1] method.

In this study, the MR images were applied for evaluating results. The MR images were resliced in the same space as the PET images. Because in practise reslicing reduces resolution, a higher resolution MR image is resliced instead of a PET image. With the traditional method, all ROIs are drawn manually on the MR image by using CTI Imagetool program. The ROI positions were evaluated by displaying ROIs on the corresponding PET planes. In VOI method, VOIs were determined from the functional PET images as described here. The positions of VOI projections were displayed on the corresponding MR images. ROIs and projections are saved and further analysis could be carried out. For example, the tissue radioactivity concentration can be calculated from the PET images by using determined VOIs and ROIs.

4.2 Results

The VOI program was used to determine the functional parameters from FDOPA PET images. Table 1 represents results of analysis and the target object volumes by using the traditional method and VOI method. The time used for extracting VOIs takes about 5-10 minutes per image with manual drawing (ROI), and about 2-3 minutes per image with program (VOI). The volume of phantom striatum is determined by using program and the manual value is the true filled value.

5 Discussion and conclusions

The purpose of this study was to develop and to examine the new semi-automatic concept for determining volume of interests from brain PET. The differences between the traditional method and the introduced method are (1) source of data, (2) three-dimensional determination of target and (3) automatic segmentation of functional structure.

The traditional method determines targets manually from anatomical MR images and result is checked from corresponding functional PET images, while the introduced method determines targets semi-automatically

Table 1: Experiments with median root prior (MRP) reconstructed images.
Ki is influx constant determined with graphical Patlak analysis.

patient	average Ki value for striatum, $*10^{-2}$ manual ROI method	semi-automatic VOI method	difference VOI-ROI	VOI/ROI volume, cm^3 manual ROI method	semi-automatic VOI method
1	1.04	1.32	+0.28	7.8	29.8
2	1.35	1.25	-0.10	9.3	25.1
3	1.12	1.10	-0.02	11.0	21.5
4	1.05	1.29	+0.24	9.0	14.5
5	0.91	1.04	+0.13	10.0	13.1
average	1.05	1.20	+0.15	9.4	20.8
	average activity, kBq/cm^3 manual	VOI	VOI-manual	volume, cm^3 true	VOI method
phantom	39.5	24.3	-15.2	24.3	23.9

from functional PET images and results can be checked from corresponding anatomical MR images. This causes differences in the volume because the functional part of target may not equal to the anatomical target. Activity may also spread to several anatomical structures.

In the traditional method, the user makes segmentation by manually drawing boundaries on the image slices. With the introduced method, the user selects threshold and the target to be segmented from one slice. The segmentation is done automatically in three dimensions to extract the whole target. Three-dimensional determination of target produces more details in the target surface and larger target volume than the traditional method based on two-dimensional subjective user determination.

With the test set of images, the volume obtained from VOI method is about three times the corresponding manually determined volume. The manual method boundaries were determined only from two "best" planes from the image, while the semi-automatic method finds a true three-dimensional objects from the image causing the difference in volume. Greater volume increases the accuracy of determination of activity concentration. Still, the obtained volume is likely to differ from the true volume.

As with the studies in literature, the benefits of semi-automatic method are the reduced processing time and the reproducibility of results. Our tests show about one third time reduction for object extraction, but it is likely to be much better when there are more planes than with the test set of images.

In this study, to use only simple segmentation method is motivated by the results reported from literature [4], where complicated segmentation methods do not necessarily produce better results with real clinical situation. Obviously, it is a limitation of the program. It can find the striatum, but cannot split it to caudatus and putamen. The splitting can be done by manually editing results. Automated separation may require a prior knowledge of the structure. With pre-cautions, applying advanced three-dimensional segmentation methods with a prior konwledge is certainly interesting topic for further investigation in brain PET.

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