Analysis of PET imaging for tumour delineation

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Abstract

The primary goal of this is research is to build a statistical framework for automated PET image analysis that is closer to human perception. Although manual interpretation of the PET image is more accurate and reproducible than thresholding-based semiautomatic segmentation methods, human contouring has large interobserver and intraobserver variations and moreover, it is extremely time-consuming. Further, it is harder for humans to analyze more than two dimensions at a time and it becomes even harder if multiple modalities are involved. Moreover, if the task is to analyze a series of images it quickly becomes an onerous job for a single human. The new statistical framework is designed to mimic the human perception for tumour delineation and marry it with all the advantages of an analytic method using modern day computing environment.

Advantages of analytical techniques

- High Contrast - dealing with numbers
- Analysing data in higher dimensions
- Including multiple modality
- Objective decision
- Can be scaled to analyse multiple images. power to analyze a single image faster.

Advantages of human expert

- Different scales of information
- Combining spatial information across different resolutions
- Zooming in on local information and adjusting the contrast between signal and noise/background
- Using prior information regarding location and shape of tumours.
- "Overlay" PET and CT to use complementary information.

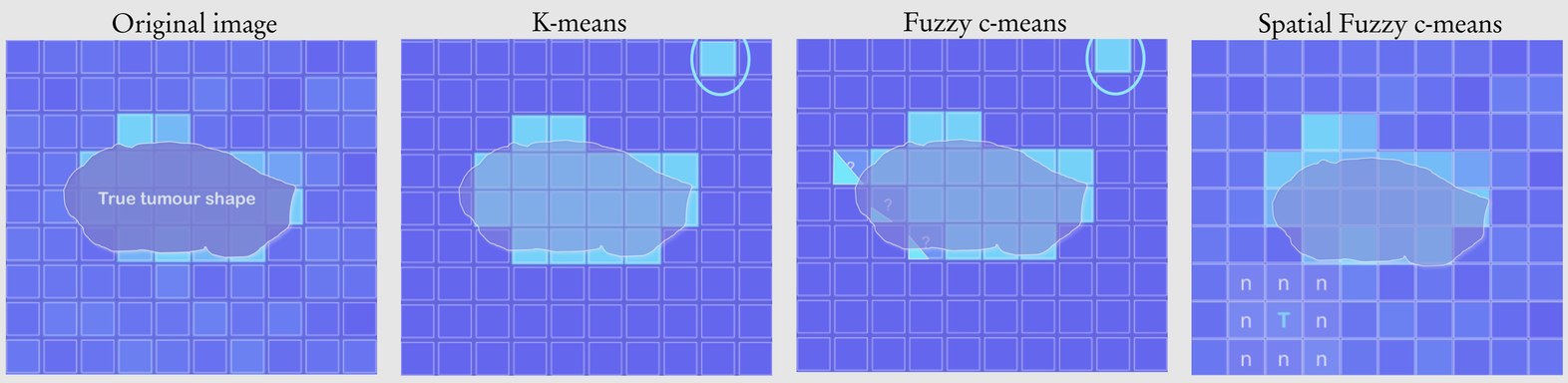
Clinical usages of PET images

- Tumour detection
- Diagnosis
- Staging
- Treatment

Commonly used analytical methods

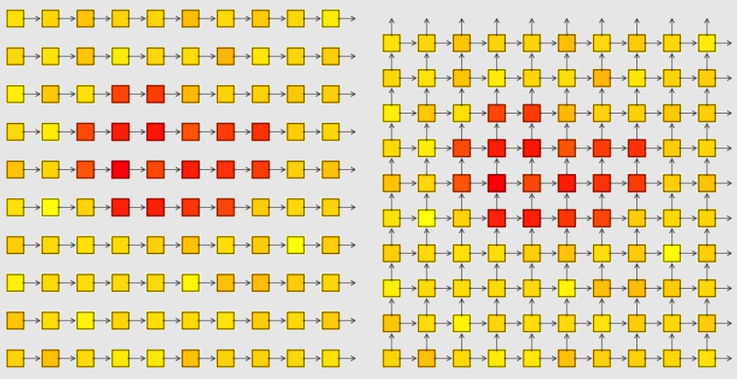
- Threshold based
- K-means clustering
- Fuzzy clustering
- Spatial Fuzzy clustering
- HMM based fuzzy clustering
- Fuzzy locally adaptive Bayesian (FLAB)

Full review available in [3]



Modal HMM

The standard approach for modal clustering [6, 2, 1], clusters i.i.d observations in any dimensions to the local high density region using a fast and parallelizable computing technique. In contrast to the i.i.d. assumption of modal clustering, to effectively cluster a 3D PET image we propose to develop a statistical framework of 3D Hidden Markov model (HMM) which will have the ability to honour the spatial coherence of tumour cells. [5, 4, 8, 7] show that this technique can achieve much improved computational efficiency even for standard clustering technique. Our framework will bring these two steps under one coherent algorithm whereby we first estimate a marginal Gaussian mixture model without spatial consideration and use modal clustering to group certain states together. In the follow up step we estimate an HMM using these states and later during tumour delineation, states claimed to be in the same cluster by modal clustering stay as the same cluster. One can also use CT images to complement or fine tune the tumour boundaries, once the two coordinate systems (PET and CT) are appropriately matched.

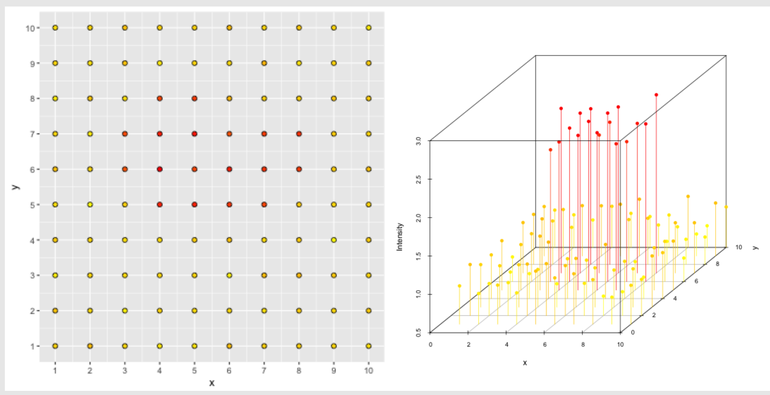


1-D HMM on a 2d grid

1-D HMM on a 2d grid

Tumour Depth

In the second approach, we don't work in the space of pixel values, but in the space of (x,y,z) coordinates. In this case, the intensity values at each coordinate is viewed as the graph of a density function. The pixel value corresponds to the weights assigned to the pixels and the density function is of the 3-D (x,y,z) coordinates. Modal clustering can be applied to find the segments. The advantage of this approach is that spatial coherence is naturally incorporated, and generalisation from 2 to 3 dimensions is very obvious. Further, this approach is extremely effective for tumour delineation as the tumour regions will have high density – but a large portion of the image is "background". Once the density is constructed one can use modes to find the regions with high density to delineate tumours. Additionally if a density function is used to approximate the image surface, besides finding modes, one can do a lot of other things to tailor to their own needs. Finally, incorporating CT is very natural as we will now have density information over 6 dimensions although partial information will be available for some pixels as CT and PET might not have been observed at the same coordinates.



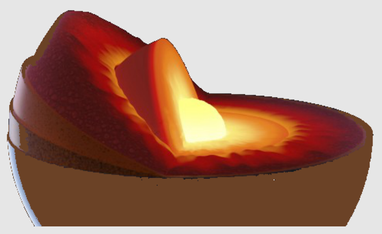
PET image as intensity values

Using the intensities to construct density shape

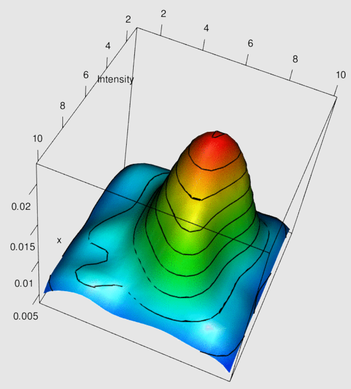
Tumour Depth for Radiotherapy

Advances in radiotherapy techniques including volumetric modulated arc therapy (VMAT) mean it is now possible to accurately deposit higher dose burdens to tumours beds whilst minimising the radiation dose to neighbouring healthy/radiosensitive tissues.

We assume that the intensity value of the PET image carries the information where more radiation is ideal. Our research will provide a Tumour Depth analysis which will enable one to treat the tumour as a non-homogeneous structure rather than a "homogeneous lump" and also ease the burden of exact boundary detection.



Representation of tumour as a non-homogeneous structure



"Wrapped" density shape obtained by smoothing intensities

Both of these methods will be fine-tuned and validated by using feedback from clinicians and radiologists at Gartnavel and will also be tested on carefully designed phantoms.

Comparison of these techniques (Modal HMM and Tumour Depth) against existing statistical and threshold based techniques will also be performed.

Algorithm Steps and Mathematical details (2D Slice)

Let x_{ij} be the image intensity at location i and j and let $y_{ij} \in 0, 1$ be the final segmentation of the image.

1. First cluster the scalar observations x_{ij} without considering their spatial location using modal clustering. Let c_{ij} be the cluster labels
2. Estimate an HMM using these states $S(ij)$ and later during tumour delineation, states claimed to be in the same cluster by modal clustering stay as the same state.
3. Since any state with an M-component Gaussian mixture can be split into M sub-states with single Gaussian distributions, we define the probability density function of feature vector x(i,j) given its corresponding hidden state $s(i,j) = m$, as

$$b_m(x(i,j)) = \frac{1}{(2\pi)^{\frac{d}{2}}|\sum_m|^{\frac{1}{2}}} e^{-\frac{1}{2}(x(i,j)-\mu_m)^T\sum_m^{-1}(x(i,j)-\mu_m)}$$

$$F^{(p)}_{m,n,k,l}(i,j) = P\Big(m = s(i-1,j), n = s(i-1,j-1), k = s(i,j-1), l = s(i,j)|O,\Theta^{(p)}\Big),$$

$$G^{(p)}_m(i,j) = P(s(i,j) = m|O,\Theta^{(p)}).$$

$$\pi^{(p+1)}_m = P(G^{(p)}_m(1,1)|O,\Theta^{(p)}), a^{(p+1)}_{m,n,k,l} = \frac{\sum_i^I\sum_j^J F^{(p)}_{m,n,k,l}(i,j)}{\sum_{l=1}^M\sum_i^I\sum_j^J F^{(p)}_{m,n,k,l}(i,j)}.$$

$$\mu^{(p+1)}_m = \frac{\sum_i^I\sum_j^J G^{(p)}_m(i,j)x(i,j)}{\sum_i^I\sum_j^J G^{(p)}_m(i,j)}.$$

$$\sum\nolimits^{(p+1)}_m = \frac{\sum_i^I\sum_j^J G^{(p)}_m(i,j)(x(i,j)-\mu^{(p+1)}_m)(x(i,j)-\mu^{(p+1)}_m)^T}{\sum_i^I\sum_j^J G^{(p)}_m(i,j)}.$$

Future work

- Extension to 3D PET images
- Including other modalities
- Validation
- Software

References

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