GDR CNRS-INSERM STIC Santé
Journée Thématique "Volumes cibles biologiques en Radiothérapie"
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Automatic PET-based target delineation: Tentative state of the art

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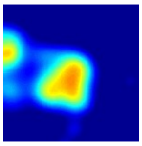
PET-based target delineation

- Positron emission tomography:
  - Tracer → Isotope → Positron → Photons → Detectors → Sinogram
  - PET image = measurement of a statistical nature
- Typical procedure:
  - PET acquisition
  - PET reconstruction
  - PET delineation
  - PET / CT registration
- Aim: ***accurate*** delineation
- Main pitfall: the ***low resolution*** of PET images →



- Delineation methodology:
  - Manual
    - PET alone *(blur → intra- & inter-observer variability?)*
    - PET/CT or PET/MR fusion *(bias introduced by anatomical modality?)*
  - Automatic
    - …

Automatic delineation methods

- State of the art to be looked for in
  - Literature
    - Radiation oncology (red/green journals)
    - Nuclear medicine
    - Medical physics
    - Engineering (IEEE journals, etc.)

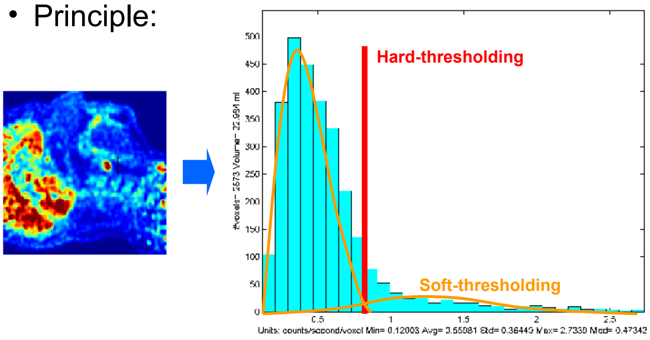
    → Many different approaches
  - Numerous conferences, congresses, symposia, …
- An exhaustive list of publications is almost impossible to establish
- There are also many
  - Methodological differences
    - Delineation algorithm
    - Validation data (simulated, phantom, or patient images)
  - Application contexts
    - Various PET systems, acquisition & reconstruction protocols
    - Several tumor sites and/or tracers
- There are only a few comparative studies with uniform experimental setup

Automatic delineation methods

- Histogram-based
  - Threshold-based
    - Hard thresholding
      - Absolute
      - Relative
    - Soft thresholding
      - Probabilistic modeling (finite mixture of probability distributions)
      - Fuzzy clustering
- Feature-based
  - (Fuzzy) Clustering
  - Clustering of Time Activity Curves
- Image-based
  - Probabilistic modeling (Hidden Markov random fields)
  - Gradient based
    - Active contours, snakes, …
    - Watersheds

Histogram-based approaches

- Principle:

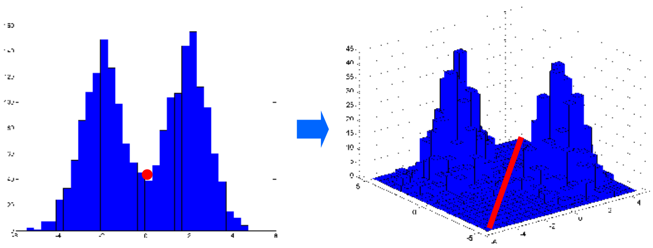


Directly fix a threshold value

Fit a finite mixture of probability density functions and find Bayesian threshold

Feature-based approaches

- Histogram thresholding is difficult due to mode overlap and badly balanced modes
- Idea: use pixel values and additional 'features'



Pixel uptake ≈ single feature **Two features → reduced mode overlap**

Feature-based approaches

- Features can be
  - Tranformed pixel values
    (e.g. filtered values, wavelet components, …)
    → can involve neighboring pixels
    → allows for taking into account the image structure
  - Time sequences in dynamic PET acquisitions
    (pixels have several values that are the features)

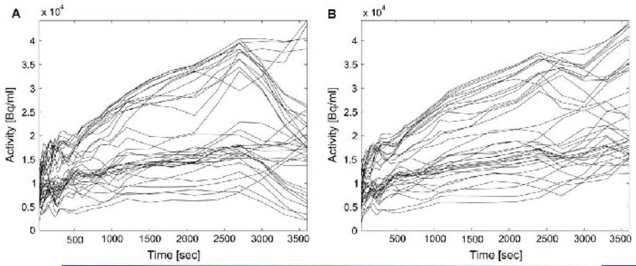
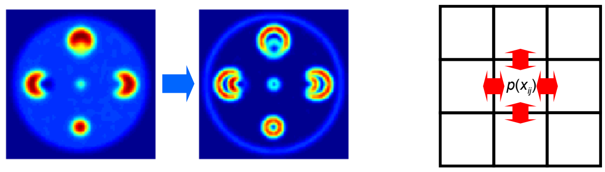
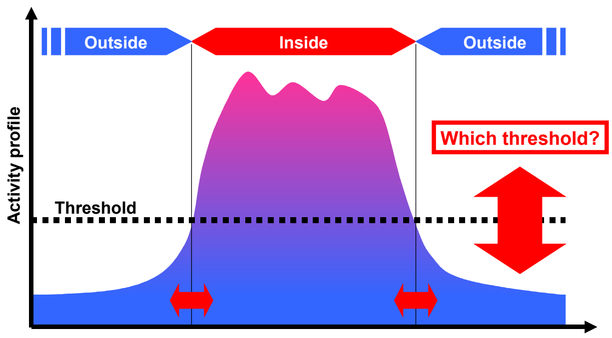


Image-based approaches

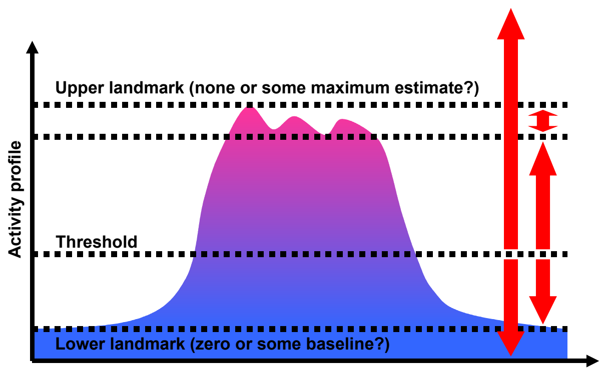
- Motivation
  - Histogram-based and feature-based methods do not (or not explicitly) take into account the image structure
  - Image-based approaches can model the idea that e.g. neighboring pixels are likely to belong to the same region
  - Allows a better control of the contour smoothness, volume connectedness, and similar properties
- Main idea: compare/combine adjacent pixels
- Examples:
  - Gradient & Laplacian operators (profile slope & curvature)
  - Hidden Markov Random Fields



Threshold-based segmentation



Threshold-based segmentation



Which threshold value?

- Examples found in the literature
  - Absolute: 2.5 SUV
  - Relative: ~40% of maximum
  - Adaptive: source-to-background ratio
  - Iterative: intersecting thr.-vol. & vol.-thr. curves
  - …
- Usual methodology:
  - Calibration with phantom images
  - Validation with
    - Phantom images (often; truth is known!)
    - Patient images (seldom; truth is difficult to measure…)
- Alternative approach: mathematical model…
  → take into account resolution blur

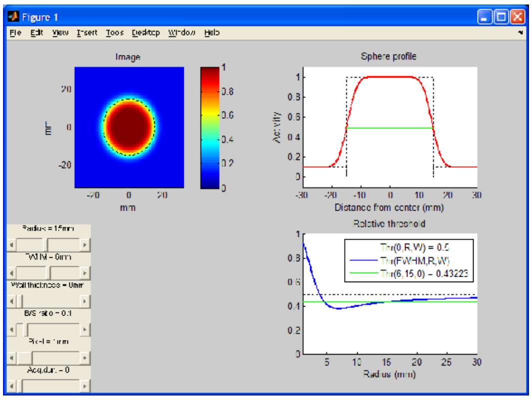
Mathematical model

- Work hypotheses (~ Jaszczak phantom)
  - Spherical objects
  - Uniform uptakes in target and background
  - Thin plexiglas wall
  - Resolution is constant in the field of view, with a PSF that is Gaussian and isotropic
- Analitically convolve a sharp image with the PSF…

Using polar coordinates in the xy plane leads to:

$$\begin{aligned}
f_{R\sigma}(u) &= \int_{-R}^{R} \frac{1}{\sigma\sqrt{2\pi}} \exp\left(-\frac{(z-u)^2}{2\sigma^2}\right) \int_{-\pi}^{\pi} \int_{0}^{R_z} \frac{1}{2\pi\sigma^2} \exp\left(-\frac{r^2}{2\sigma^2}\right) r\,dr\,d\theta\,dz \\
&= \int_{-R}^{R} \frac{1}{\sigma\sqrt{2\pi}} \exp\left(-\frac{(z-u)^2}{2\sigma^2}\right) \int_{-\pi}^{\pi} d\theta \int_{0}^{R_z} \frac{1}{2\pi\sigma^2} \exp\left(-\frac{r^2}{2\sigma^2}\right) r\,dr\,dz \\
&= \int_{-R}^{R} \frac{1}{\sigma\sqrt{2\pi}} \exp\left(-\frac{(z-u)^2}{2\sigma^2}\right) 2\pi \left[-\frac{1}{2\pi} \exp\left(-\frac{r^2}{2\sigma^2}\right)\right]_{0}^{R_z} dz \\
&= \int_{-R}^{R} \frac{1}{\sigma\sqrt{2\pi}} \exp\left(-\frac{(z-u)^2}{2\sigma^2}\right) \left(1-\exp\left(-\frac{R_z^2}{2\sigma^2}\right)\right) dz \\
&= \left[\frac{1}{2}\left(1+\operatorname{erf}\left(\frac{z-u}{\sigma\sqrt{2}}\right)\right)\right]_{-R}^{R} - \int_{-R}^{R} \frac{1}{\sigma\sqrt{2\pi}} \exp\left(-\frac{(z-u)^2+R_z^2}{2\sigma^2}\right) dz\,.
\end{aligned}$$

Mathematical model



Mathematical model

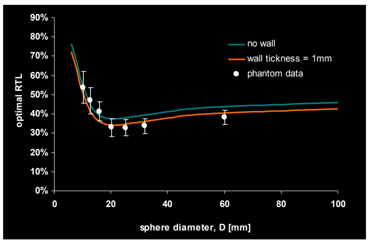
- Mathematical analysis says:
  If
  - Point-spread function is isotropic
  - Target is spherical
  - Target activity is uniform
  - Background activity is uniform

  Then
  - Target contours can be 'exactly' recovered
  - Threshold must be relative to
    - Background activity
    - Maximum target activity
  - Threshold depends on ratio (target_radius/FWHM) → **The problem turns out to be circular!**

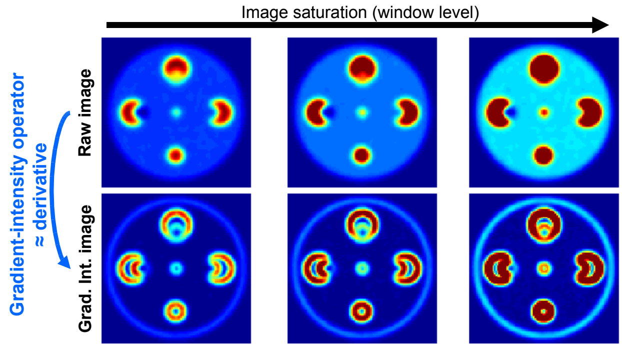
  Otherwise
  - Contours cannot be accurately recovered with a ***single*** threshold per target
- Conclusions are already bad in a ***simplistic*** case
- No need to come up with ***real*** cases…

Mathematical model

- Sphere wall thickness is not negligible
  → **Threshold calibration with phantoms leads to overestimating tumor volumes**
- Optimal threshold and radius depend on each other
  → **Circularity is broken only with an iterative approach (convergence for non-spherical objects?)**

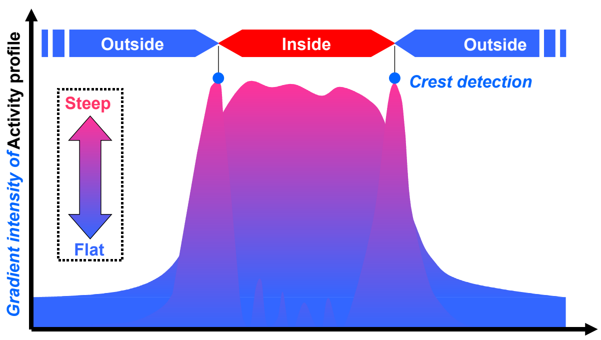


Interest of gradient information



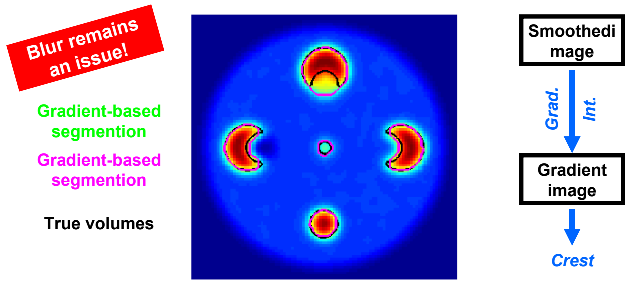
Boundaries do not move for gradient!

Gradient-based segmentation



Gradient-based segmentation

- Naive approach:
  - Smooth image to attenuate noise
  - Apply gradient intensity operator and determine crest



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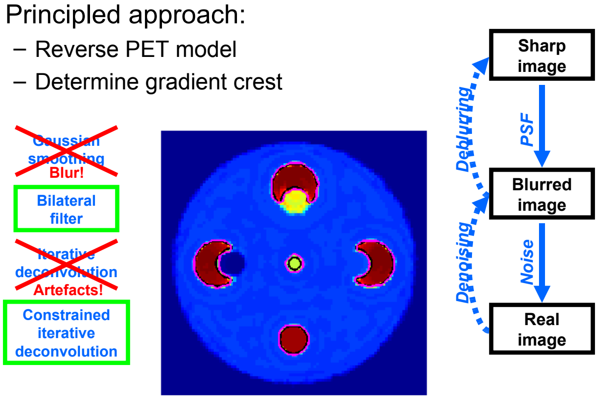
Gradient-based segmentation

- Principled approach:
  - Reverse PET model
  - Determine gradient crest

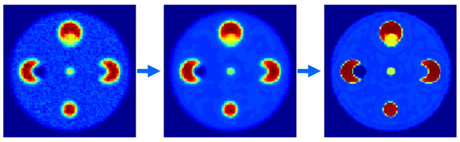


Gradient-based PET segmentation

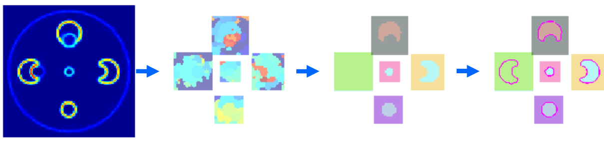
- Image processing
  - Denoising (edge-preserving filter)
    - Bilateral filter for Poisson noise
    - Denoise without smoothing edges
  - Deblurring (edge enhancement)
    - Iterative deconvolution to roll back PSF-induced blur
    - Min & Max local constraints prevents ringing artifacts
- Gradient-based segmentation
  - Gradient-intensity image (≈ derivative)
    - Plains & Plateaus → Mountain chains & Valleys
  - Crest detection (Watershed Transform)
    - Detect moutain crests → Compute watersheds
    - Practically: flooding simulation
  - Cluster analysis (hierarchical Ward's clustering)

Gradient-based PET segmentation

- Image processing



- Gradient-based segmentation



Methodological issues

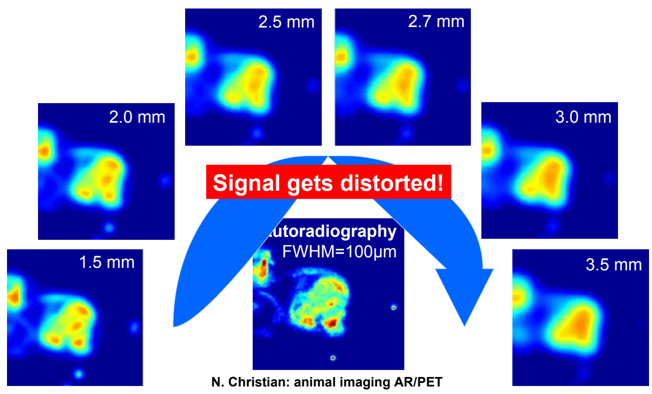
- Experimental conditions are too different
  - Acquisition hardware
  - Reconstruction software
  - Segmentation technique
  - Specific patient / disease sets
- Validation sets are
  - Too small and difficult to build **(ground truth is difficult to observe)**
  - Rarely exchanged
- There are too many empirical studies:
  - Pick a random segmentation method
  - Adjust its parameters with some data
  - **(evidence-based strategies are effective in medicine, not in engineering)**
- Key questions are often neglected
  - How can we model the shortcomings of PET images?
  - How can we compensate for them with delineation in mind?
  - What is the best attainable accuracy?

Methodological issues

- PET segmentation is complex because multidisciplinary
  (dialog between physicists/engineers/physicians is tedious)
  (learning curves are rather flat)
- There is a tendency toward YAPETISM
  (Yet Another PET Image Segmentation Method)
  - It is easier and fancier to design new methods
  - This is more cost-effective in terms of publications
  - Analogy with a regression problem:
    - Learn Y as a function of X with some regression model
    - If the model is complex enough,
      if the learning and validation sets are small and similar,
      then some parameter tuning suffices to obtain good results
    - But generalization to other data sets will be poor
- The quality of PET images is low
  - Automatic PET delineation is a difficult problem
  - Can we circumvent the problem with dose painting?
    → No! Resolution remains an issue…

Resolution blur: illustration

Resolution ≠ pixel size (mm) **Resolution = amount of blur → PSF FWHM (mm)**



N. Christian: animal imaging AR/PET

Conclusions

- Resolution is the main bottleneck of PET-based for target delineation
- Threshold-based segmentation
  - Relies on questionable assumptions
    - Uniform background and target
    - Spherical target
  - Is intrinsically inaccurate (except in unrealistic conditions)
- Other segmentation paradigms
  - Can handle more complex cases
  - But still critically depends on careful image reconstruction and processing
- Candidate take-home messages
  - Target delineation ≠ target detection ≠ quantification !
  - PET-based target delineation is a difficult problem with
    - No simple solution
    - Specific requirements w.r.t. acquisition & reconstruction
  - Develop your acquisition and reconstruction protocols hand-in-hand with the nuclear medicine department
  - Pick a segmentation method that accounts for the shortcomings of PET (resolution, noise) in a simple and principled way

Literature

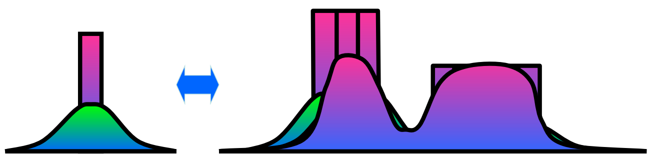
- Key paper
  - **Partial-Volume Effect in PET Tumor Imaging**
    M. Soret, S.L. Bacharach, and I. Buvat
    JNM 48 (6): 932. (2007)
- Comparison papers
  - **Comparison of Different Methods for Delineation of 18F-FDG PET–Positive Tissue for Target Volume Definition in Radiotherapy of Patients with Non–Small Cell Lung Cancer**
    U. Nestle, S. Kremp, A. Schaefer-Schuler, Ch. Sebastian-Welsch, D. Hellwig, Ch. Rübe, and C.-M. Kirsch
    JNM 46 (8): 1342. (2005)
  - **Comparison of five segmentation tools for 18Ffluoro-deoxy-glucose-positron emission tomography-based target volume definition in head and neck cancer**
    D.A. Schinagl, W.V. Vogel, A.L. Hoffmann, J.A. van Dalen, W.J. Oyen, J.H. Kaanders
    Int J Radiat Oncol Biol Phys 69: 1282. (2007)
  - **Assessment of various strategies for 18F-FET PET-guided delineation of target volumes in high-grade glioma patients**
    H. Vees, S. Senthamizhchelvan, R. Miralbell, D.C. Weber, O. Ratib, and H. Zaidi
    Eur J Nucl Med Mol Imaging 36: 182. (2009)
- Iterative thresholding
  - **Iterative threshold segmentation for PET target volume delineation**
    L. Drever, W. Roa, A. McEwan, and D. Robinson
    Med Phys 34: 1253. (2007)
  - **Development of a generic thresholding algorithm for the delineation of 18FDG-PET-positive tissue: application to the comparison of three thresholding models**
    S. Vauclin, K. Doyeux, S. Hapdey, A. Edet-Sanson, P. Vera, and I. Gardin
    Phys Med Biol 54 6901. (2009)
  - **Segmentation of PET volumes by iterative image thresholding**
    W. Jentzen, L. Freudenberg, E.G. Eising, M. Heinze, W. Brandau, and A. Bockisch
    JNM 48: 108. (2007)
  - **A novel iterative method for lesion delineation and volumetric quantification with FDG PET**
    J.A. van Dalen, A.L. Hoffmann, V. Dicken, W.V. Vogel, B. Wiering, T.J. Ruers, N. Karssemeijer, and W.J.G. Oyen
    Nucl Med Comm 28: 485. (2007)
- Gradient-based segmentation
  - **A gradient-based method for segmenting FDG-PET images: methodology and validation**
    X. Geets, J.A. Lee, A. Bol, M. Lonneux, and V. Grégoire
    Eur J Nucl Med Mol Imaging 34: 1427. (2007)
- …

Thank you for your attention!

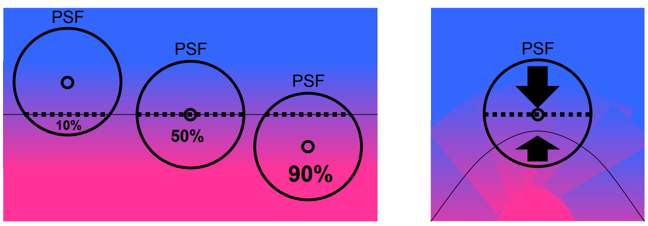
If you have any question…

Resolution: convolution

- Abstract mathematical operation (close to 'times')
- How it can model resolution blur:
  - (blurred image) = (sharp image) * PSF
  - Convolution:
    - Decompose the neat image into a sum of point sources
    - Spread each source (replace each source with the scaled PSF)
    - Sum everything back to obtain the blurred image
  - Dual interpretation: weighted average of neighbors



Resolution: convolution



Resolution blur *distorts* the image:
***curved* edges and region boundaries look displaced!**
Segmentation will be problematic…