Medical image registration

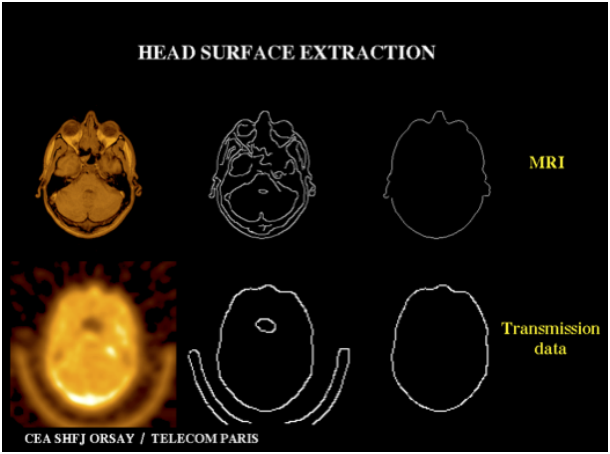
Isabelle Bloch

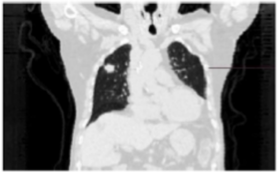
LIP6, Sorbonne Université

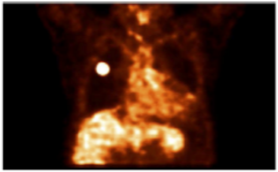
isabelle.bloch@sorbonne-universite.fr

Introduction

- Usefulness of registration
- Multi-modal imaging
- Complementary information
- Preprocessing for fusion
- More information and better decisions


HEAD SURFACE EXTRACTION
MRI
Transmission
data
CEA SHFJ ORSAY / TELECOM PARIS





Definition

Finding the best spatial correspondence

General formulation:

$$\min_{t \in \mathcal{T}} f(I_1, t(I_2))$$

- I_1 andt I_2: images to register (or features extracted from the images)
- t: transformation
- $\mathcal{T}$: set of possible / admissible transformations
- f: distance (or similarity $\Rightarrow \max f$)

Main components of a registration system

- nature of the transformation (t and its domain $\mathcal{T}$)
- features (on which t and f are applied)
- distance or similarity criterion f
- optimization method

non mutually independent
depend on the type of images, modalities,
and on the registration problem to solve

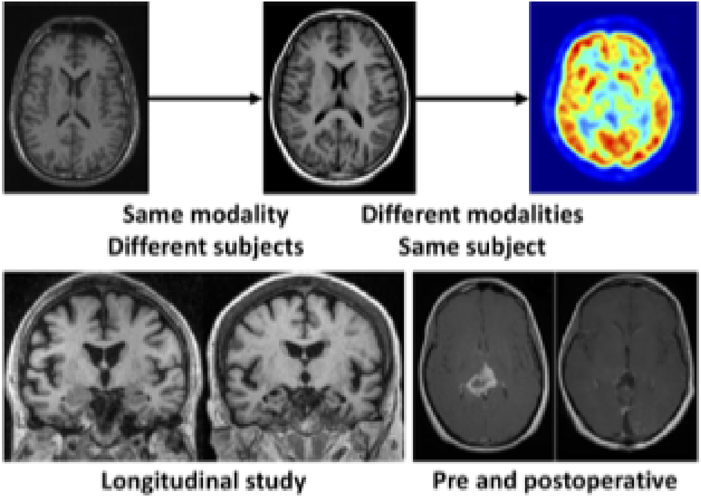
Difficulties due to

- complexity of problems
- discrete nature of images
- evaluation of registration results

Types of problems

- 2D/2D, 2D/3D, 3D/3D
- mono-modal images
- multi-modal images
- image / model (e.g. anatomical atlas)
- inter-patient registration

Example


Same modality
Different subjects
Different modalities
Same subject
Longitudinal study
Pre and postoperative

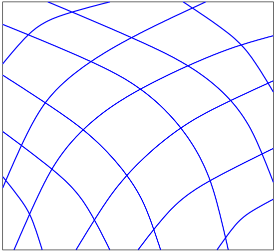
Transformations

- Rigid: only translation and rotation $X' = RX + T$
- Affine: parallel lines are transformed into parallel lines $X' = SRX + T$
- Projective
- Non linear
  - polynomial
  - composition of basis functions (e.g. splines)
  - free-form deformations
  - elastic deformations

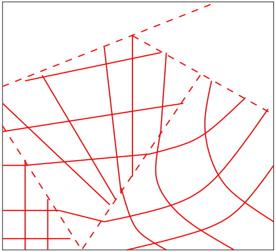
$$\mu \nabla^2 u(x, y, z) + (\lambda + \mu) \nabla (\nabla \dot{u}(x, y, z)) + f(x, y, z) = 0$$

    $u(x, y, z)$: deformation field, f: external forces, λ and μ: elasticity constants
  - fluid transformations (u replaced by velocity field)
  - diffeomorphisms

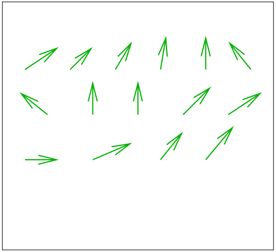
Gobal / local model



modèle global



modèle par morceaux
(régional)



modèle local

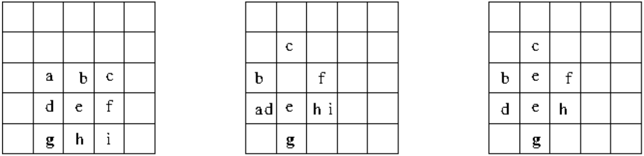
$$(x', y') = t(x, y)$$

Problems:

- (x, y) = integer coordinates $\Rightarrow (x', y')$?
- Calculation?
- Properties?

Example: rotation by $\pi/4$

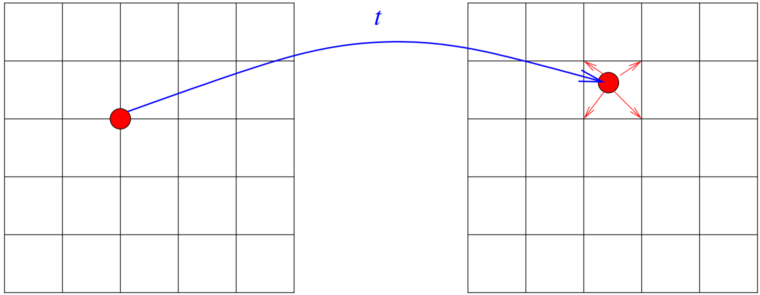
$$x' = (x - y)\frac{\sqrt{2}}{2} \quad y' = (x + y)\frac{\sqrt{2}}{2}$$



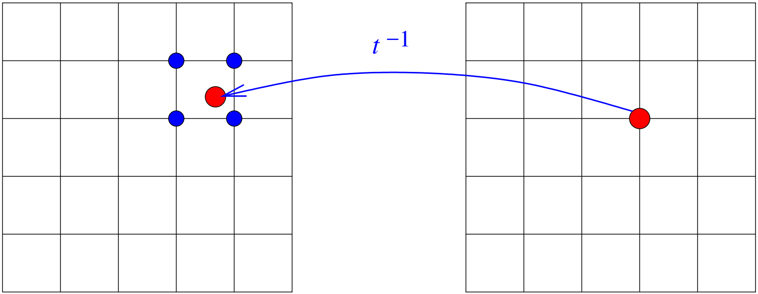
Direct transformation

Inverse transformation (closest point interpolation)

Direct transform:

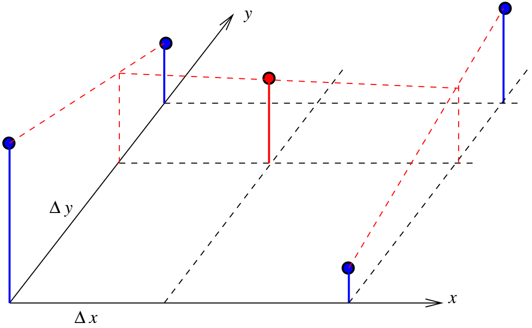


Inverse transform (better when t^{-1} can be computed:



Interpolation

- Closest neighbor
- Linear



$$f(x,y)[(1-\Delta x)(1-\Delta y)] + f(x+1,y)[\Delta x(1-\Delta y)] +$$
$$f(x,y+1)[(1-\Delta x)\Delta y] + f(x+1,y+1)[\Delta x \Delta y]$$

- Higher order

Example

10 rotations by 36 degrees of the original image, with different interpolations:

Original

Closest neighbor

Linear

Degree 4 Bspline

Source: http://bigwww.epfl.ch/demo/jaffine/index.html (Michael Unser)

Features

- extrinsic:
  - stereotaxic frame
  - markers
  - calibration of acquisition systems
- intrinsic: related to image content
  - extracted from images:
    - anatomical key points
    - anatomical structures (organs)
    - geometric or differential features (crest lines...)
  - pixel of voxel intensity

Choice: modalities, influence on the distance or similarity criterion

Similarity and distance (or dissimilarity) criteria

Many!

Distance between corresponding points

- Hypotheses:
  - same number of points n
  - known correspondence between x_i and y_i
  - any dimension
  - no outliers
- Criterion:

$$E = \sum_{i=1}^{n} \|x_i - (R(y_i) + T)\|^2$$

- Optimal translation: matching the centers of gravities
- Optimal rotation: closed formula in 2D, quaternion method in 3D, or using SVD.
- Outliers: Replace mean square errror by a robust estimator.

Quaternions

- Definition

$$q = (q_1, q_2, q_3, q_4)^t = (s, v)$$

$s =$ real part
$v =$ imaginary part

- Product:

$$q \times q' = (ss' - v \cdot v', sv' + s'v + v \wedge v')$$

- Conjuguate: $\bar{q} = (s, -v)$
- Norm:

$$|q|^2 = \bar{q} \times q = q \times \bar{q} = (s^2 + \|v\|^2, 0) = (\|q\|^2, 0)$$

- $\mathcal{Q}_1 =$ set of quaternions of norm 1

Representing rotations by quaternions

- $\mathcal{R}^3$ = set of 3D rotations
- Rotation of axis $\vec{u}$ and angle θ: equivalent to (s, v) and $(-s, -v)$ with:

$$s = \cos\frac{\theta}{2}$$

$$v = \sin\frac{\theta}{2}\vec{u}$$

- Equivalence relation: $\mathcal{R}(q, q') \Leftrightarrow q = -q'$

$$\boxed{\mathcal{R}^3 \text{ isomorphic to } \mathcal{Q}_1/\mathcal{R}}$$

$$Rx = q \times x \times \bar{q}$$

Application to rigid registration

Minimization of $E = \sum_{i=1}^{n} \|x_i - R(y_i)\|^2$
(after applying the best translation)

$$
\begin{aligned}
E &= \sum_{i=1}^{n} |x_i - q \times y_i \times \bar{q}|^2 \\
&= \sum_{i=1}^{n} |x_i - q \times y_i \times \bar{q}|^2 |q|^2 \\
&= \sum_{i=1}^{n} |x_i \times q - q \times y_i \times \bar{q} \times q|^2 \\
&= \sum_{i=1}^{n} |x_i \times q - q \times y_i|^2 = \sum_{i=1}^{n} q^t A_i^t A_i q
\end{aligned}
$$

Optimal rotation by computing the eigenvalues of

$$A = \sum_{i=1}^{n} A_i^t A_i.$$

Solution = quaternion which is the eigenvector of norm 1 associated with the smallest eigenvalue of A

Unknown correspondence

- Reduce complexity:
  - progressive registration starting with the most relevant features
  - constraints (geometry, topology...)
- graph matching
- distance between surfaces

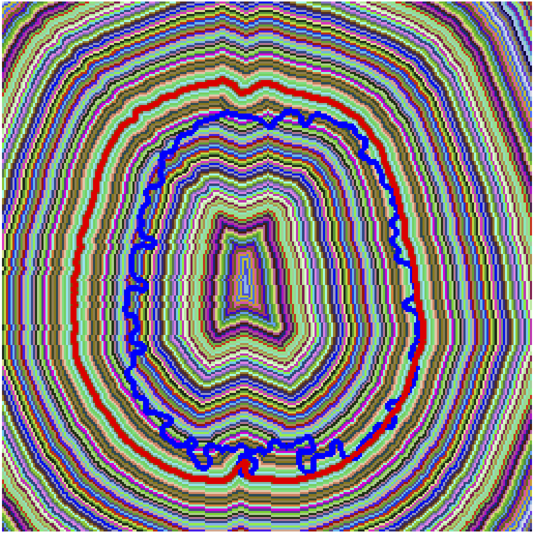
$$d(x, Ref) = \min_{y \in Ref} d(x, y)$$

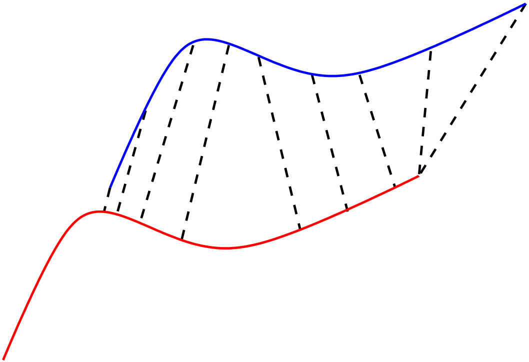
(fast computation, only once)

$$d(S, Ref) = g(d(x, Ref), x \in S)$$

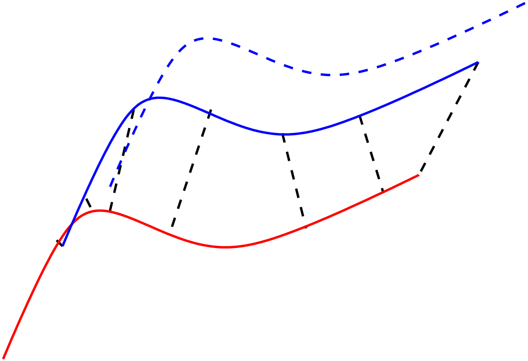
$g = \min, \max$, average...

Distance map





ICP (Iterative Closest Point)



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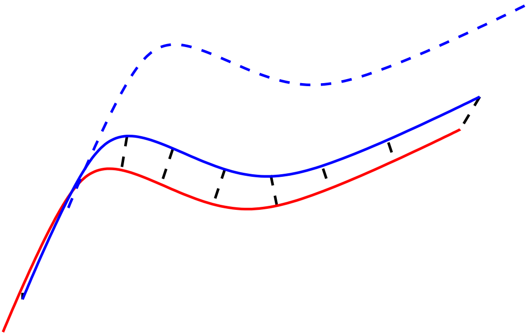


Intensity based registration: mono-modal case

- Quadratic:

$$E(\Theta) = \sum_x [I_{ref}(x) - I_{rec}(T_\Theta(x))]^2$$

- Quadratic with normalization:

$$E(\Theta) = \sum_x [\frac{\overline{I}_{rec}}{\overline{I}_{ref}} I_{ref}(x) - I_{rec}(T_\Theta(x))]^2$$

- Correlation:

$$R(\Theta) = \frac{\sum_x [I_{ref}(x) - \overline{I}_{ref}][I_{rec}(T_\Theta(x)) - \overline{I}_{rec}]}{\sqrt{\sum_x [I_{ref}(x) - \overline{I}_{ref}]^2 \sum_x [I_{rec}(T_\Theta(x)) - \overline{I}_{rec}]^2}}$$

(max for the best transformation)

- Robust similarity: $\rho =$ M-estimateur

$$E(\Theta) = \sum_x \rho[I_{ref}(x) - I_{rec}(T_\Theta(x))]$$

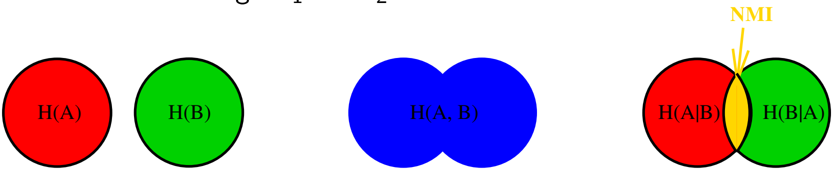
Examples of robust estimators

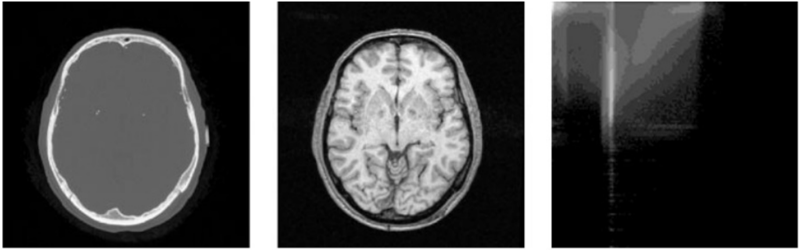
- quadratic
- truncated quadratic
- attenuated quadratic (Geman - McLure)
- quadratic for small errors, then linear (Huber)

Use of the joint histogram: maximization of mutual information

$$E(\Theta) = -\sum_g \sum_k p(g,k) \log \frac{p(g,k)}{p(g)p(k)}$$

g, k: intensities in images I_1 and I_2





(a) (b) (c)

Fig. 1. Example of a feature space for (a) a CT image and (b) an MR image. (c) Along the axes of the feature space, the gray values of the two images are plotted: from left to right for CT and from top to bottom for MR. The feature space is constructed by counting the number of times a combination of gray values occurs. For each pair of corresponding points $(\mathbf{x}, \mathbf{y})$, with $\mathbf{x}$ a point in the CT image and $\mathbf{y}$ a point in the MR image, the entry $(I_{\mathrm{CT}}(\mathbf{x}), I_{\mathrm{MR}}(\mathbf{y}))$ in the feature space on the right is increased. A distinguishable cluster in the feature space is the stretched vertical cluster, which is the rather homogeneous area of brain in the CT image corresponding to a range of gray values for the MR image.

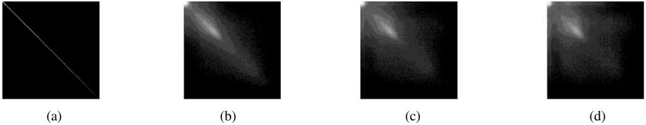


Fig. 2. Joint gray value histograms of an MR image with itself. (a) Histogram shows the situation when the images are registered. Because the images are identical, all gray value correspondences lie on the diagonal. (b), (c), and (d) show the resulting histograms when one MR image is rotated with respect to the other by angles of 2°, 5°, and 10°, respectively. The corresponding joint entropy values are (a) 3.82; (b) 6.79; (c) 6.98; and (d) 7.15..

Figures from [Pluim et al. 2003]

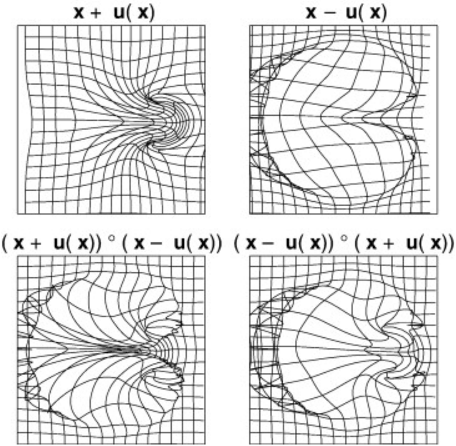
Back to transformations: non-linear registration

1. Small displacement:

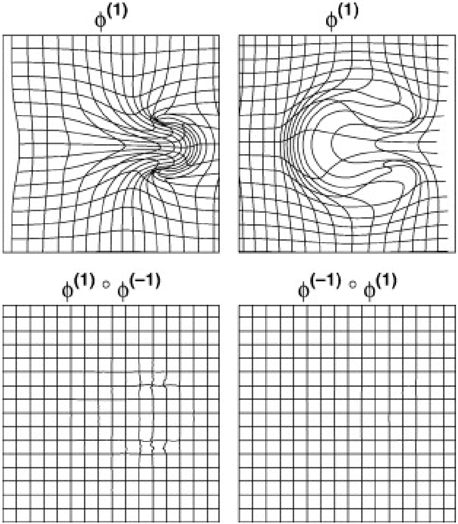
$$T(x) = x + u(x)$$

   where $u(x)$ is computed from neighbor landmarks. Does not work for large displacements!

2. Large displacement: diffeomorphism (differentiable, bijective, differentiable inverse). Example: integrating instantaneous velocity at each point over time.



First row: forward and inverse transformation. The first one is a one-to-one mapping whereas the second one presents intersections. Second row: composition of transformations. They should be the identity. (Source: Younes, 2010).



First row: forward and inverse diffeomorphic transformations (both are one-to-one). Second row: composition of forward and inverse transformations. The result is the identity (no deformation). (Source: Younes, 2010).

Optimization

- Typical algorithms: gradient, conjugated gradient, Powell, simplex, Levenberg-Marquardt, Newton-Raphson, geometric hashing...
- Local minima $\Rightarrow$ importance of initialization
- Stochastic optimization, genetic algorithms, simulated annealing...
- Multi-scale
- Specific methods in some cases (e.g. ICP)

Interactivity?

- Automatic: not always desirable
- Interactive: difficult in 3D, lacks reproducibility
- Semi-automatic: defining the right level of interaction (initialization, control, corrections...)

Validation and evaluation

$\boxed{\text{Ground truth?}}$

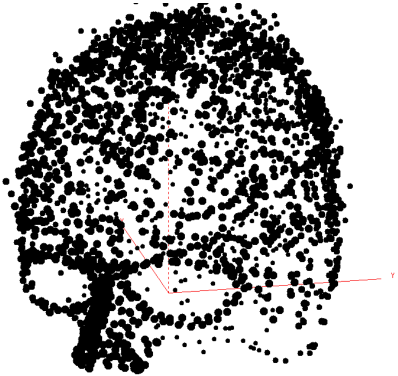
Criteria:

- intrinsic precision of the algorithm
- precision, robustness
- reliability
- resources required
- algorithmic complexity
- practical use

Different levels of test:

- simulations
- phantoms
- real data

MRI + headshape in EEG/MEG (Jérémie Pescatore)



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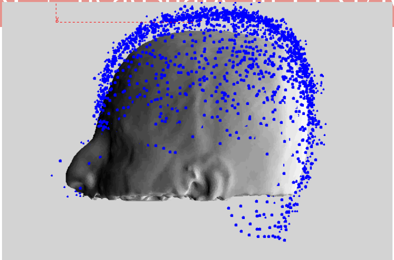
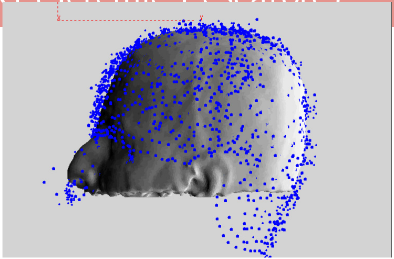
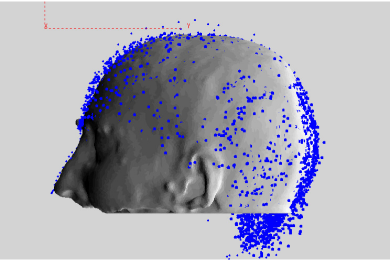
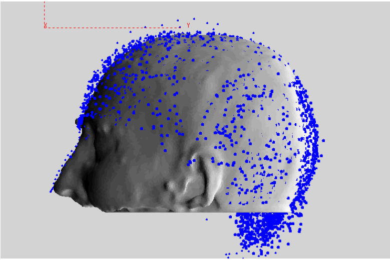




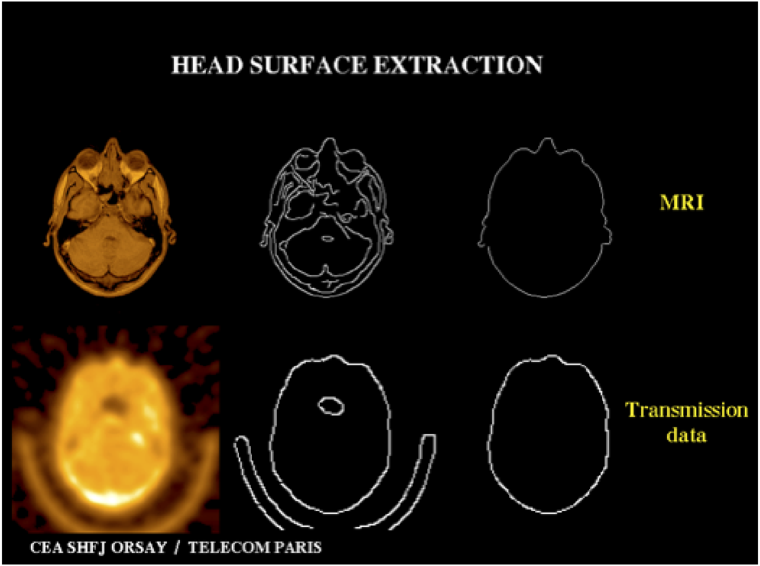
fonction de proximité=2.1 mm





fonction de proximité=1.80 mm

Rigid registration of brain images (Jean-François Mangin)



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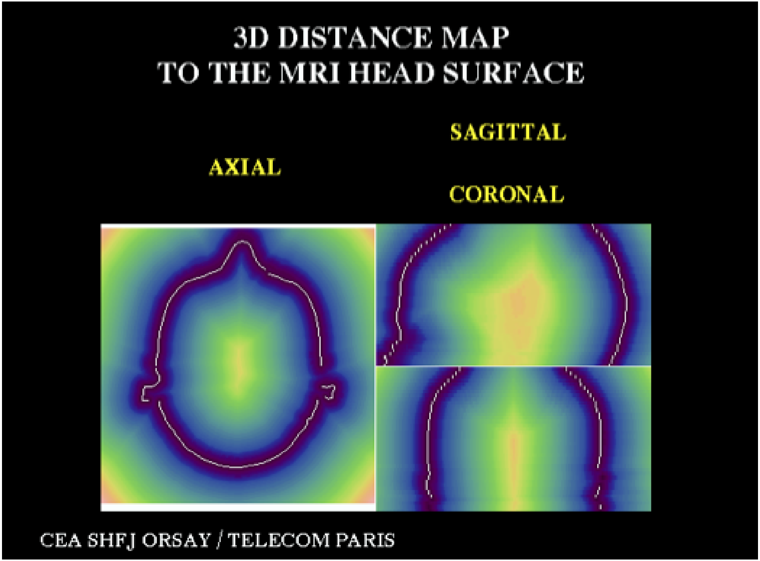

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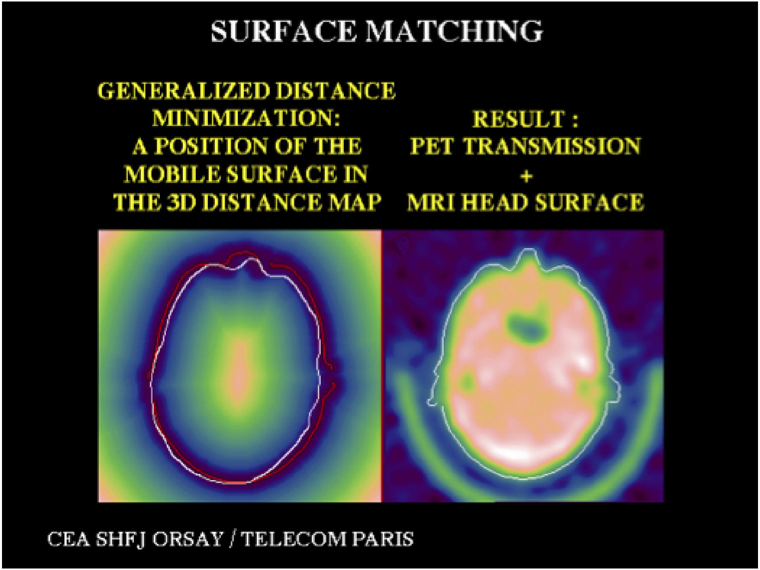

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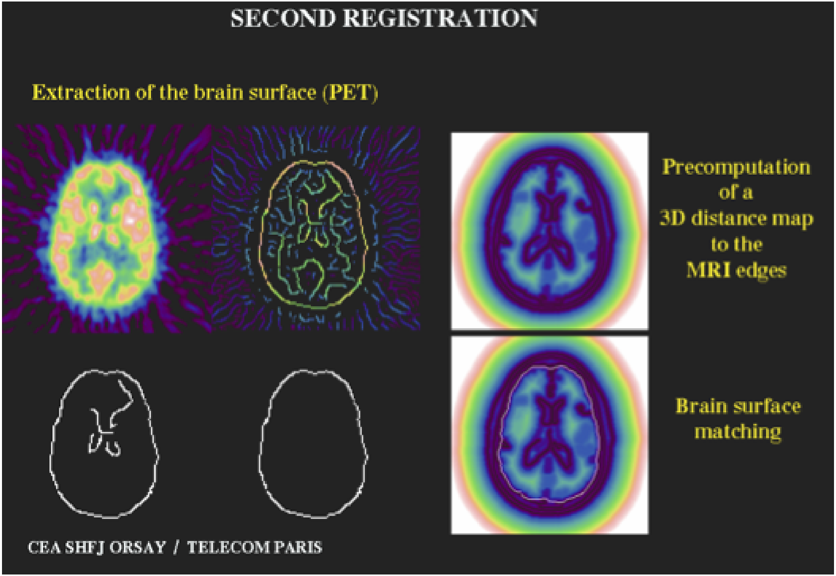

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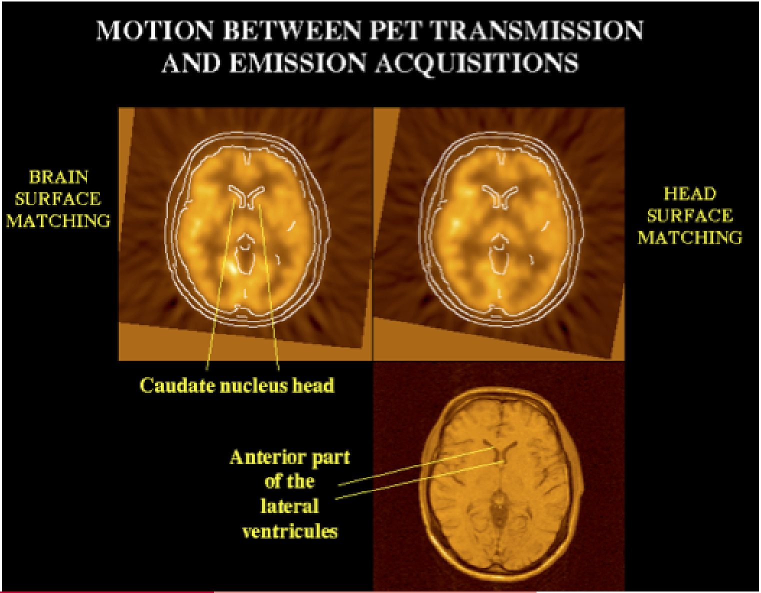

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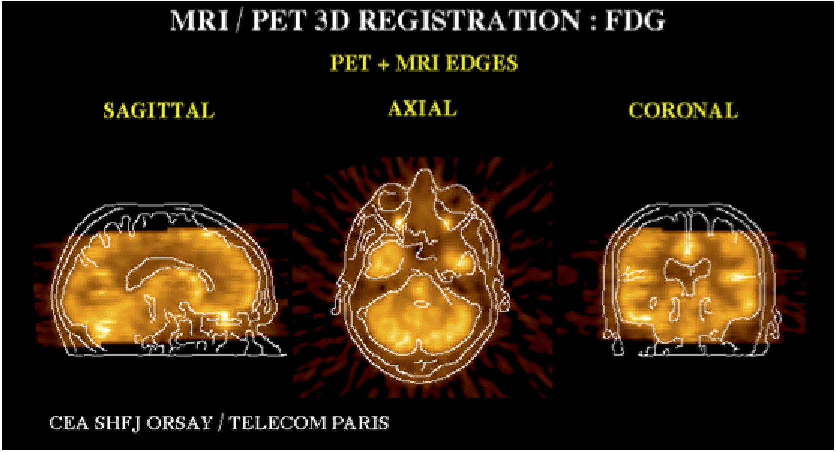
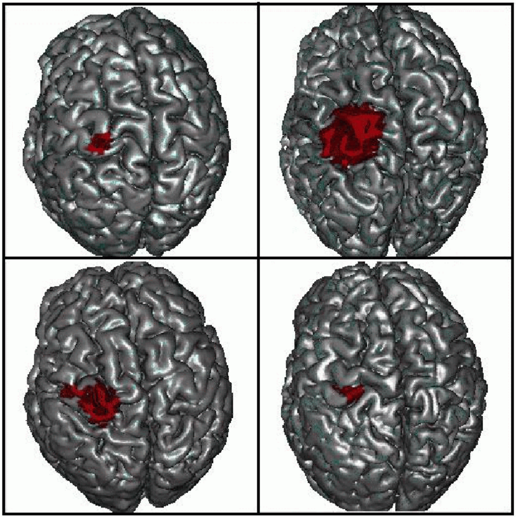
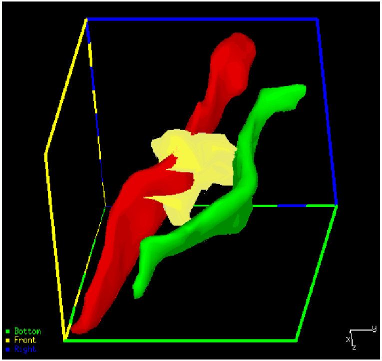


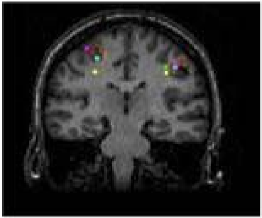
Rigid registration of brain images (Jean-François Mangin)

Anatomo-functional registration

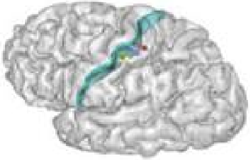


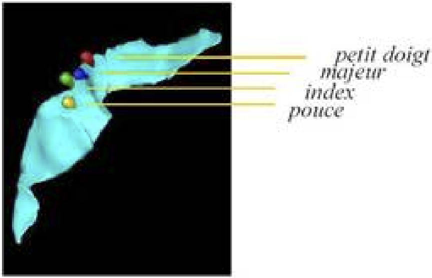


SOMESTHESIE : Somatotopie des doigts



Distance entre doigt ~ 0.9 cm
Distance I - V ~ 1.5 cm

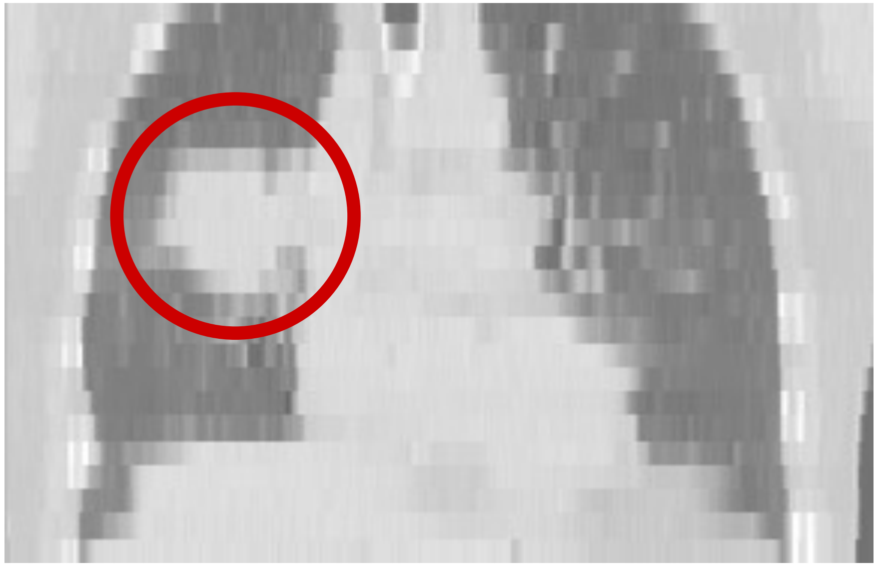


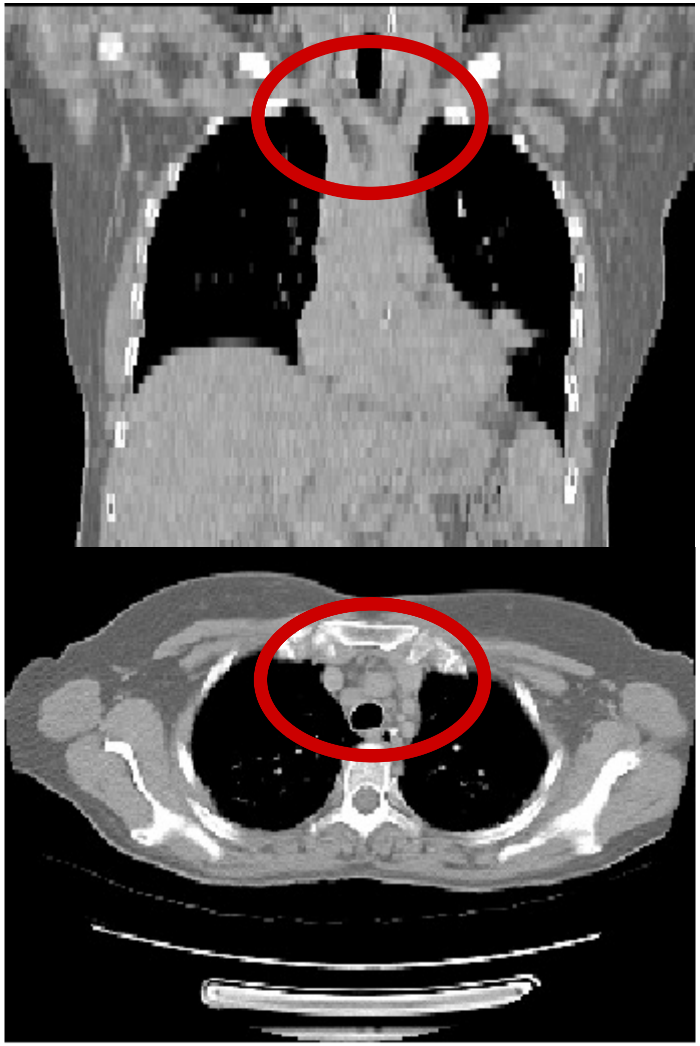


Non linear registration: chest images (Oscar Camara)

Introduction: CT images

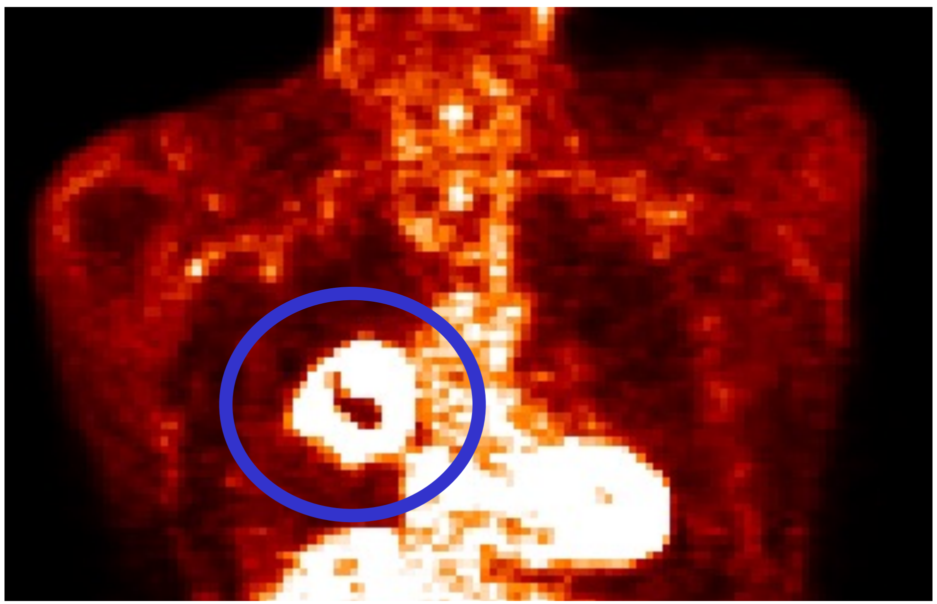
- Anatomical information
- Accurate localization and morphology of organs
- No lesion malignancy information
- Sometimes tumours not distinguishable

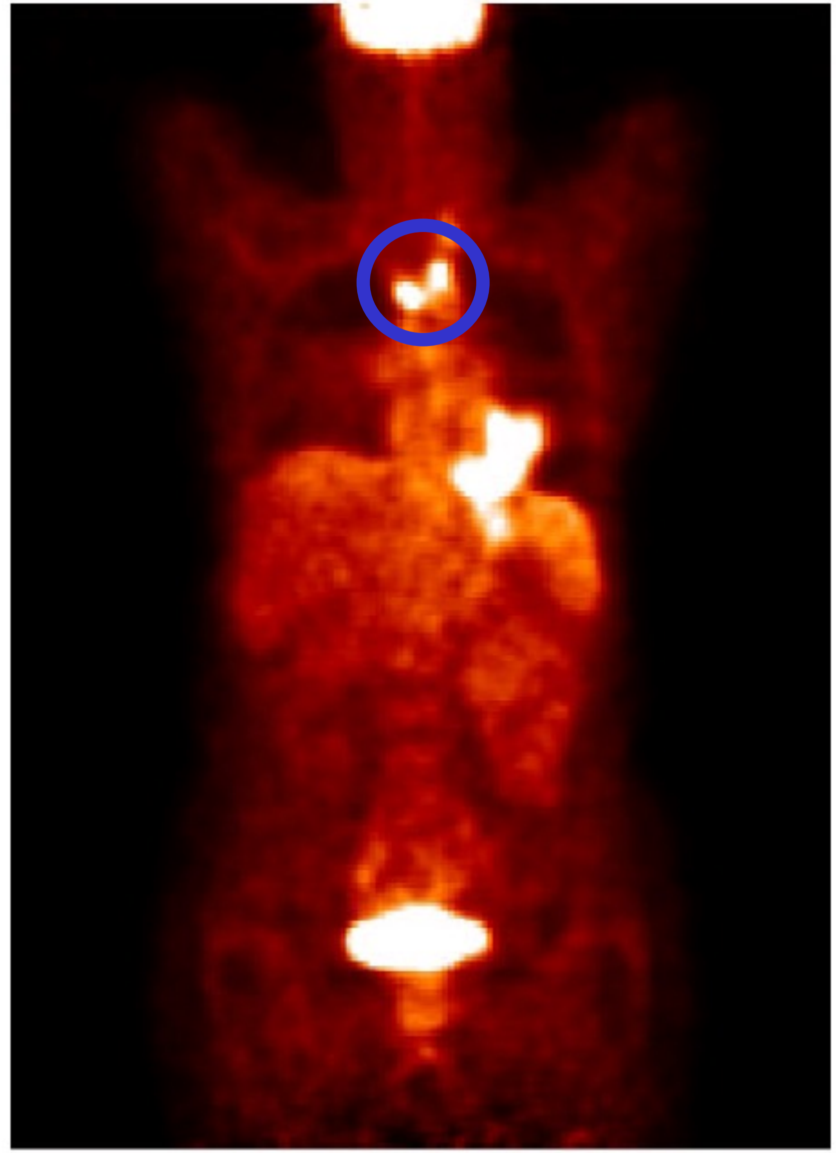




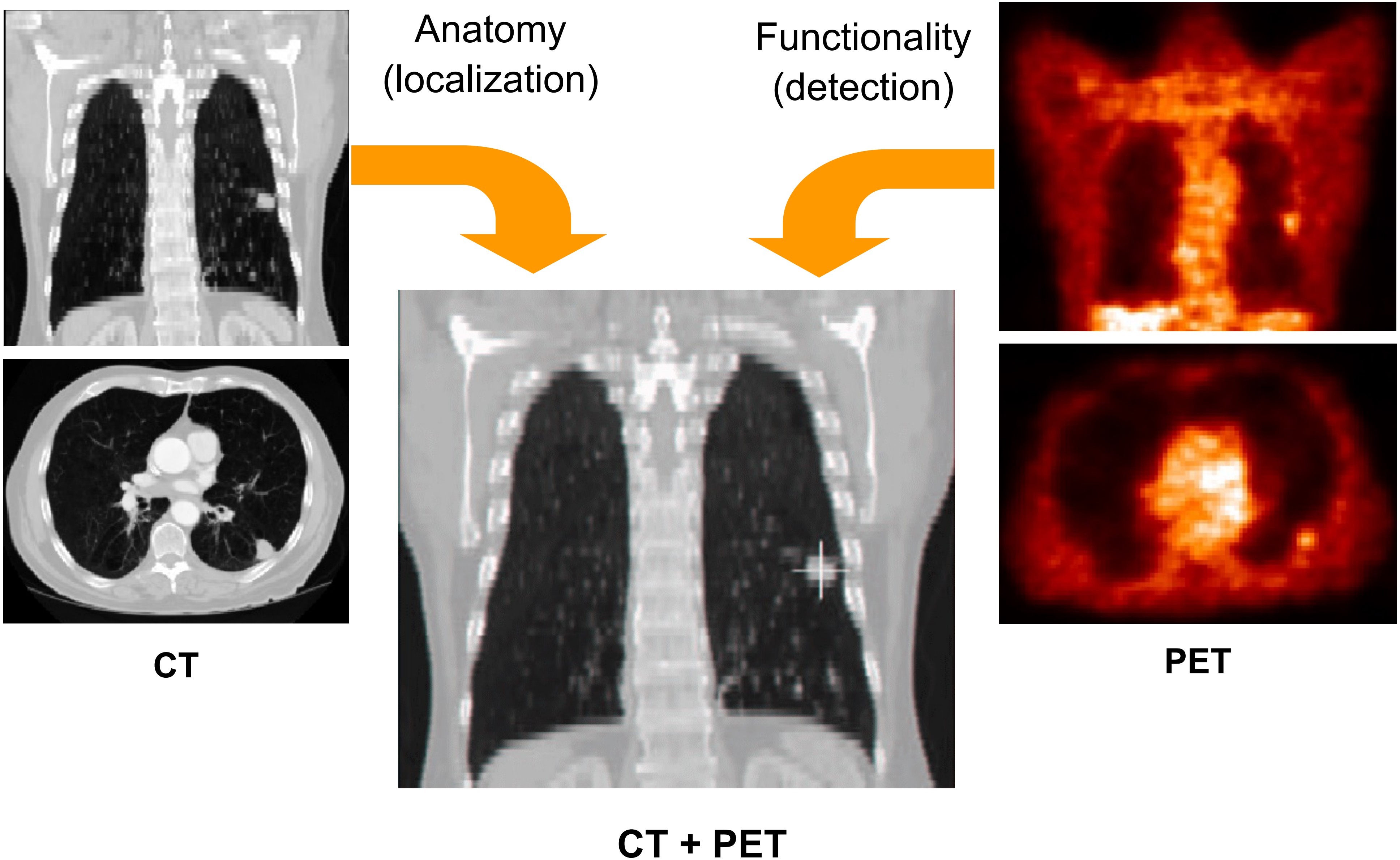
Introduction: PET images

- Metabolic information, staging
- High sensitivity and specificity
- Poor image quality
- Little anatomical information



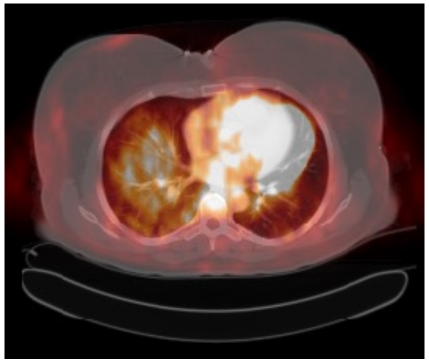


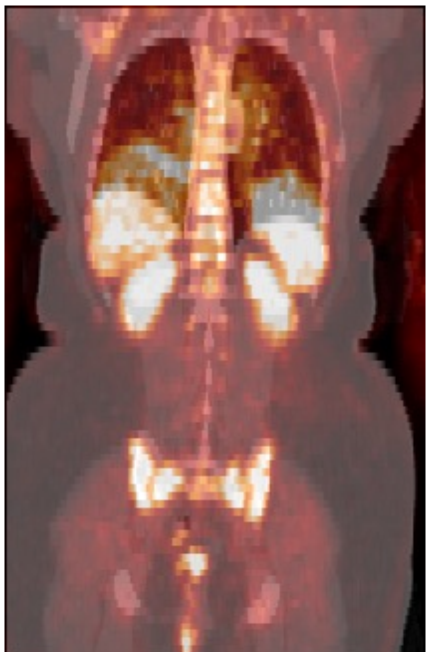
Introduction: PET-CT application



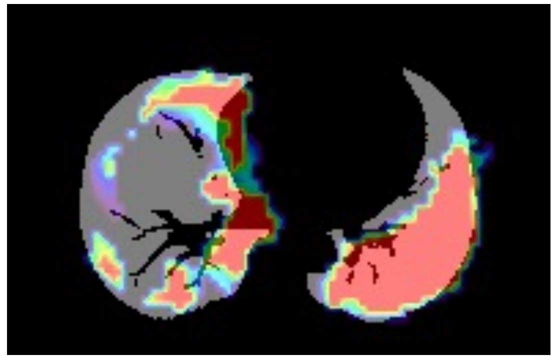
Registration context: linear registration

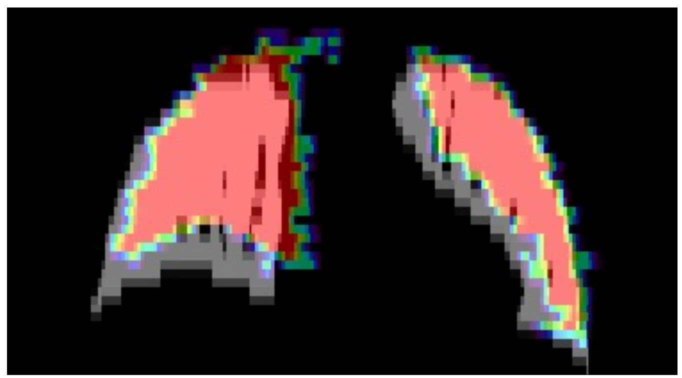
Grey level





Segmented lungs, 2D





- *CT lungs*
- *PET lungs*

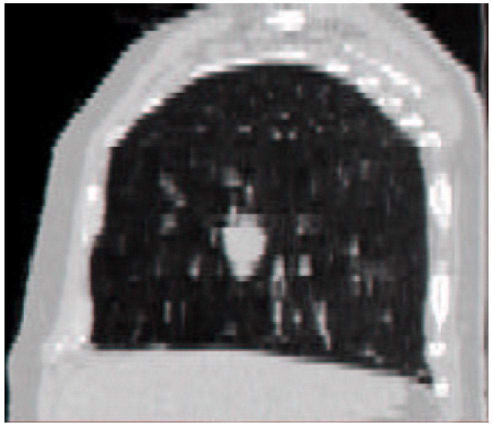
Segmented lungs, 3D

- *CT lungs*
- *PET lungs*

Registration context: structure-based methods

No information far from the landmarks

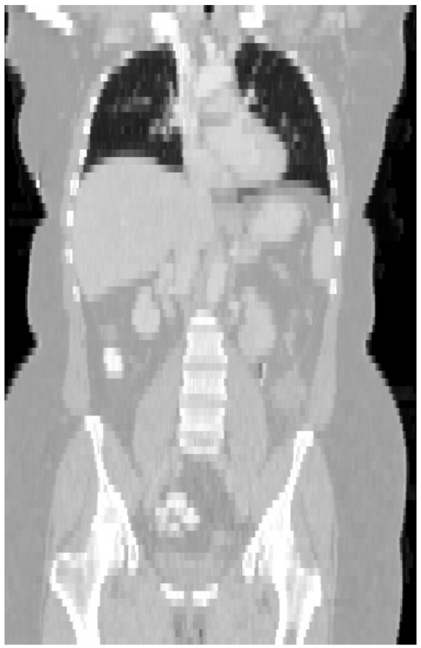
Loss of information “within” the structure



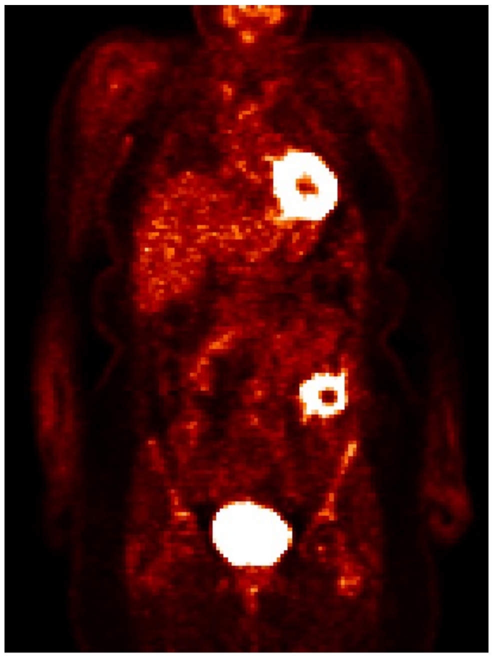
Registration context: Free-Form Deformations

- FFD with a previous affine registration phase

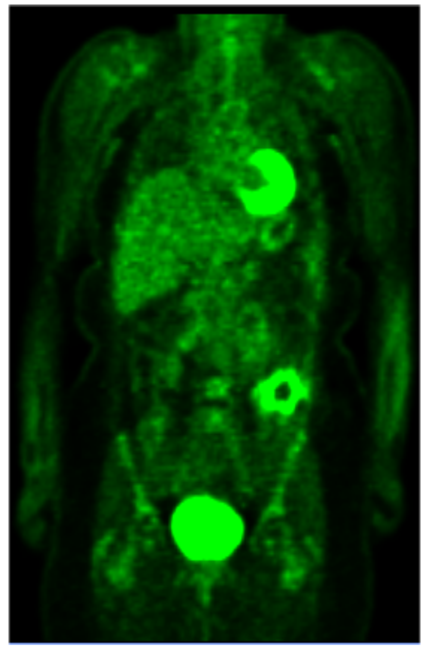
CT



PET



PET linear



PET non-linear FFD

Proposed methodology

Structure-based

- accuracy limited by segmentation
- no information far from segmented structures

Grey level-based methods

– difficulty of working with PET images

– computational cost

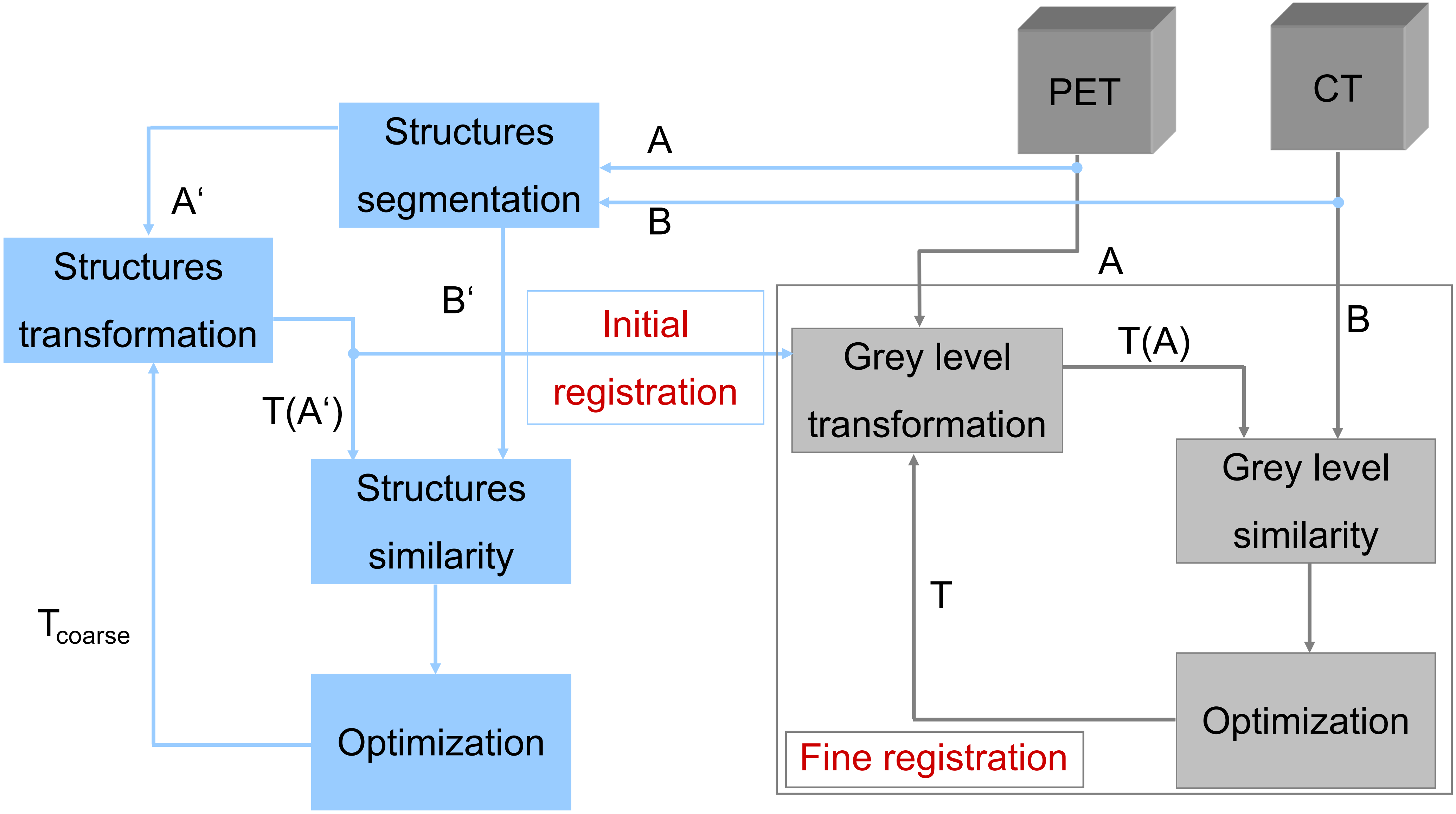
Original solution:

– combine both strategies

– anatomical 2-level scheme

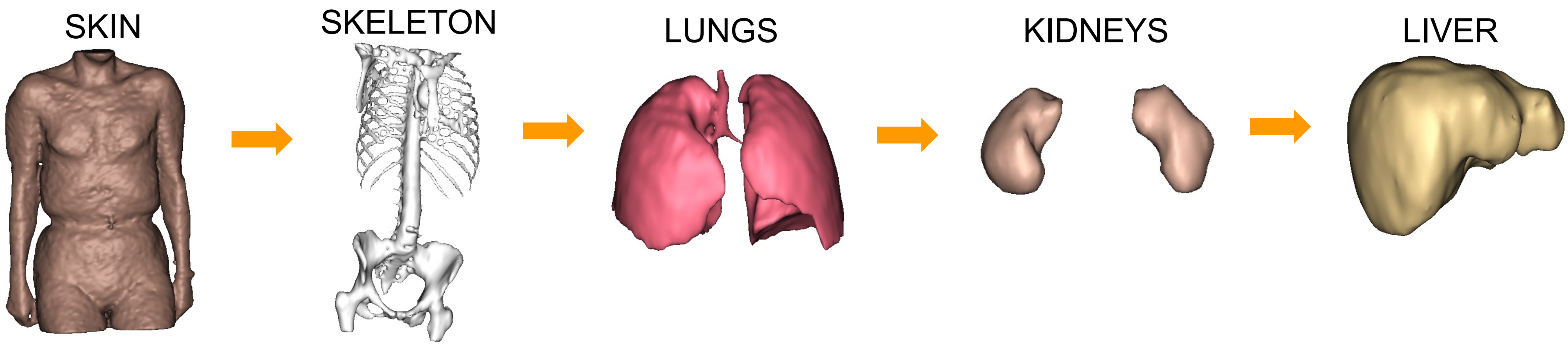
– use of anatomical information to constrain the search of global solution

Proposed methodology

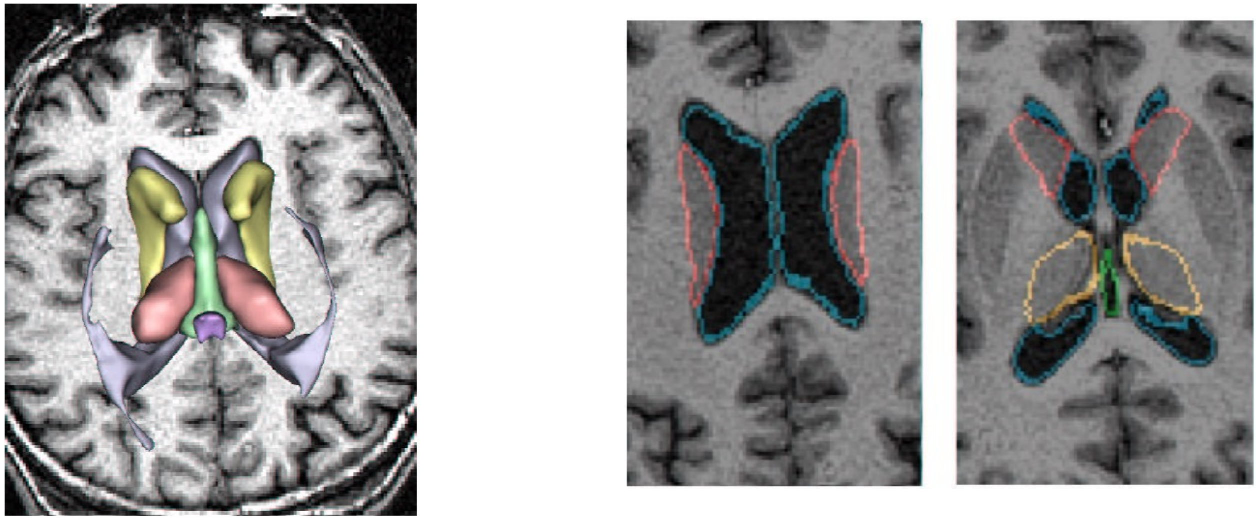


Initial registration: structure segmentation

- Choice and order of structures to segment

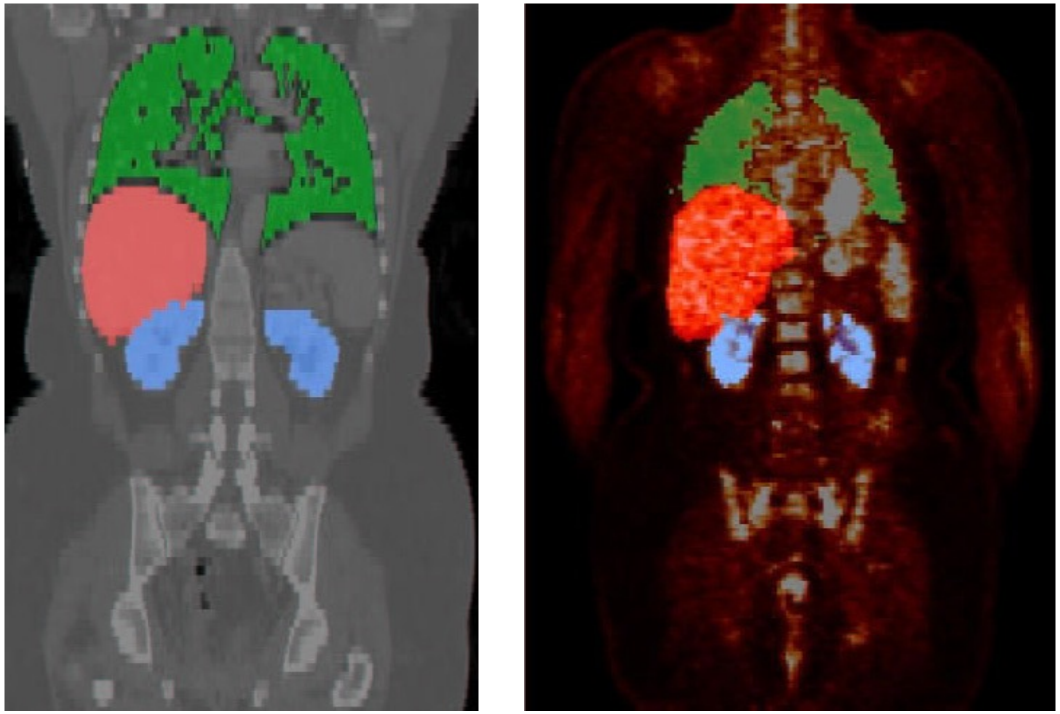


- Similar strategy used in a brain internal structure segmentation application [Colliot-Camara, SPIE’04]

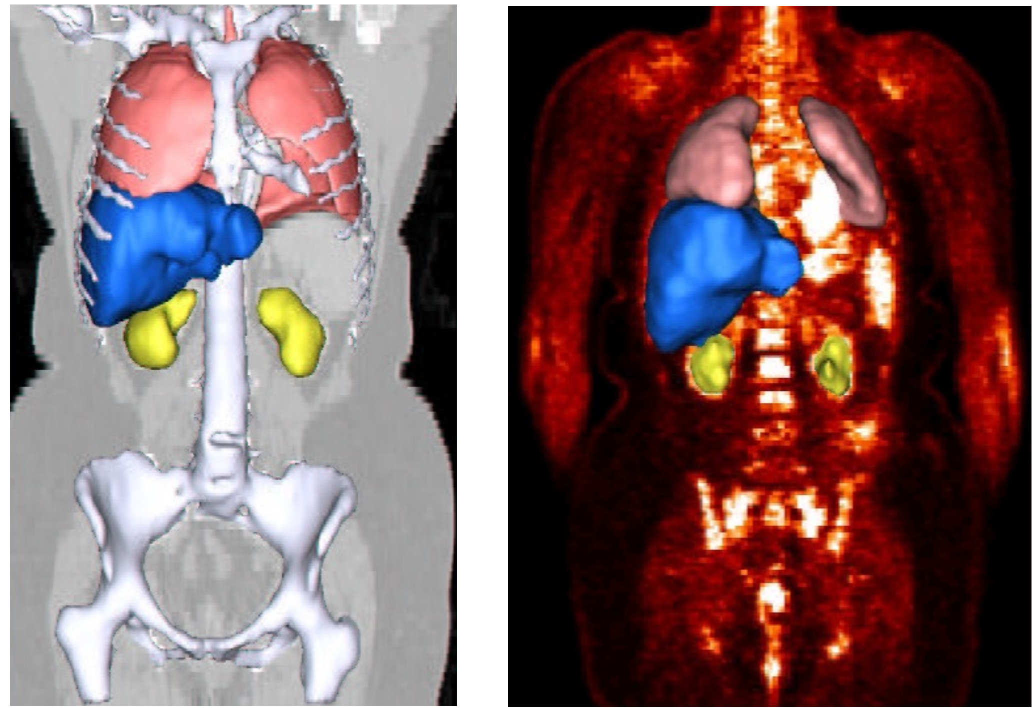


Initial registration: structure segmentation

2D segmentation results

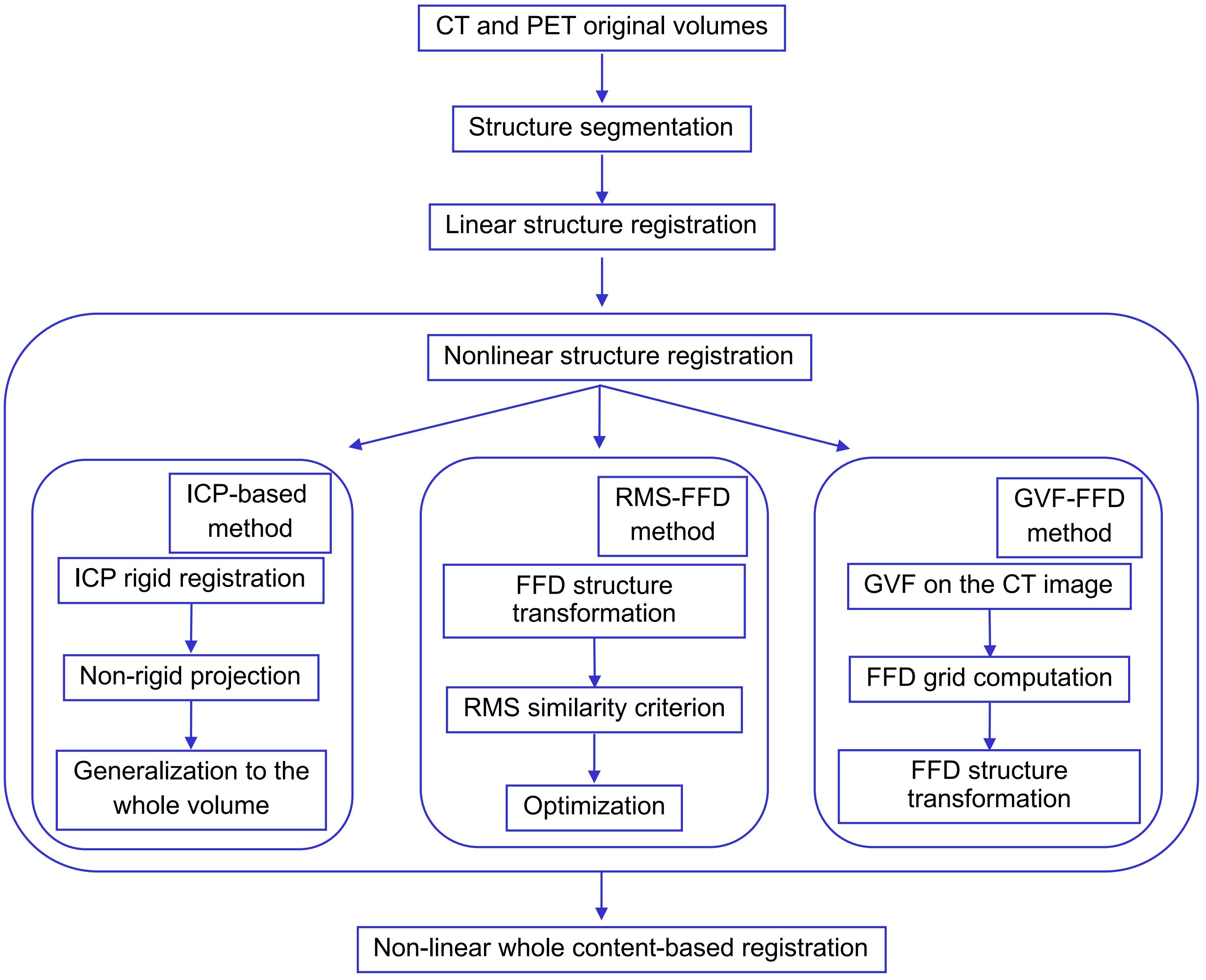


3D segmentation results



O. Camara et al., RFIA, 2004

Initial registration: structure registration



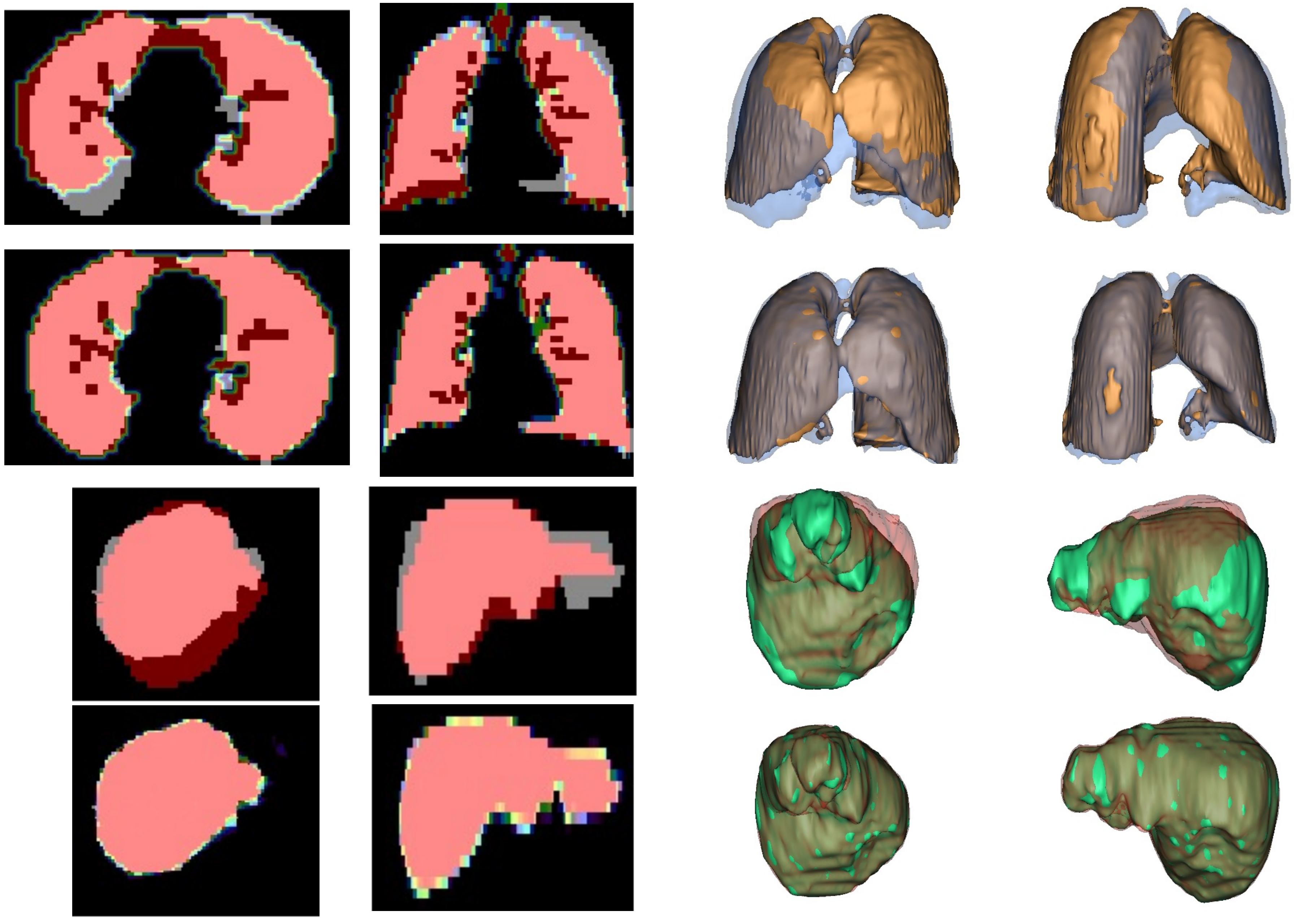
Initial registration: structure registration, RMS-FFD

Linear

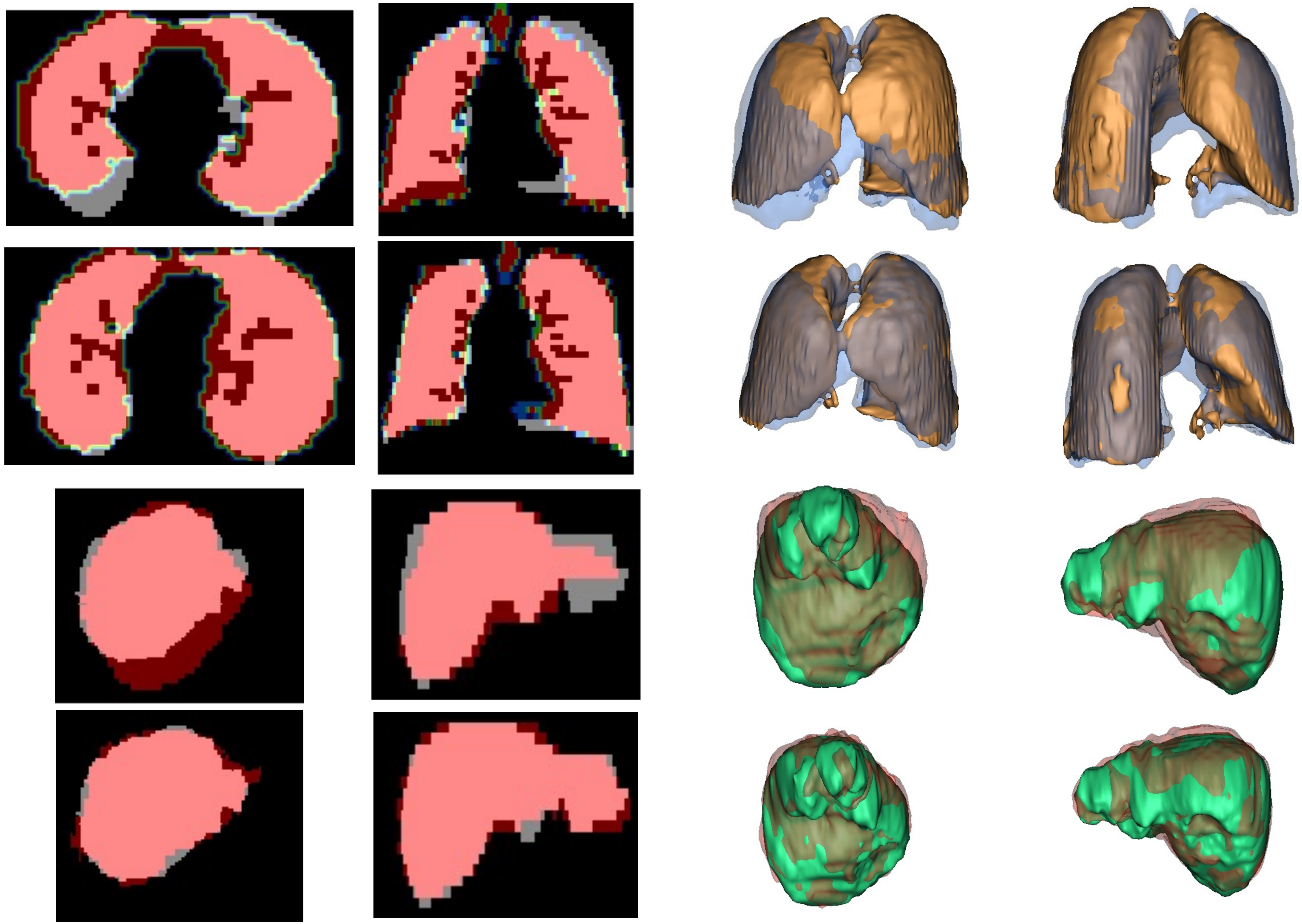
RMS-FFD

Linear

RMS-FFD



Initial registration: structure registration, GVF-FFD



Linear

RMS-FFD

Linear

RMS-FFD

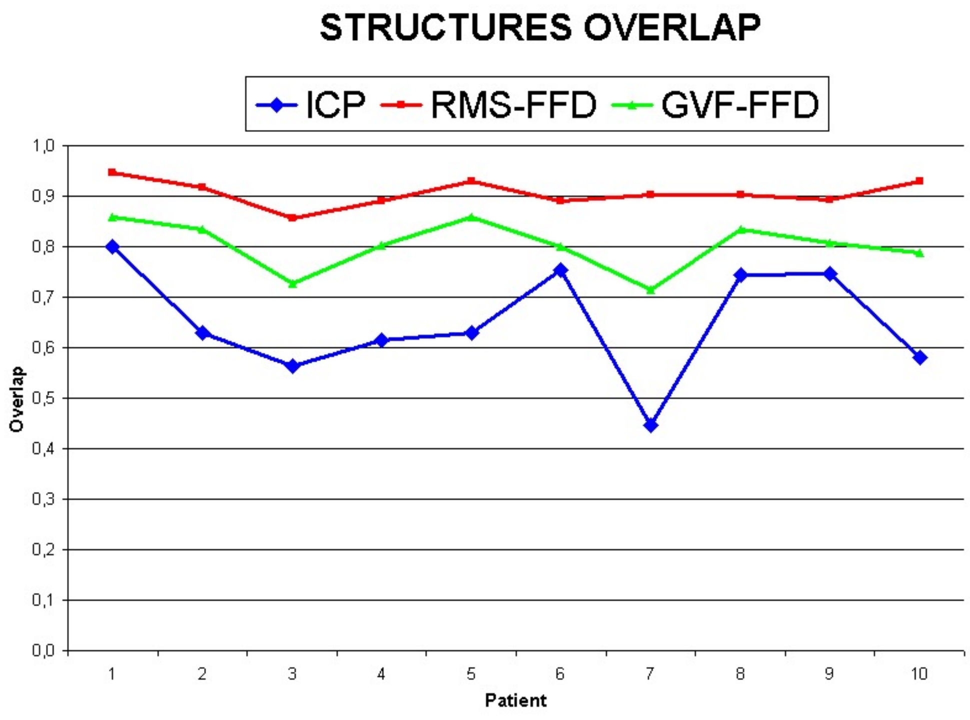
Initial registration: structure registration

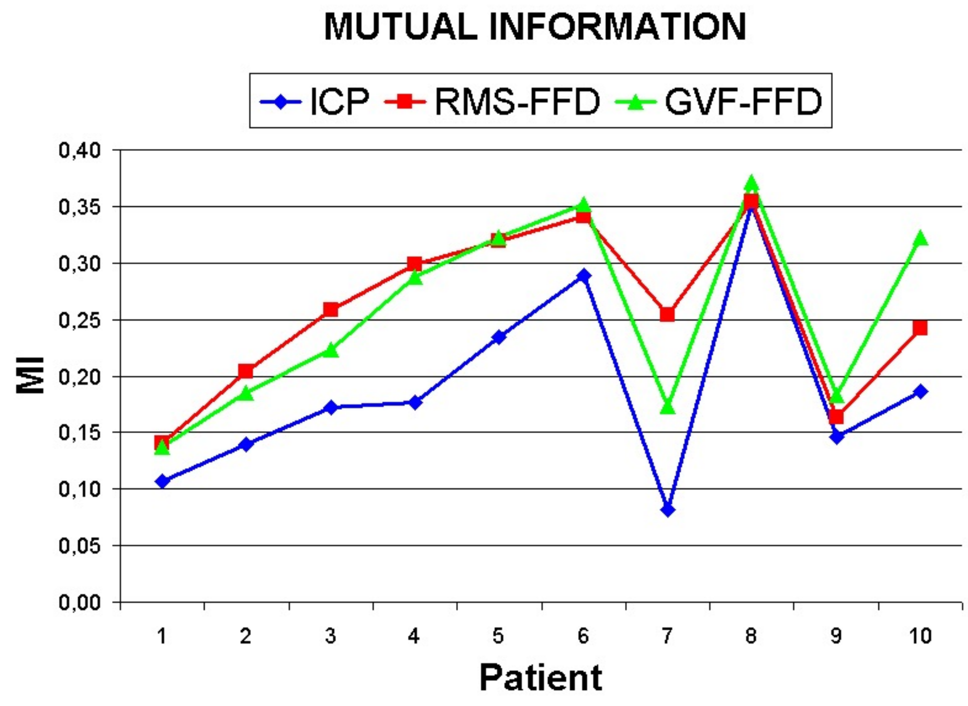
- Evaluation of the structure registration phase
  - comparison between ICP-based, RMS-FFD and GVF-FFD
  - two quantitative measures:
    - Overlap Measure (OM) applied on segmented structures

$$OM = \frac{|A \cap B|}{|A \cup B|}$$

    - Mutual Information (MI) between:
      - grey-level CT
      - grey-level PET, registered by applying the transformation computed over the surfaces

Initial registration: structure registration





Method	ICP	RMS-FFD	GVF-FFD
Overlap(value/%)	0.6586/100	0.9030/137.095	0.8275/122.081
MI(value/%)	0.1888/100	0.2592/137.286	0.2486/131.697
Time (μs/pixel)	6.60723	699.365	52.610

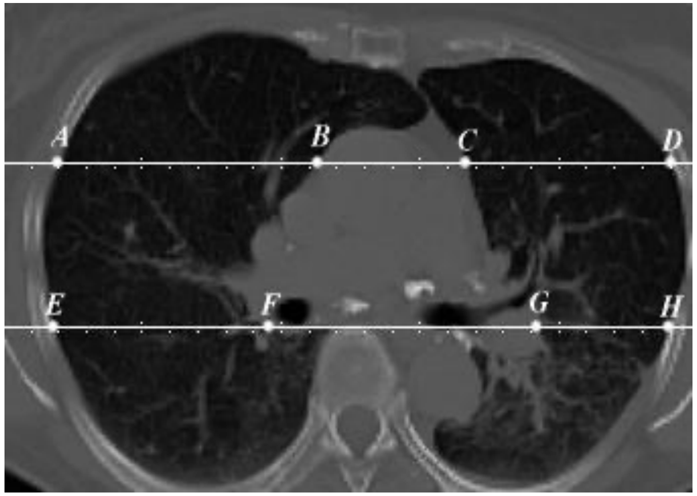
Fine registration: similarity measure

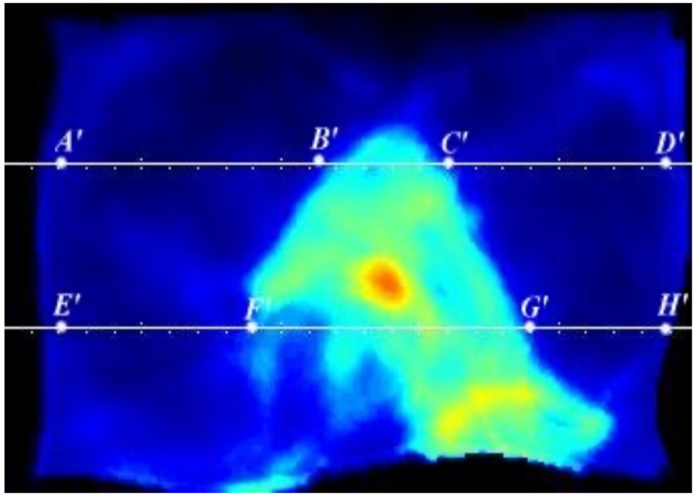
- Problem
  - in multimodal applications, non-functional relation among image grey-level values

- Solution
  - Mutual Information, MI [Viola95, Collignon95], and its variant, Normalized Mutual Information, NMI [Studholme99]

Evaluation of the algorithm

- Original fast evaluation protocol designed with medical experts:
  – several anatomically significant slices are presented, marked with a ruler that defines some reference points





A/A‘=Anterior Left Chest Wall
C/C‘=Anterior Right Mediastinal Wall
E/E‘=Posterior Left Chest Wall
G/G‘=Posterior Right Mediastinal Wall

B/B‘=Anterior Left Mediastinal Wall
D/D‘=Anterior Right Chest Wall
F/F‘=Posterior Left Mediastinal Wall
H/H‘=Posterior Right Chest Wall

Evaluation of the algorithm

- Registration in each reference point is classified according to a scoring scale

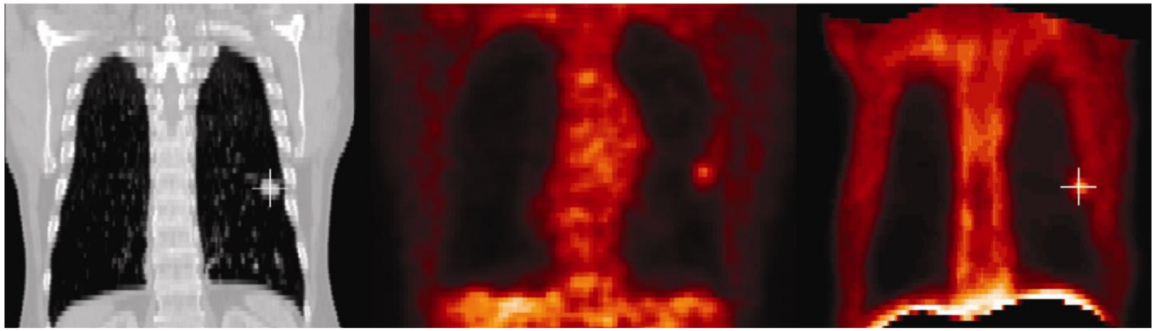
Scale	mm	quality
0	0-5	Good
1	5-15	Acceptable
2	15-	Unacceptable

- Inter-observer consistency is good enough (3 evaluators)

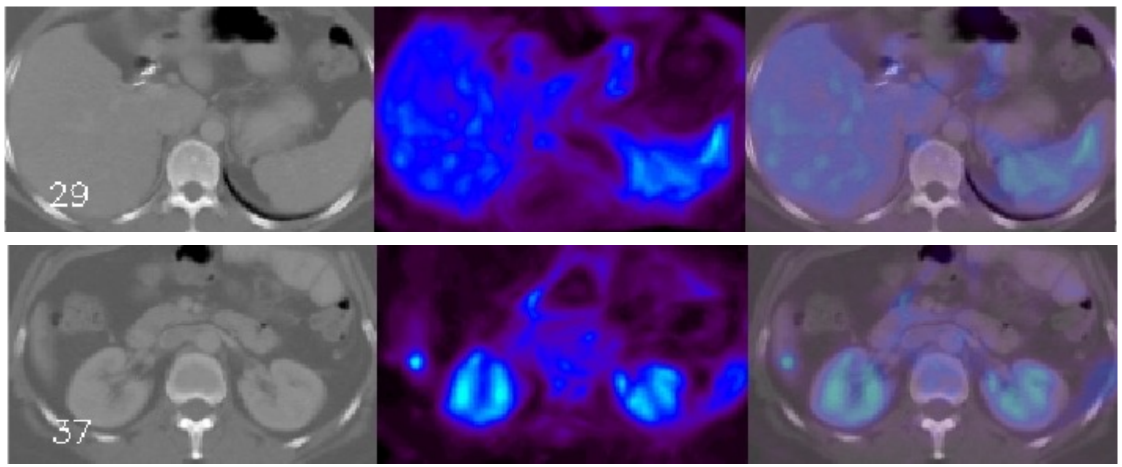
Region	**Mean**	**Variance**
Lungs	0.670	0.02
Kidneys	0.172	0.01
Liver	0.720	0.11
Heart	0.935	0.09
Stomach	1.833	0.08

Results

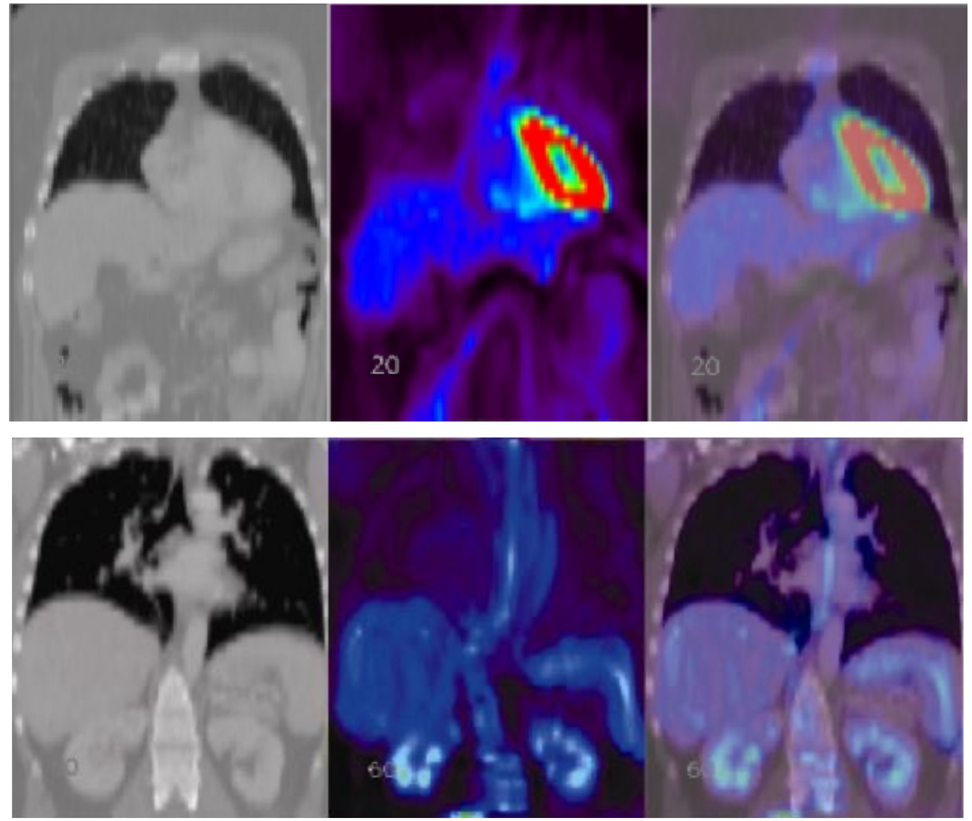
CT | *PET: linear transformation* | *PET: non-linear transformation*



CT | *PET: non-linear transformation* | *Fusion*



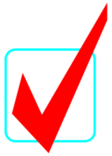
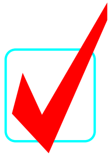
CT | *PET: non-linear transformation* | *Fusion*



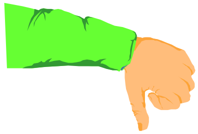
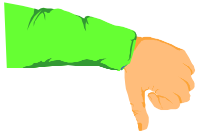
Results

- 3 independent evaluators from 3 different hospitals
- Evaluation of 5 different thoracic and abdominal cases
- Statistics on the scoring scale

Inter-patient results

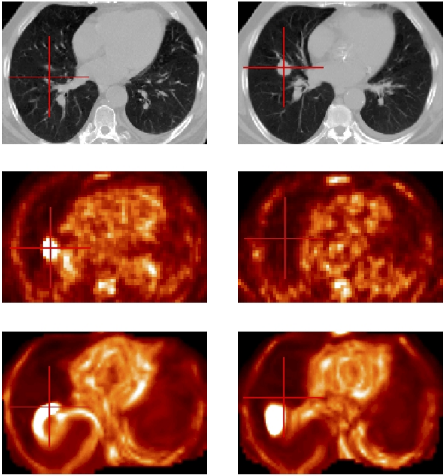



Region	Mean	Variance	Max	Min
Lungs	0.615	0.01	0.64	0.60
Kidneys	0.120	0.01	0.21	0.05
Liver	0.467	0.15	0.87	0.16
Heart	0.597	0.15	1.44	0.54
Stomach	1.833	0.11	2.00	1.33

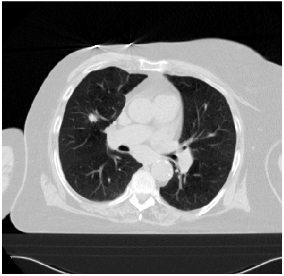
Pathological cases (Antonio Moreno)

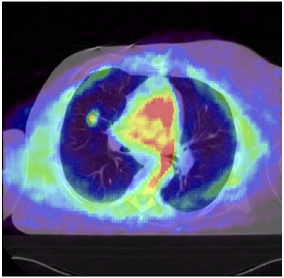
Without contrainsts:

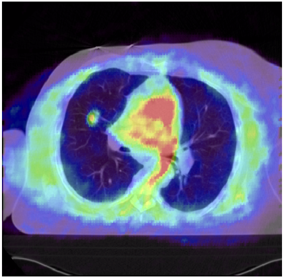


Pathological cases (Antonio Moreno)

With constraints on the tumor:

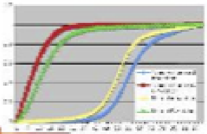






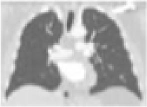
Using a breathing model (Antonio Moreno, Sylvie Chambon)

- Breathing model

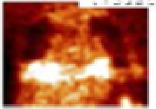


- Image data

CT at end-expiration

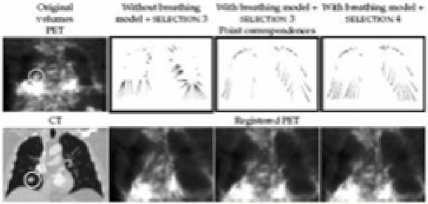


CT at end-inspiration



PET

- Optimal model-based registration of PET & CT lung images



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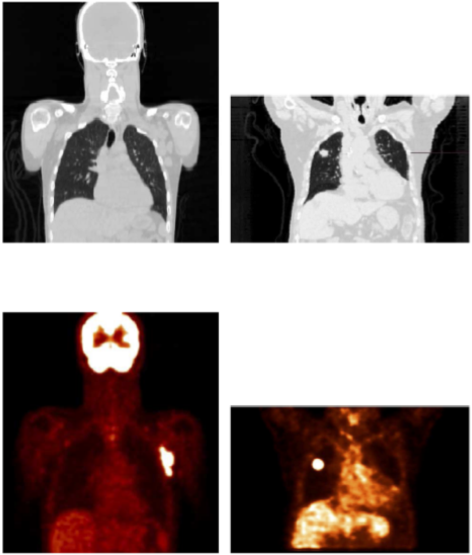
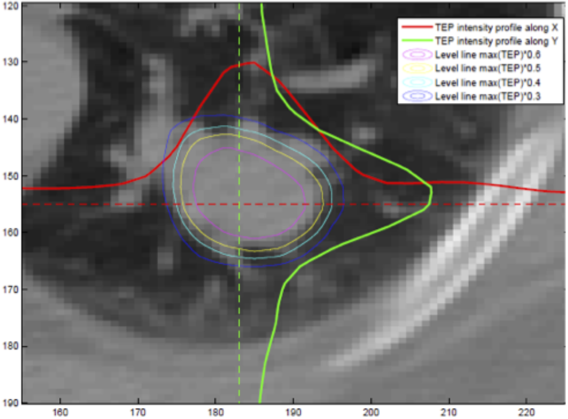
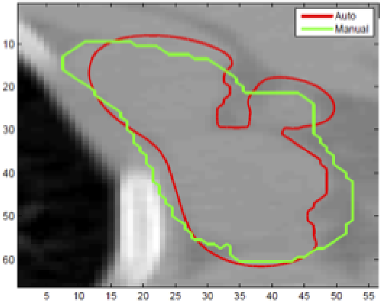
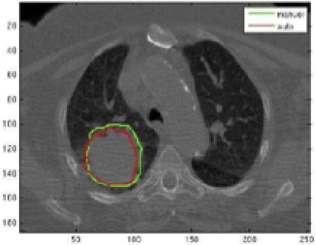
PET-CT fusion (Julien Wojak)

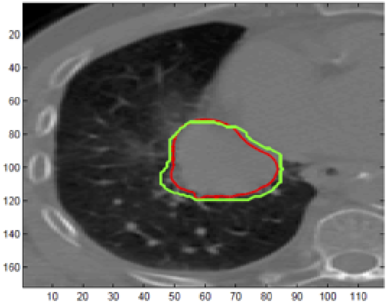


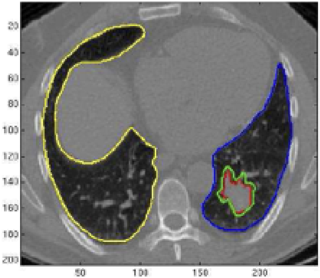
PET-CT fusion (Julien Wojak)



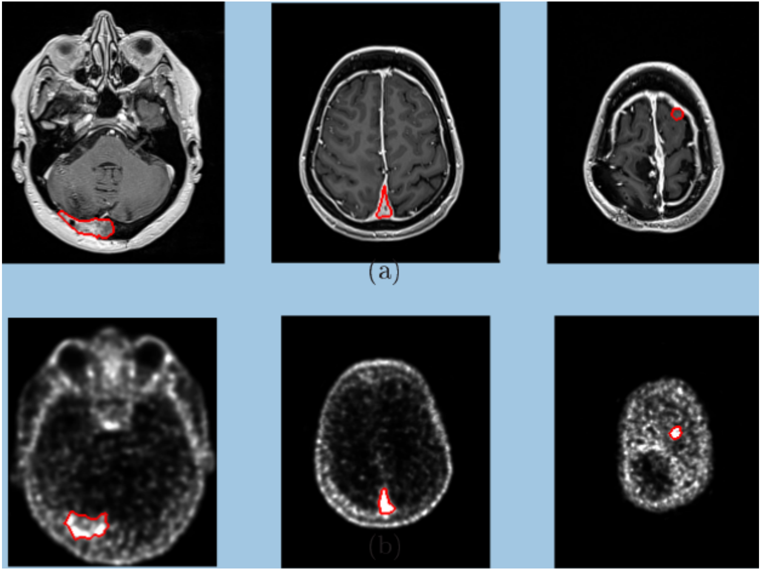

Auto
Manual



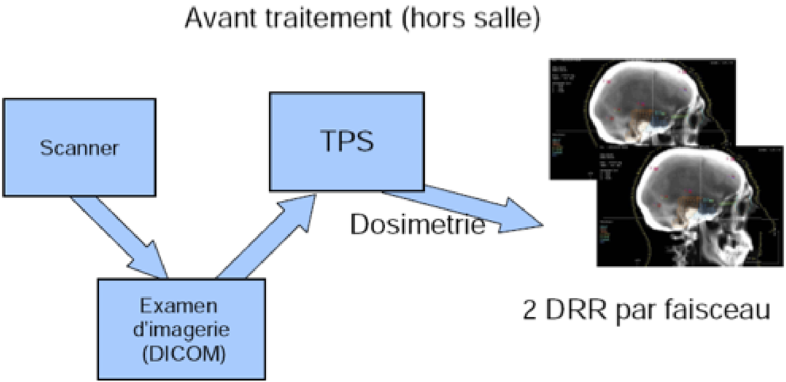

20
40
60
80
100
120
140
160
10 20 30 40 50 60 70 80 90 100 110


20
40
60
80
100
120
140
160
180
200
50 100 150

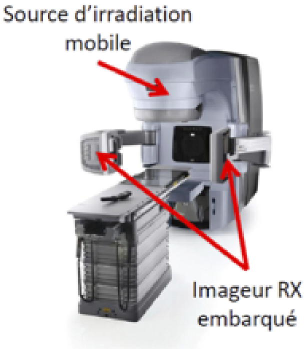
PET-MRI fusion (Hélène Urien)

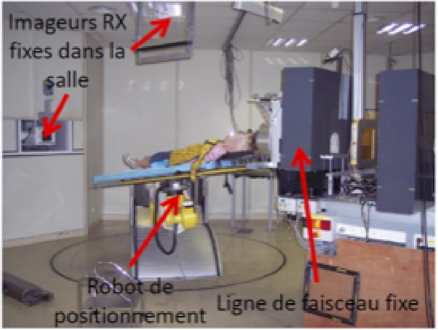


Protontherapy



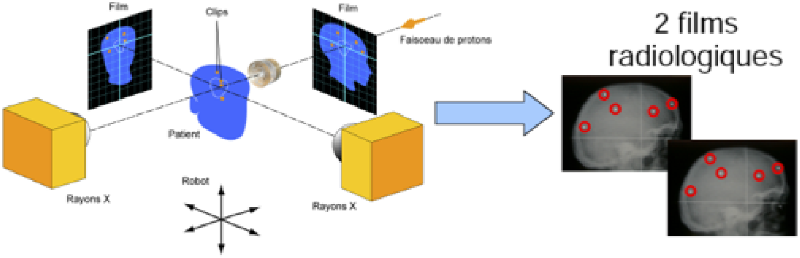
Protontherapy





Protontherapy

Etapes avant traitement (dans la salle de traitement)



Confrontation et recalage films / DRR

Examples of registration software tools

- ITK: `http://www.itk.org/`
- Brain Visa: `http://brainvisa.info/`
- FSL: `http://www.fmrib.ox.ac.uk/fsl/`
- Mipav: `https://mipav.cit.nih.gov/pubwiki/index.php/Optimized_automatic_registration_3D`
- 3D Slicer: `https://www.slicer.org/wiki/Slicer3:Registration`
- Elastix: `https://elastix.dev/`
- Ants, AntsPy: `https://antspyx.readthedocs.io/en/latest/index.html`
- ...

A few references

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- J. V. Hajnal, D. L.G. Hill, D. J. Hawkes (2001). Medical image registration. CRC press.
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- S. Klein, M. Staring, K. Murphy, M.A. Viergever, J.P.W. Pluim (2010), elastix: a toolbox for intensity based medical image registration. IEEE Transactions on Medical Imaging, vol. 29, no. 1, pp. 196 - 205.
- B. B. Avants, N. Tustison, G. Song (2009). Advanced normalization tools (ANTS). Insight j, 2(365), 1-35.