Non-Linear Registration and Patient-Adapted Atlases For Segmentation

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September 18, 2011.

Introduction

- Atlas
  - An image of an anatomy
  - Attached to various information
    - Segmentation (labels, shapes, …)
    - Statistics (diffusion tensors, fibers, …)

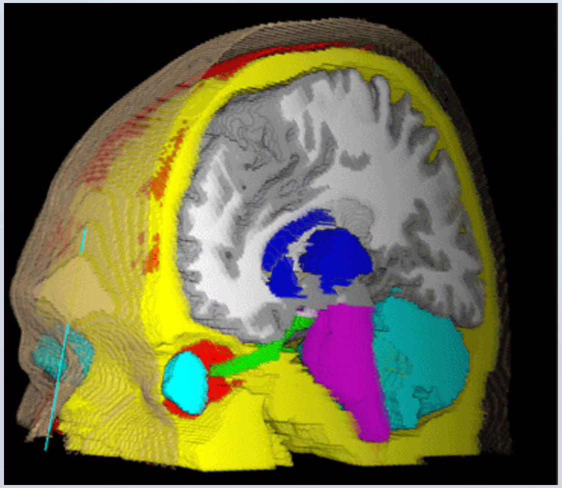
- Very powerful and generic tool
  - Study of a population (e.g. : study of functional organization)
  - In-depth comparison of populations
  - Segmentation of structures
  - In-depth characterization of disease in a patient

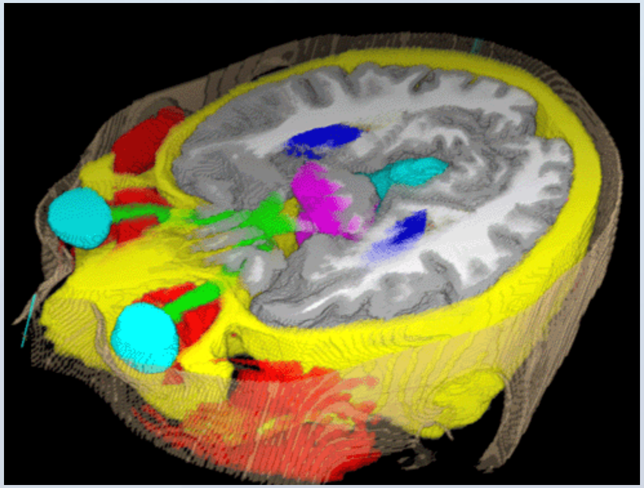
Atlas Based Segmentation

- Goal: Delineate structures on a patient/subject image
- Some applications
  - Therapy planning
  - Study of brain evolution (brain growth, atrophy due to disease, …)
- Composed of three major steps
  - Atlas construction (if needed)
  - Registration of the atlas onto the patient
  - Propagate atlas segmentation onto the patient

Atlas Construction Strategies

- Single image approach
  - One image manually segmented by an expert
    - Brain atlas [Bondiau et al., 2005]
  - Has to be representative of the patient anatomy

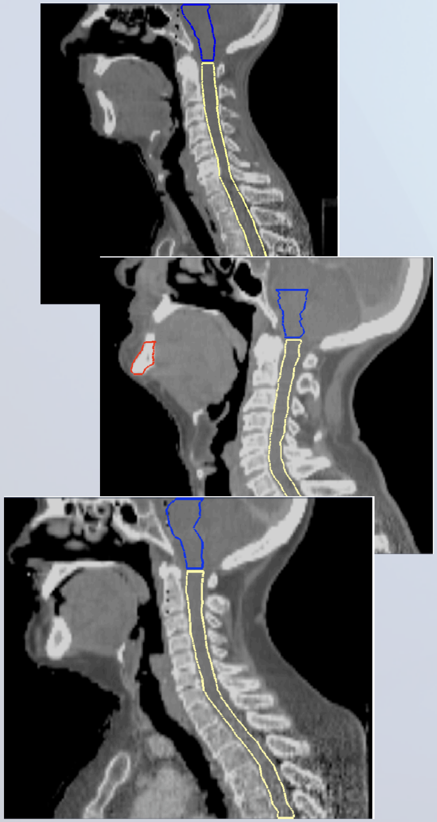




[Bondiau et al., 2005]. Atlas-based Automatic Segmentation of MR Images: Validation Study on the Brainstem in Radiotherapy. Int J Rad Onc Biol Phys, 61(1):289-98, 2005.

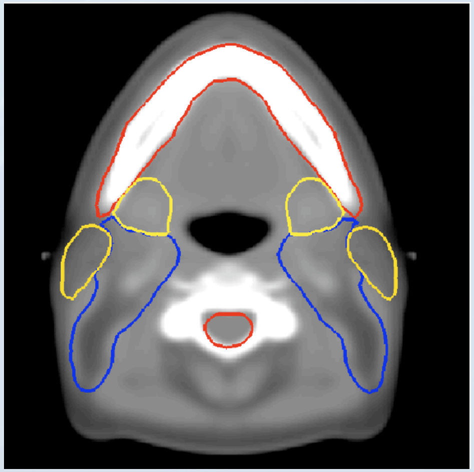
Average Atlas Construction Method

- Average anatomy built from a database

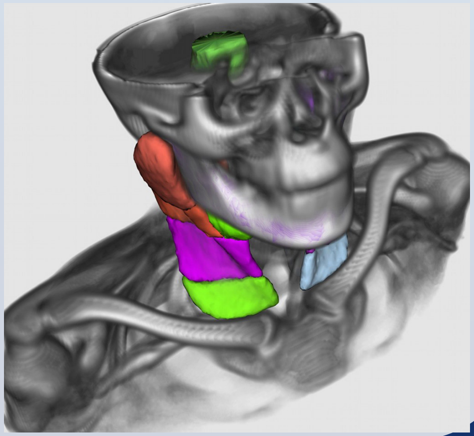


Mean Image Construction (1)

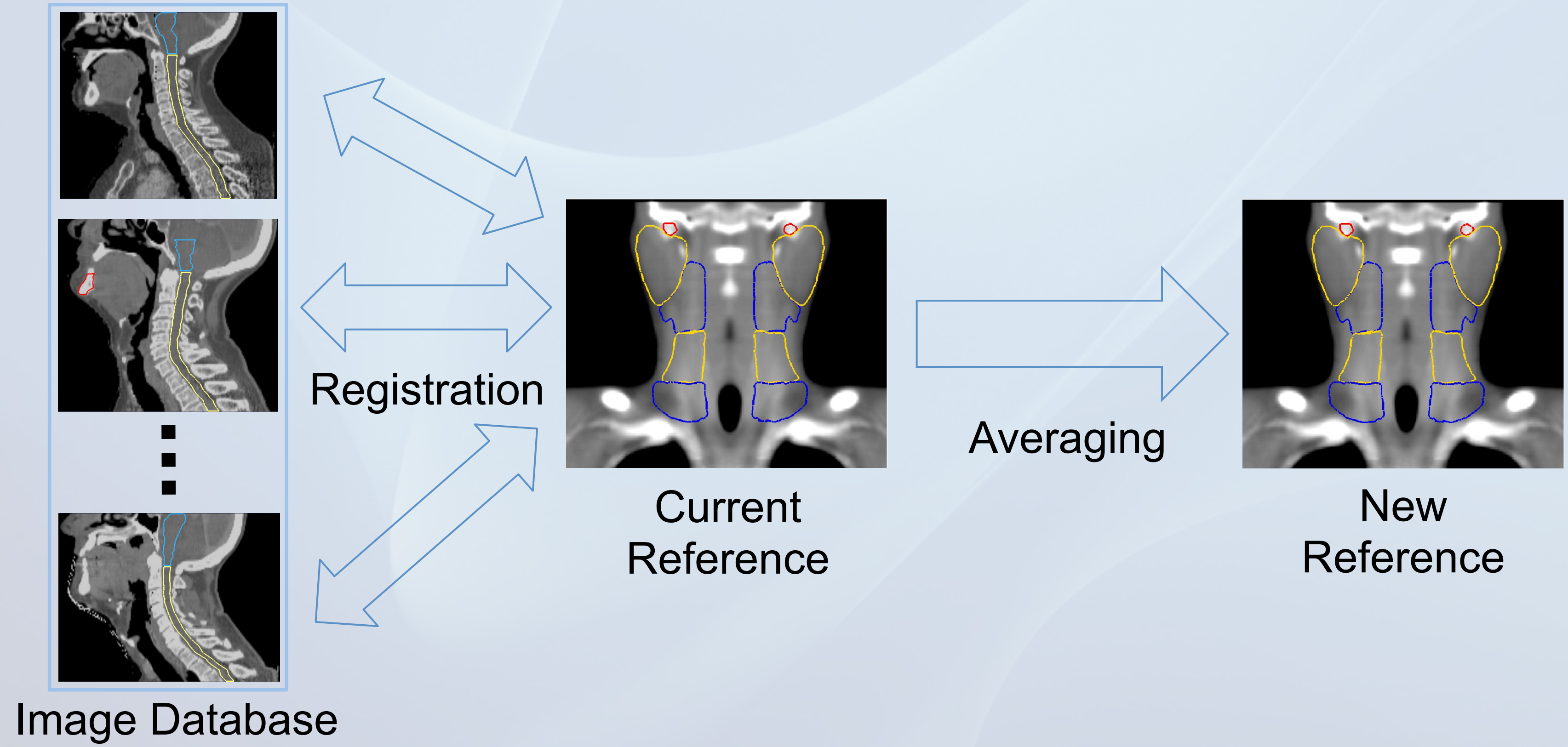
Average Segmentations Computation (2)



Average Atlas



Average Image Construction



- New reference: Averaging of registered images intensities

$$M_{k+1}(x) = \frac{1}{N} \sum_{j} I_j \circ T_j(x)$$

Average Image Construction

- Unbiased atlas construction [Guimond et al., 2000]
  - Iteration over two steps
    - Registration of all images on reference
    - "Unbiasing" the new reference

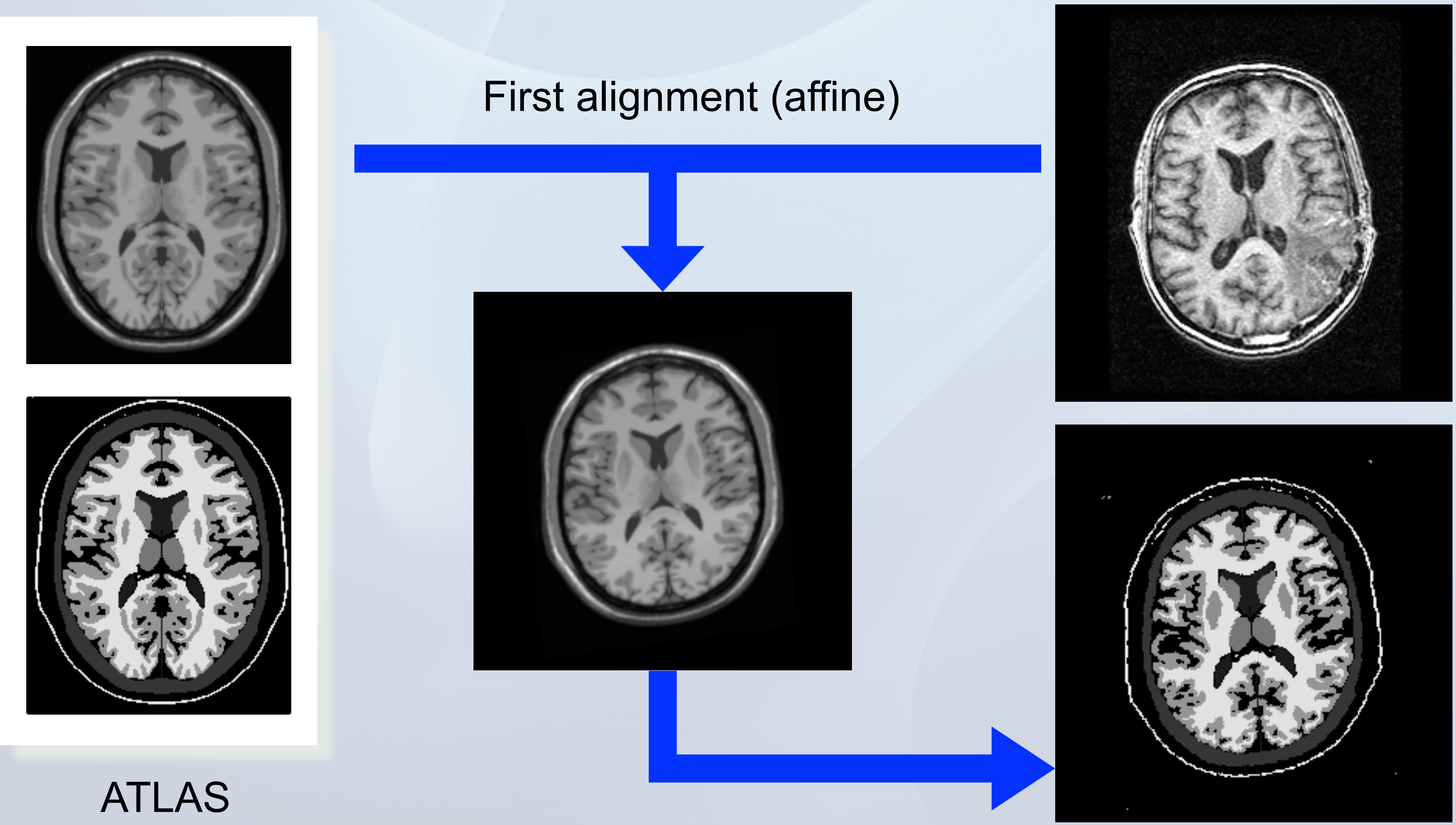
- Registration → non linear transformations to the reference
- Unbiasing step
  - Compute an average transformation [Arsigny et al., 2006]

$$\bar{T} = \exp\left(\frac{1}{N}\sum_{j}\log(T_j)\right)$$

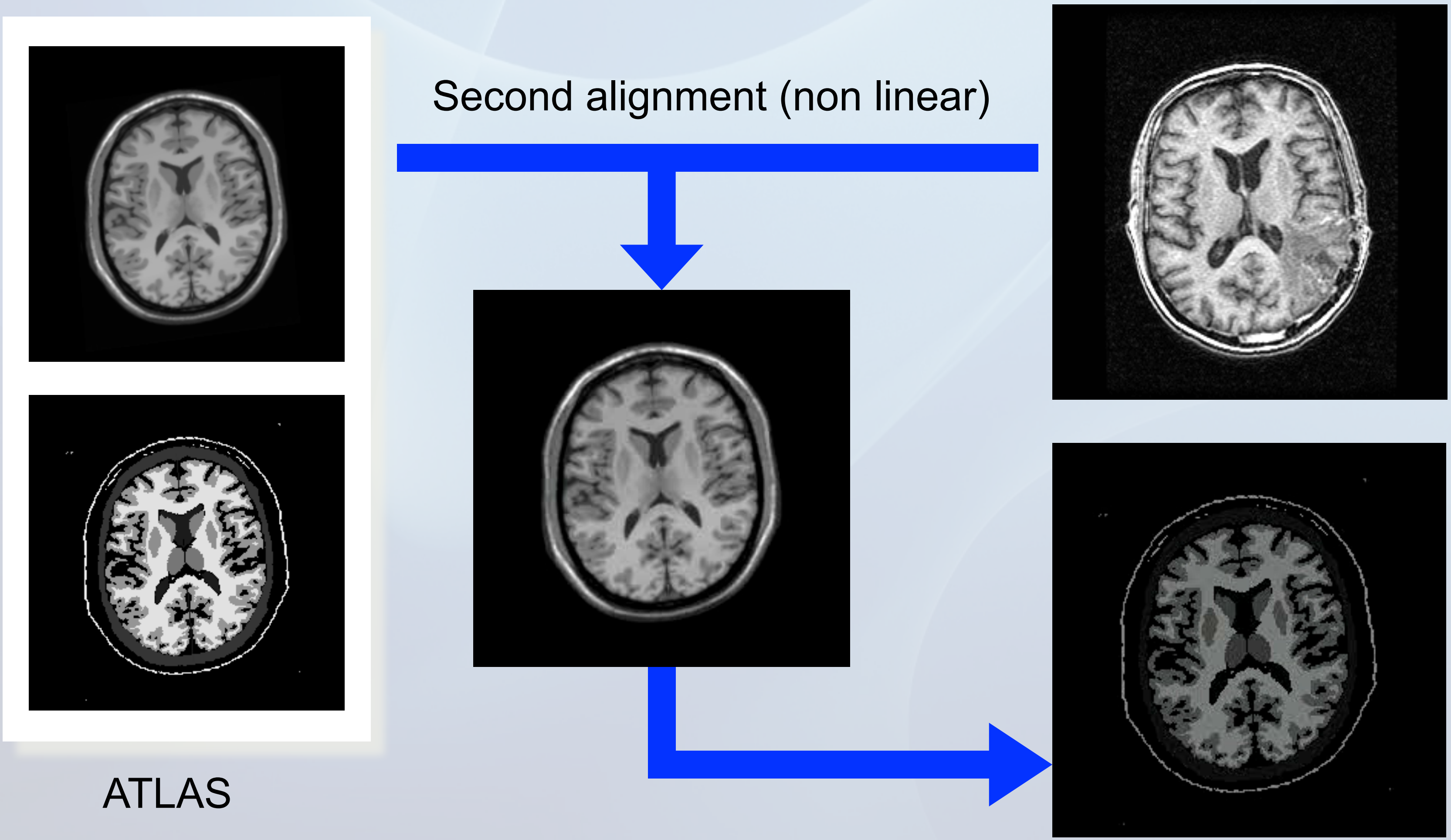
  - Application of $\bar{T}^{-1}$ to the new reference $\tilde{M}_{k+1} = M_{k+1} \circ \bar{T}^{-1}$

[Guimond et al., 2000]: Average Brain Models: A Convergence Study, CVIU, 2000.
[Arsigny et al., 2006]: A Log-Euclidean framework for statistics on diffeomorphisms, MICCAI, 2006.

Atlas Based Segmentation Principle



Atlas Based Segmentation Principle



Challenges in Atlas-Based Segmentation

- Atlas-based segmentation
  - Segmentation of many structures in one step
- Non linear registration
  - Central technique for atlas-based segmentation
  - Able to handle atlas/subject variability
  - Robust registration method, smooth transformation
- Atlas Construction
  - Need for a representative, unbiased atlas
  - How to build atlas segmentations ?

Road Map

- Introduction
- Image Registration for Atlas Based Segmentation
  - Challenges and Review
  - One Adapted Technique: Locally Affine Registration
  - Example Results
- Adapting the Atlas to the Patient
  - Adapted Atlas Construction
  - Results
- Conclusion

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Registration Techniques Classification

- Registration pipeline
  - Crucial to build the atlas (e.g. average atlas)
  - Crucial to register the atlas on the patient
  - Needs to be carefully chosen

- Registration algorithm: three main bricks [Brown, 1992]
  - Similarity measure
    - SSD, correlation coefficient, mutual information, …
  - Transformation
  - Optimization algorithm
    - Gradient descent, block matching, …

[Brown, 1992]: L.G. Brown. A Survey of Image Registration Techniques. ACM Computing Surveys, 1992.

Which transformation to register the atlas ?

- Needs to be adapted to the task
- Tradeoff in non linear registration
  - Able to handle atlas / patient variability
  - Robust and smooth
- Classes of transformations
  - Parametric: interpolated between points or regions
    - Arbitrary number of degrees of freedom
    - FFD [Rueckert et al.], …
  - Dense: one displacement vector per voxel
    - Maximal number of degrees of freedom
    - Diffeomorphic demons [Vercauteren et al.], …

Increasing degrees of freedom

[Rueckert et al.] Non-Rigid Registration Using Free-Form Deformations: Application to Breast MR Images. TMI, 1999.
[Vercauteren et al.] Diffeomorphic demons: Efficient non-parametric image registration. Neurimage, 2009.

Some Examples of Registration Algorithms

- Parametric Registration Algorithm
  - Transformation
    - defined on a grid of control points, interpolated in between

- Free-Form Deformations
  - Regular grid of cubic B-Splines
  - Gradient descent on the control points displacement
- Advantage: any number of degrees of freedom
- Disadvantage: how to choose this number?

Some Examples of Registration Algorithms

- Dense Registration Algorithm
  - Transformation: one displacement vector per voxel

- Diffeomorphic Demons
  - Similarity: optical flow (similar to SSD)
  - Gauss Newton scheme to optimize the transform

- Advantages
  - Log-Euclidean framework: guaranteed diffeomorphism
  - Fast and symmetric transform
- Disadvantages
  - many degrees of freedom, needs good regularization
  - SSD may not be adapted for some tasks

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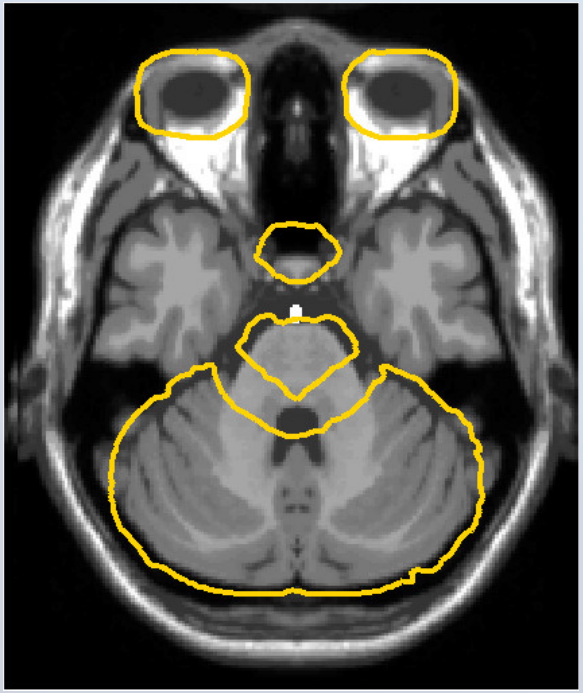
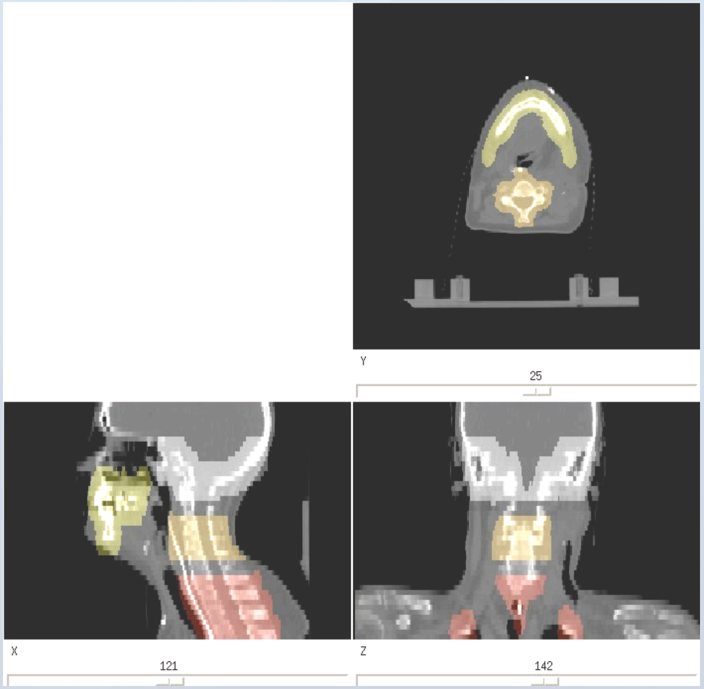
Locally Affine Registration for Atlas Registration

- Principle:
  - Register only anatomic areas of interest
  - Interpolate a global transformation from all local transformations





[Commowick et al., 2008]: An Efficient Locally Affine Framework for the Smooth Registration of Anatomical Structures. Medical Image Analysis,12(4):427-441, 2008.

Locally Affine Transformation

- Local transformation
  - Affine transformation A_i associated to each region R_i
  - Weight function $w_i(x)$
    - Relative influence of each region at point x

$$w_i(x) = \frac{1}{1 + \lambda d(x, R_i)}$$

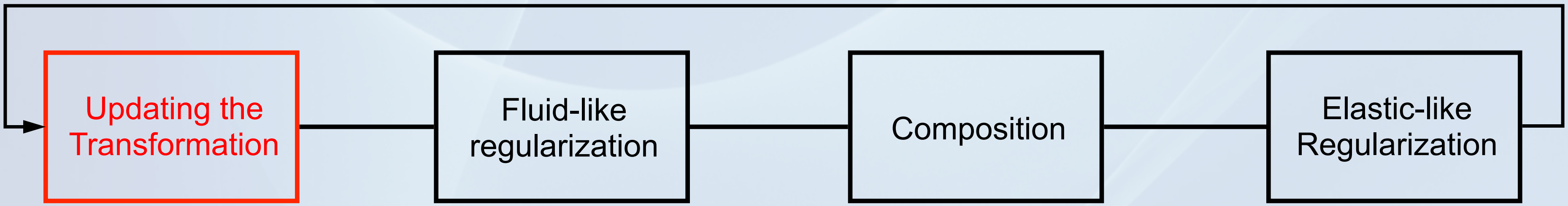
- Global transformation:
  - Solution 1: Weighted interpolation of affine components

$$T(x) = \sum_{i=1}^{N} w_i(x) A_i(x)$$

  - Solution 2: Using an ordinary differential equation [Arsigny et al., 2009]

[Arsigny et al., 2009] A Fast and Log-Euclidean Polyaffine Framework for Locally Linear Registration. Journal of Mathematical Imaging and Vision, 33(2):222-238, 2009.

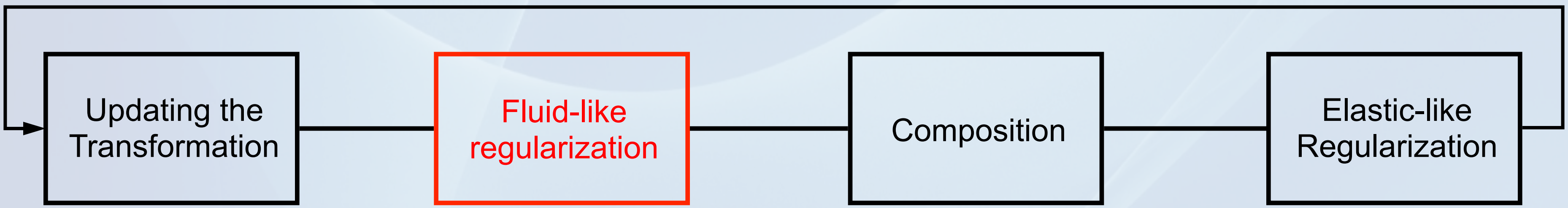
LAF: Updating the transformation



- Local affine correction δA_i estimation

- Block-Matching algorithm
- Outlier rejection in the estimation process
- Least Trimmed Squares Weighted Estimation
  - Weighted by similarity measure values
  - Weighted by $w_i(x_v)$

LAF: Fluid-like Regularization

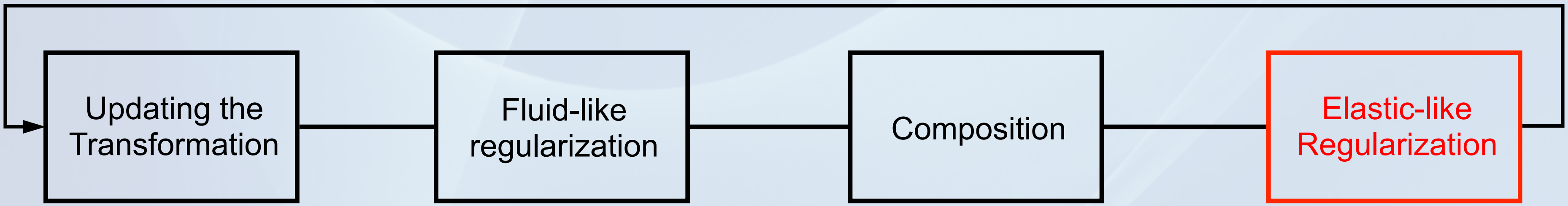


- Fluid-like regularization of local transformation corrections
- Gradient descent on

$$\mathrm{Reg}(\delta A_i, w_i) = \sum_{i=1}^{N} \sum_{j \neq i} p_{i,j} \| \log(\delta A_i) - \log(\delta A_j) \|^2$$

- Log-Euclidean polyaffine framework
  - $\log(A_i)$ belongs to a vector space
  - Generalization of usual regularization energies

LAF: Elastic-like Regularization



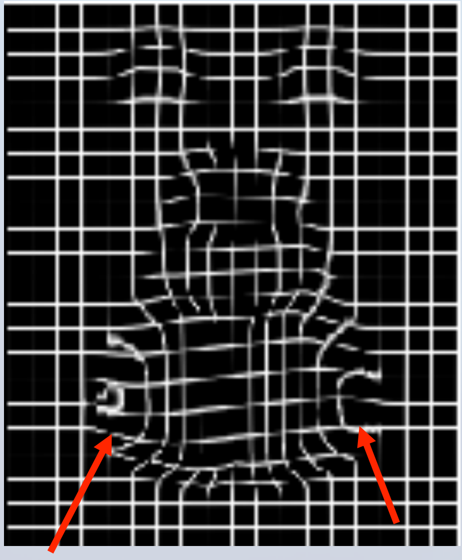
- Gradient descent on

$$\mathrm{Reg}(A_i^l, w_i) = \sum_{i=1}^{N} \sum_{j \neq i} p_{i,j} \| \log(A_i^l) - \log(A_j^l) \|^2$$

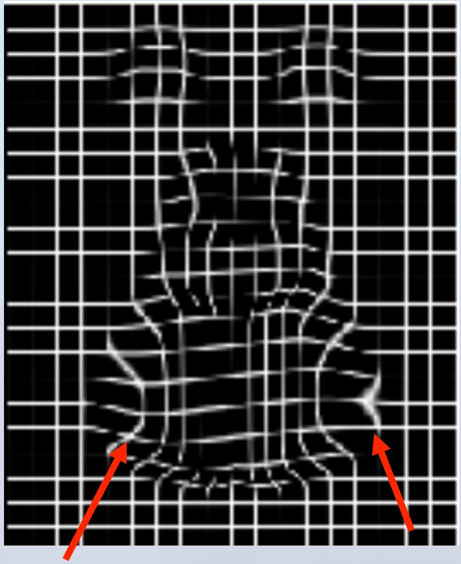
- Similar to fluid-like regularization
  - Regularization on transformations A_i^l

LAF: Transformation Interpolation

- Global transformation computation
  - Solution 1 (weighted interpolation): Fast but not always invertible
  - Solution 2 (polyaffine): Slower but always invertible



Transformation using solution 1



Transformation using solution 2

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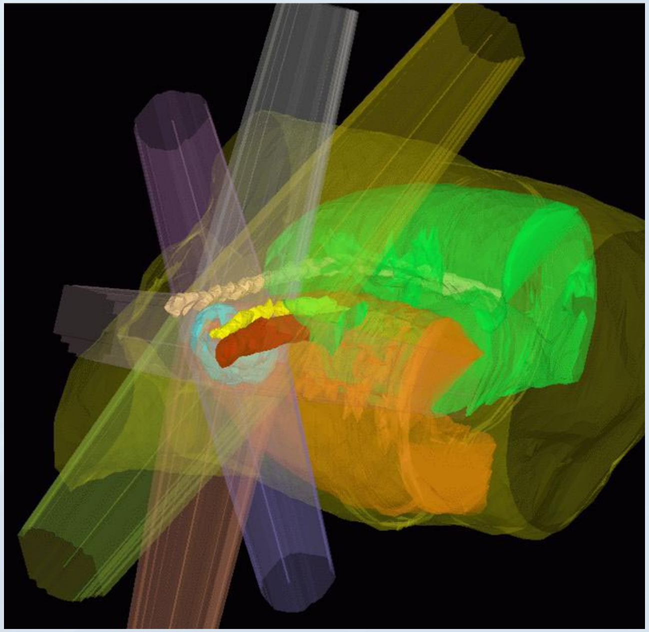
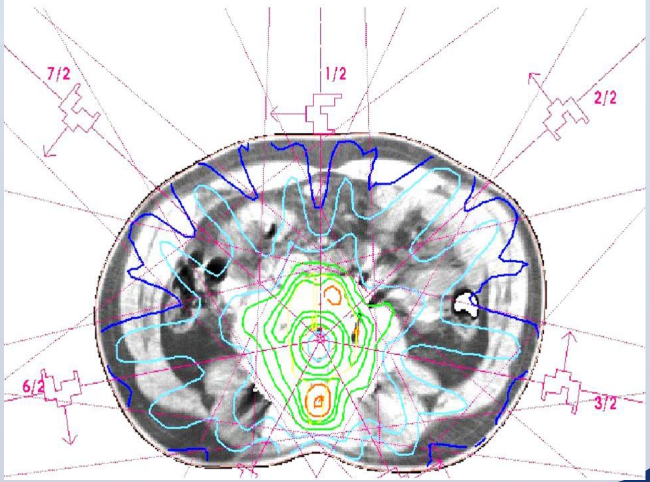
Example: Radiotherapy Planning



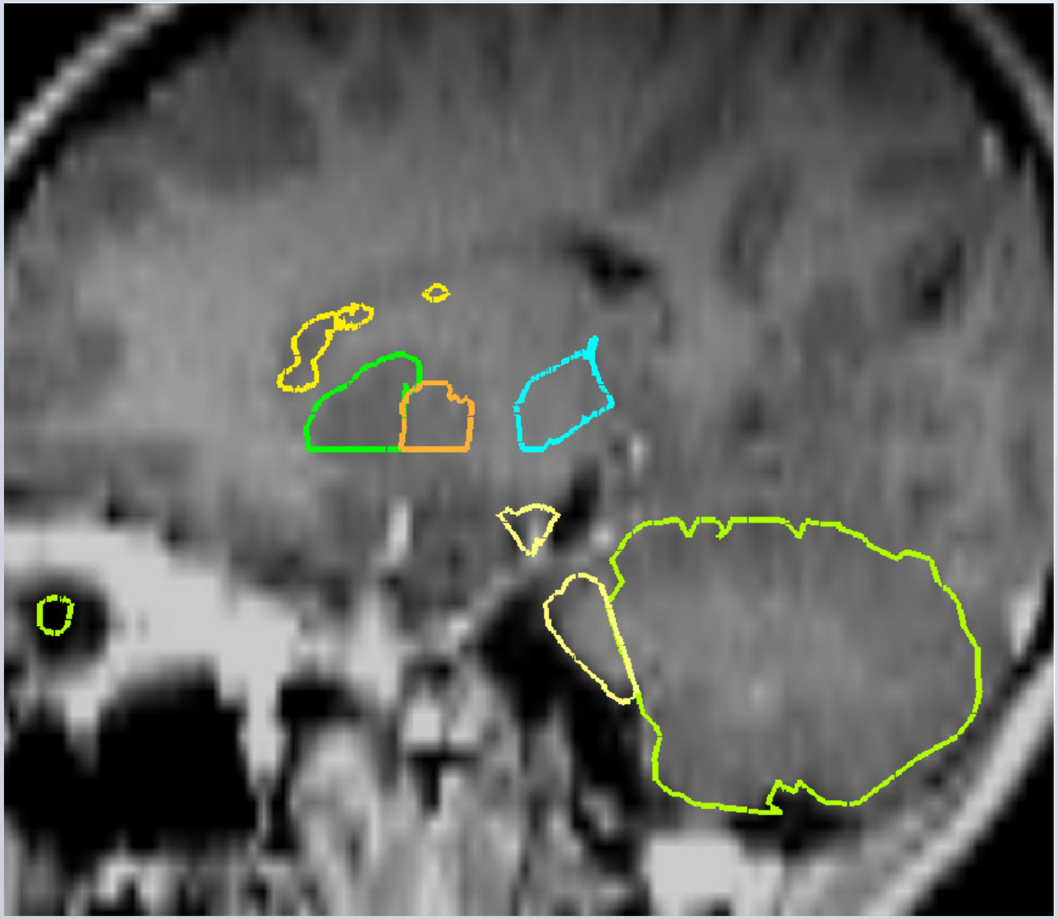
- Radiotherapy principle:
  - Use of high energy irradiation beams
  - Optimize dose on the tumor
  - Control irradiation of critical structures (OAR)

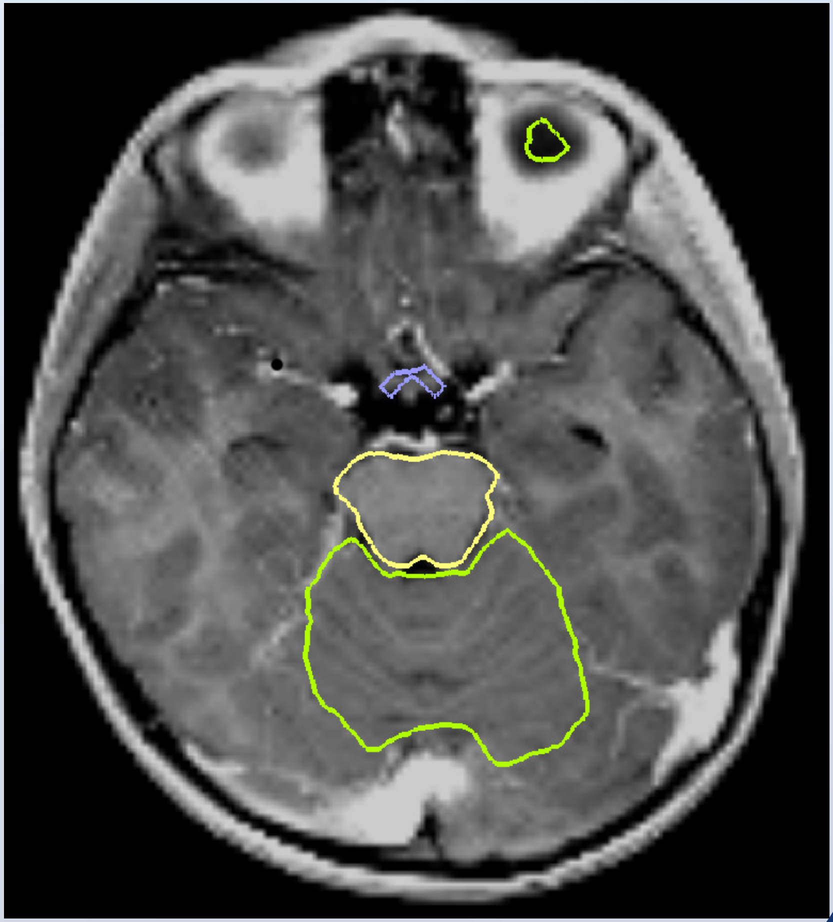
➔ Need for high precision planning
  - Irradiation doses computed on each organ
  - Compare doses with expected levels
  - Requires delineation of structures

- Objective: fast and robust automatic segmentation

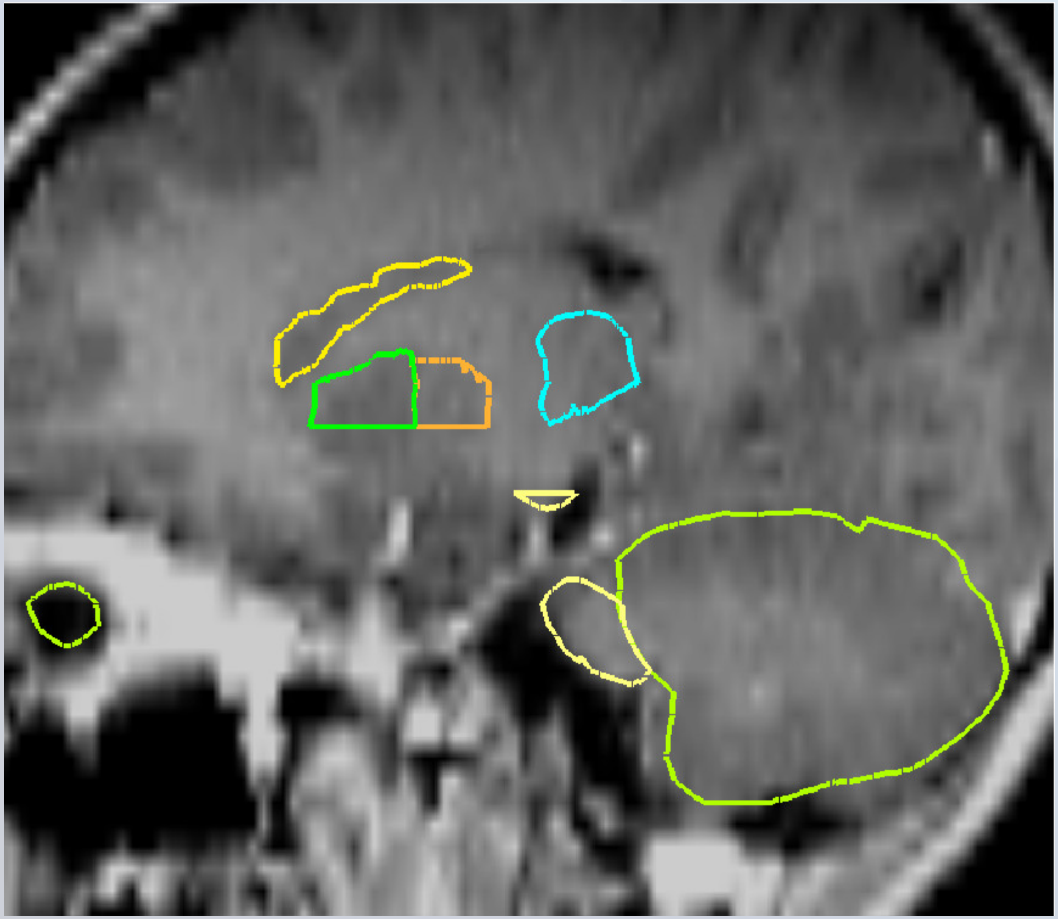


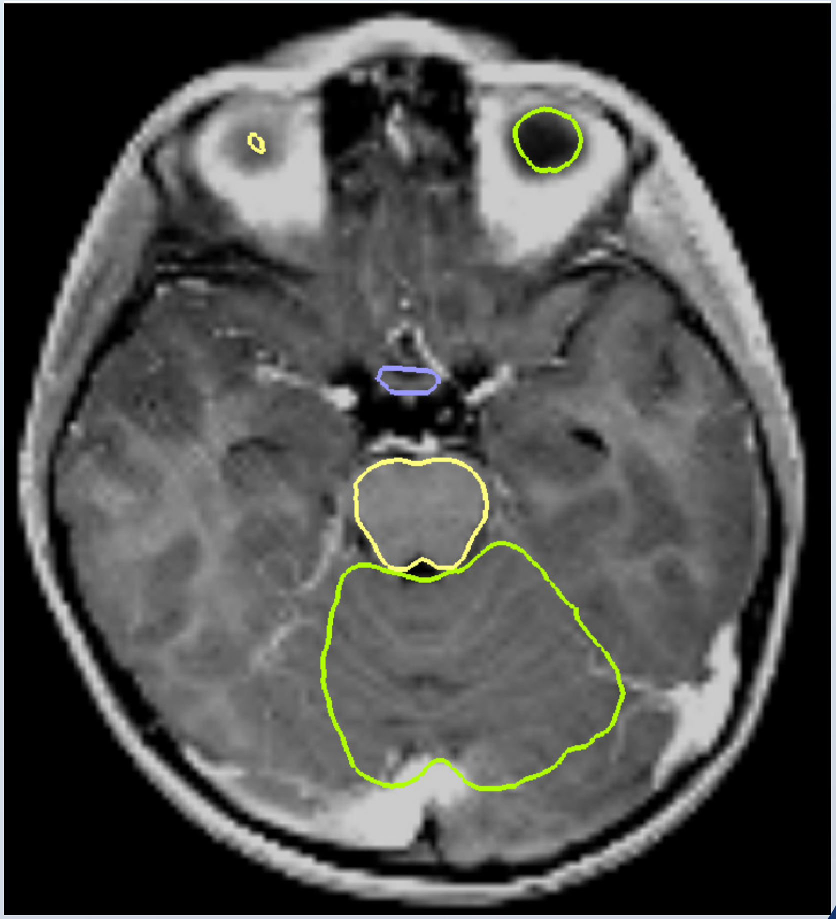
Evaluation in Clinical Conditions (Dense)





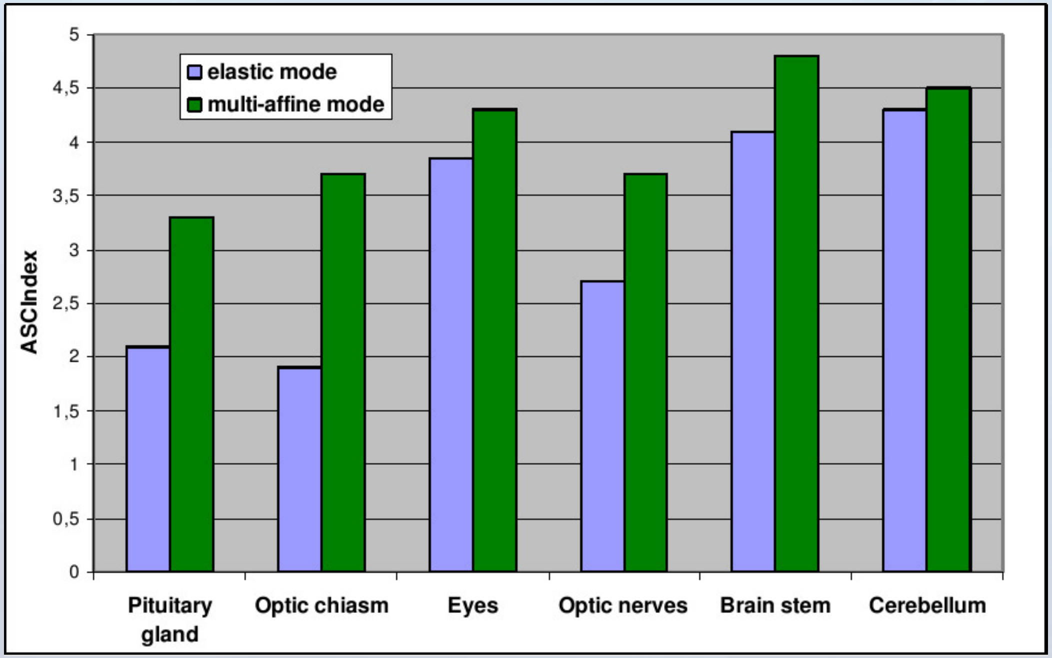
Evaluation in Clinical Conditions (LAF)





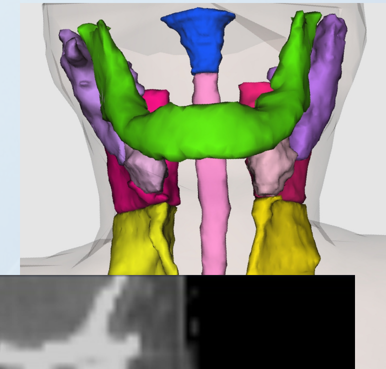
Semi-Quantitative Evaluation in Clinical Conditions

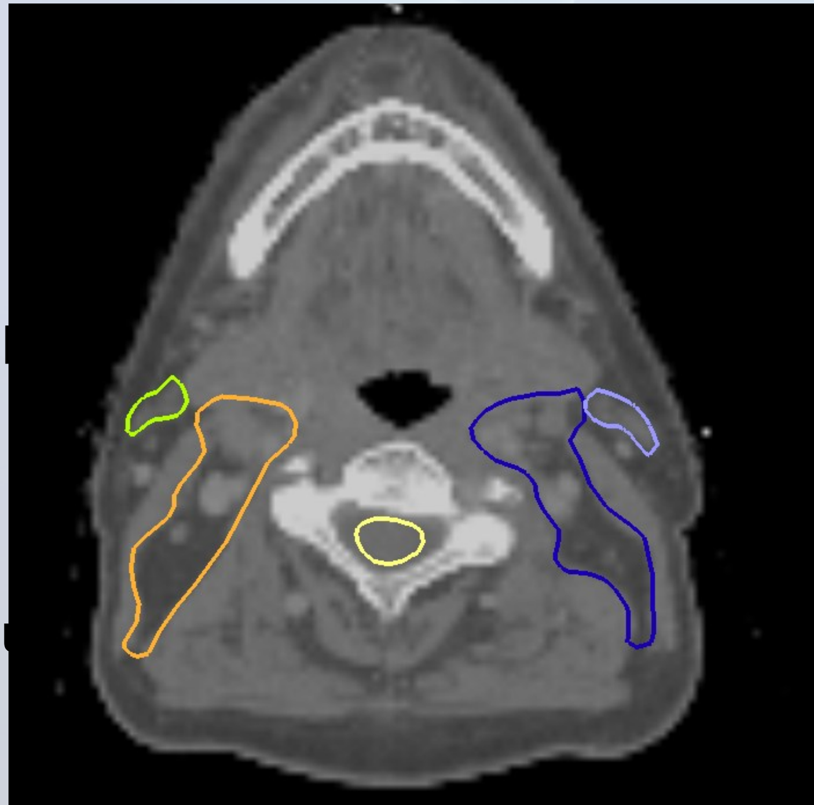
- Evaluation in clinical conditions [Isambert et al., 2008]
  - Done at Institut Gustave Roussy
  - In the frame of MAESTRO European project

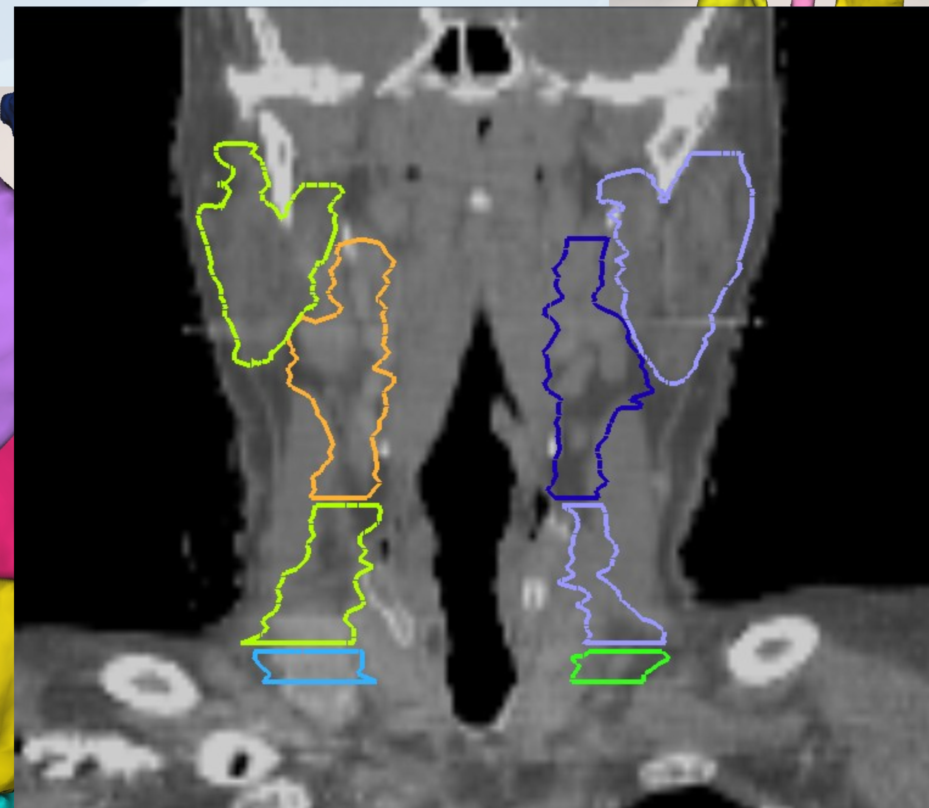


A. Isambert, F. Dhermain, F. Bidault, **O. Commowick**, P.-Y. Bondiau, G. Malandain and D. Lefkopoulos. Evaluation of an atlas-based automatic segmentation software for the delineation of brain organs at risk in a radiation therapy clinical context. Radiotherapy Oncology, 87(1):93-99, 2008.

Head and Neck Anatomy





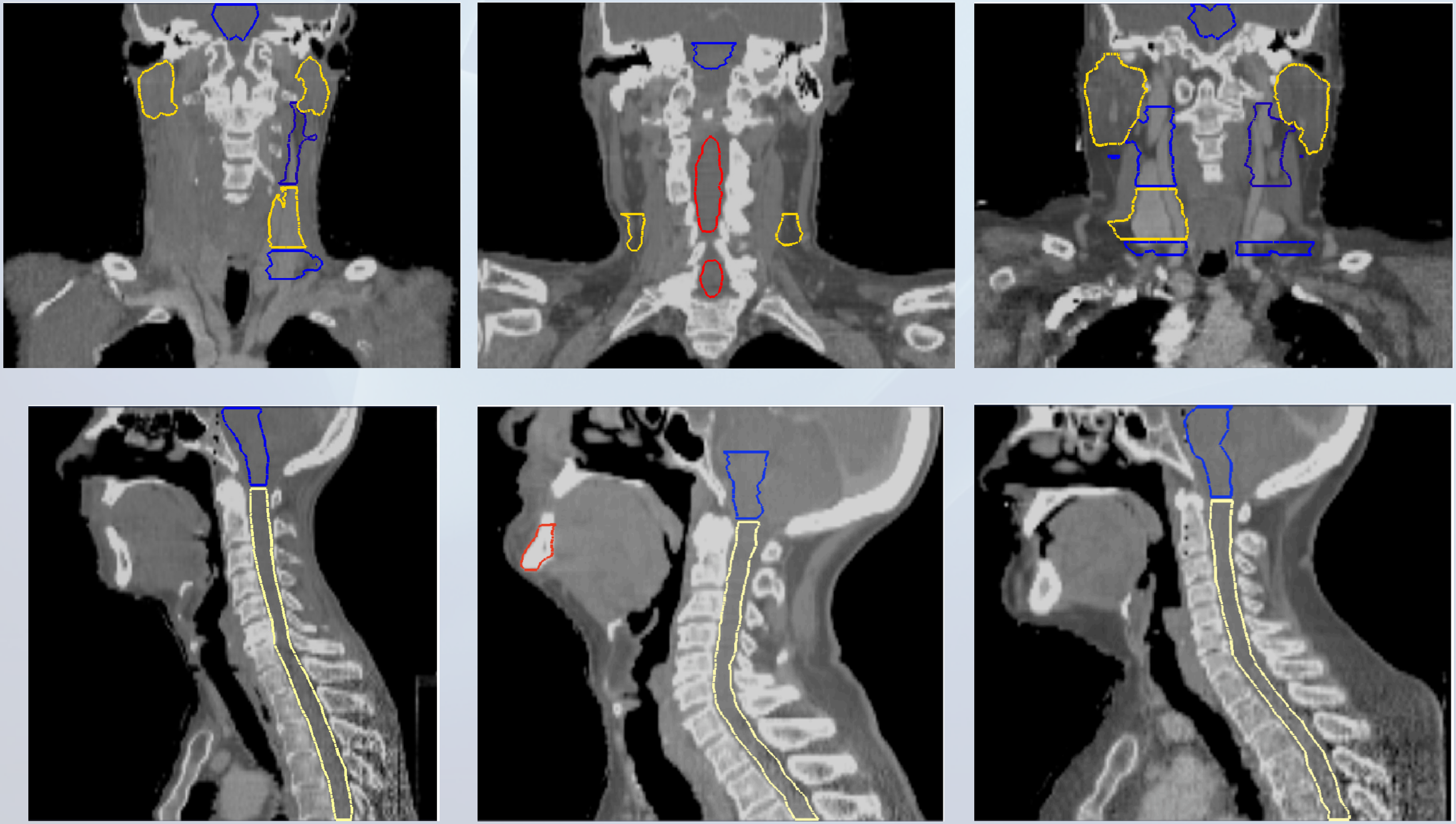


[Grégoire et al., 2003] CT-based delineation of lymph node levels and related CTVs in the node-negative neck : DAHANCA, EORTC, GORTEC, NCIC, RTOG consensus guidelines. Radiotherapy Oncology, 2003.

Evaluation protocol

- Image database
  - 105 patient CT-scan images (Pr. V. Grégoire, MAESTRO)
  - Small tumors not deforming the surrounding anatomy (N0 grade)
  - Various patient position and anatomy
- Evaluation of atlas construction and segmentation
  - Leave-one-out approach
  - M_1: Dense registration
  - M_2: Locally affine registration

Image Database Examples

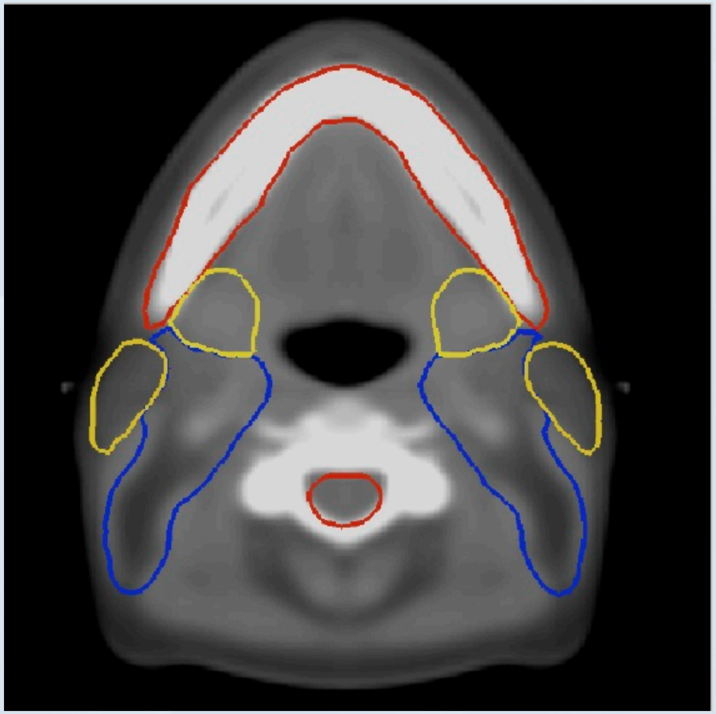


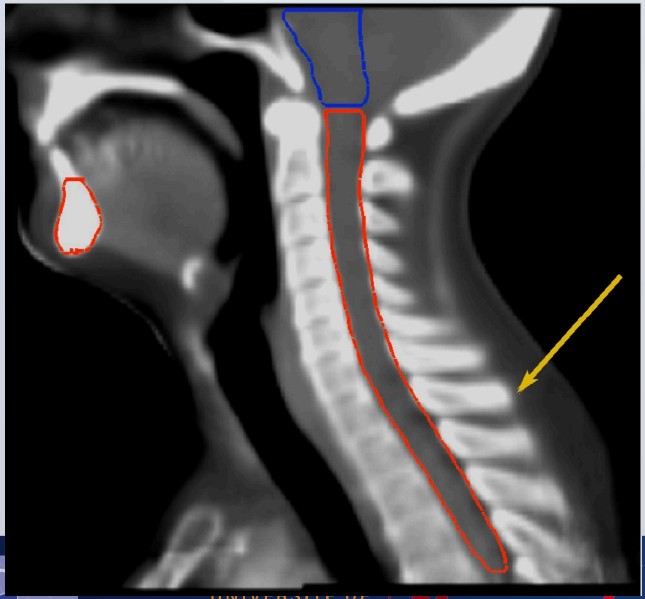
Obtained Atlases

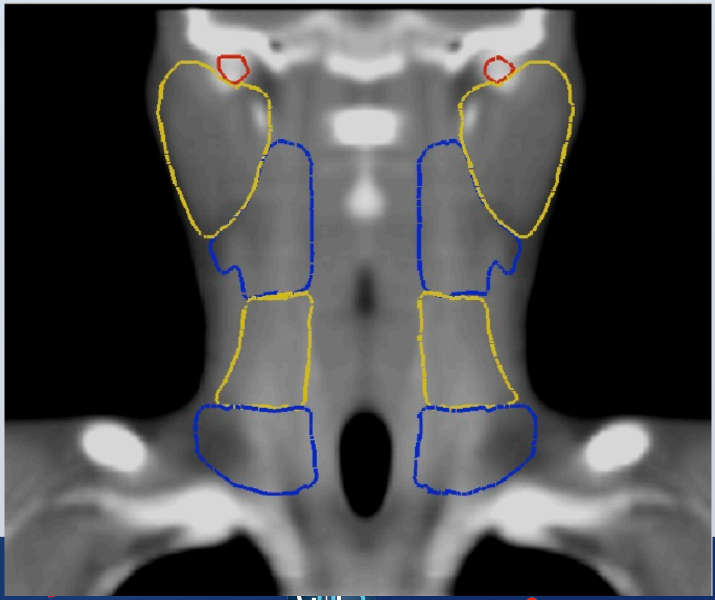
M_1 Atlas

Obtained Atlases

M_2 Atlas

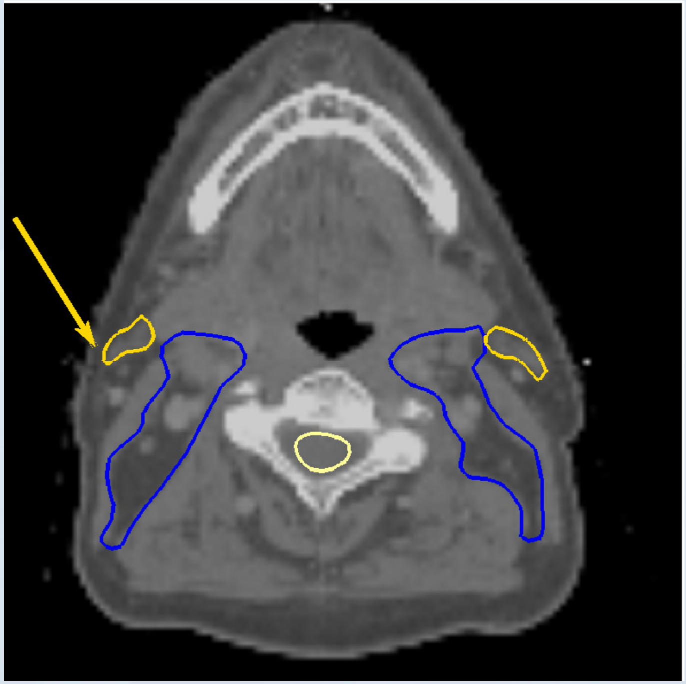


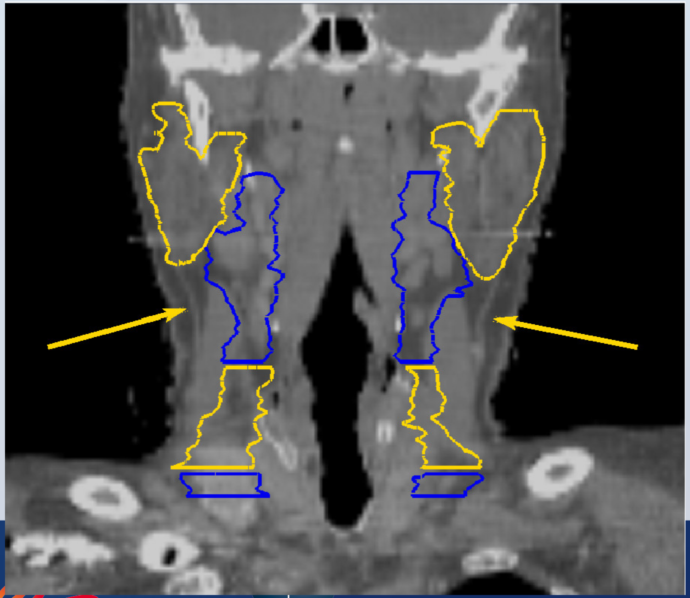




Qualitative Results

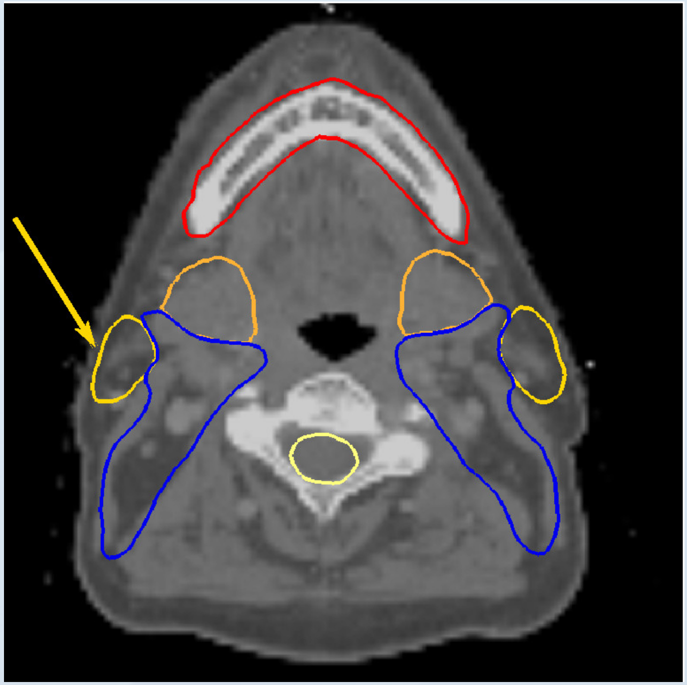
Manual Segmentation

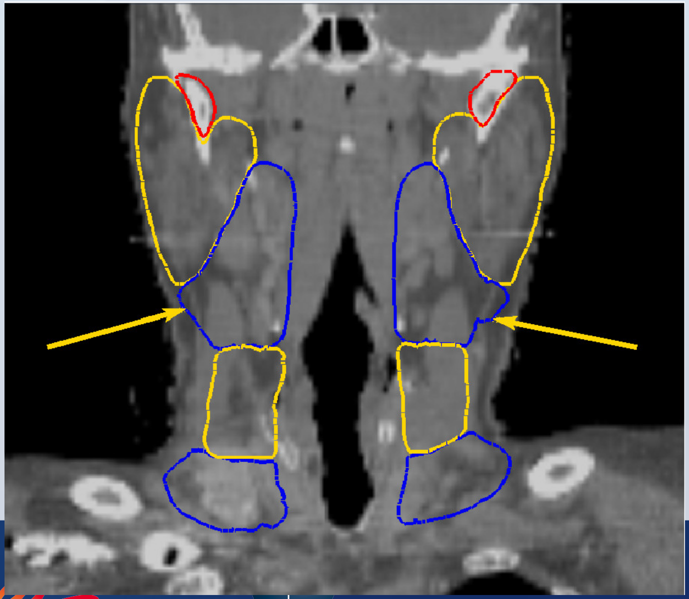




Qualitative Results

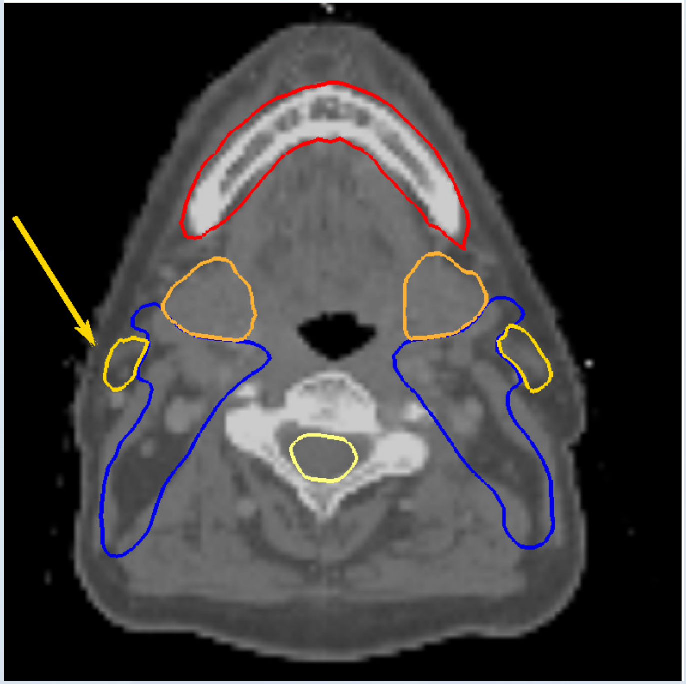
M_1 Atlas Segmentation

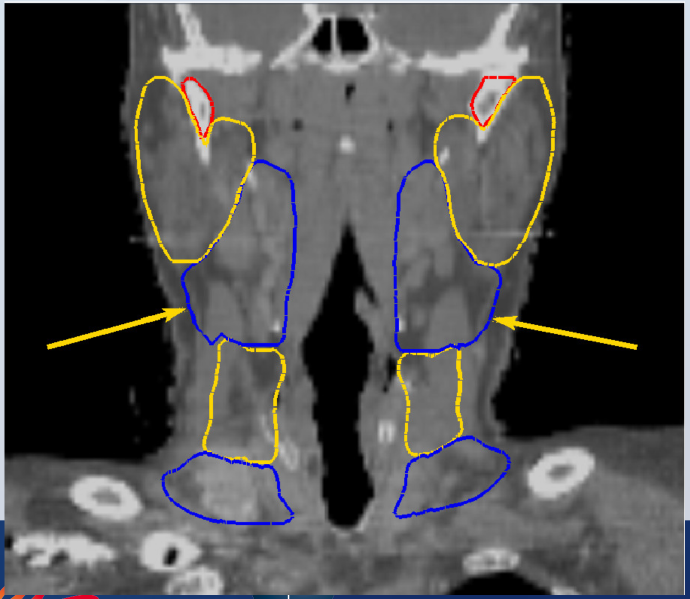




Qualitative Results

M_2 Atlas Segmentation





Summary

- Registration has to be adapted to the task
  - Enough freedom to recover deformations
  - Enough constrained to be smooth and robust
- Constrained parametric transformations
  - Locally affine registration: particularly adapted to this task
    - Robust: one parameter set for all tested acquisition protocols
    - Ideal for articulated structures (head and neck)
- Registration is important
  - But an adapted atlas may be even more
  - Mis-registrations and over-segmentations may appear

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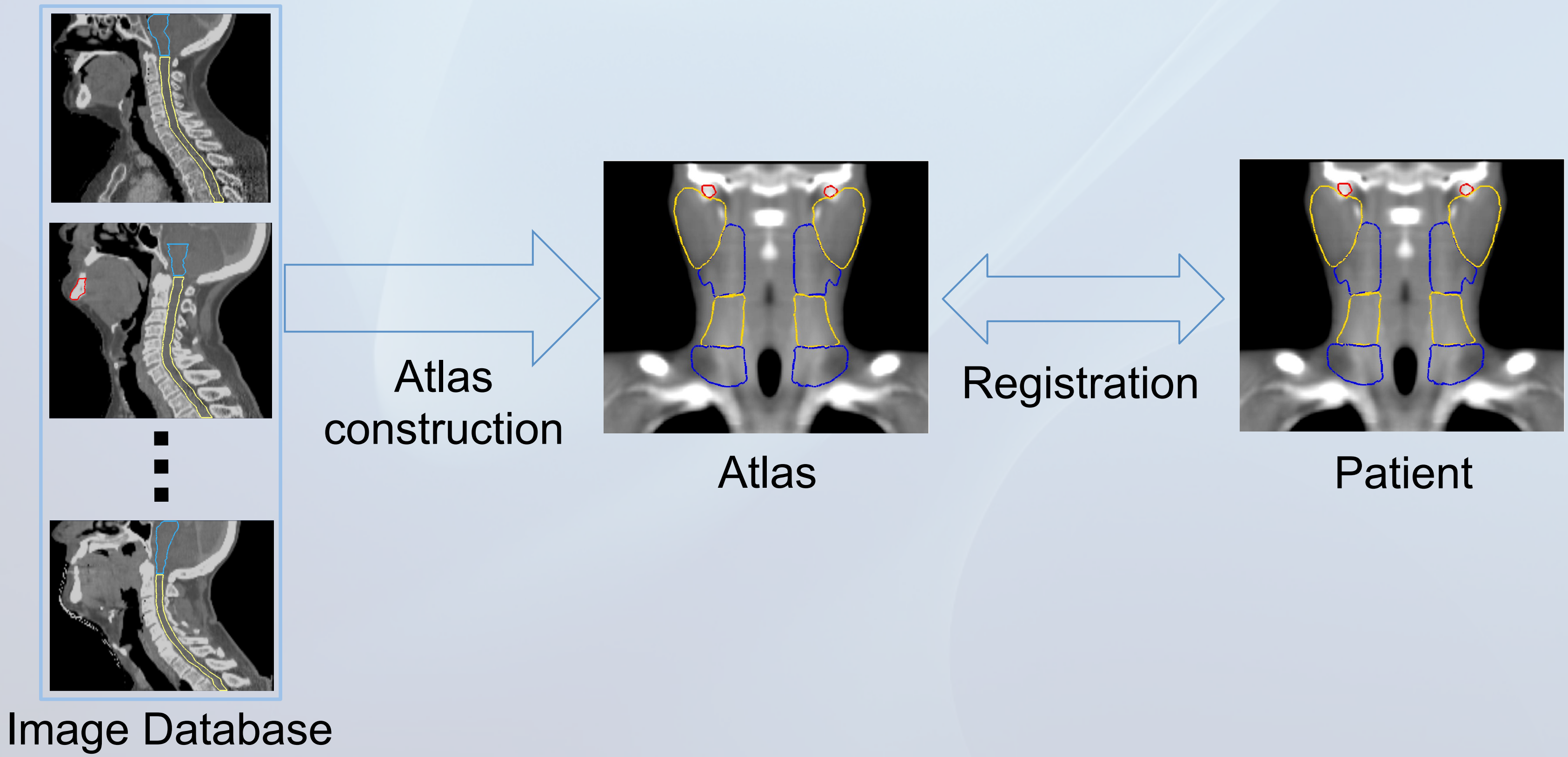
Adapting Atlas to Specific Anatomies

- Challenge
  - Anatomy may greatly vary between patients
  - Very difficult to handle with a single atlas
- Objective: get robust atlas-based segmentation
  - Other approaches to atlas construction
  - Selection of images close to the patient
    - A posteriori selection
    - A priori selection

Adapting Atlas to Specific Anatomies

- First solution: utilizing multiple atlases



Adapting Atlas to Specific Anatomies

- First solution: utilizing multiple atlases
  - Remove atlas construction step

[Artaechevarria et al., 2009]: Combination Strategies in multi-atlas image segmentation: Application to brain MR data. IEEE TMI, 2009.

Multiple Atlas Segmentation

- Utilize several template images
  - Each one associated to manual segmentations
  - Register each one on the patient to delineate
  - Combine segmentations on the patient

- Segmentation combination becomes the key
  - Getting rid of mis-registered images
  - Equal weighting of each image: majority voting (MV)
  - A posteriori selection of the images to be used for segmentation
    - SIMPLE, STAPLE, weighted MV, …

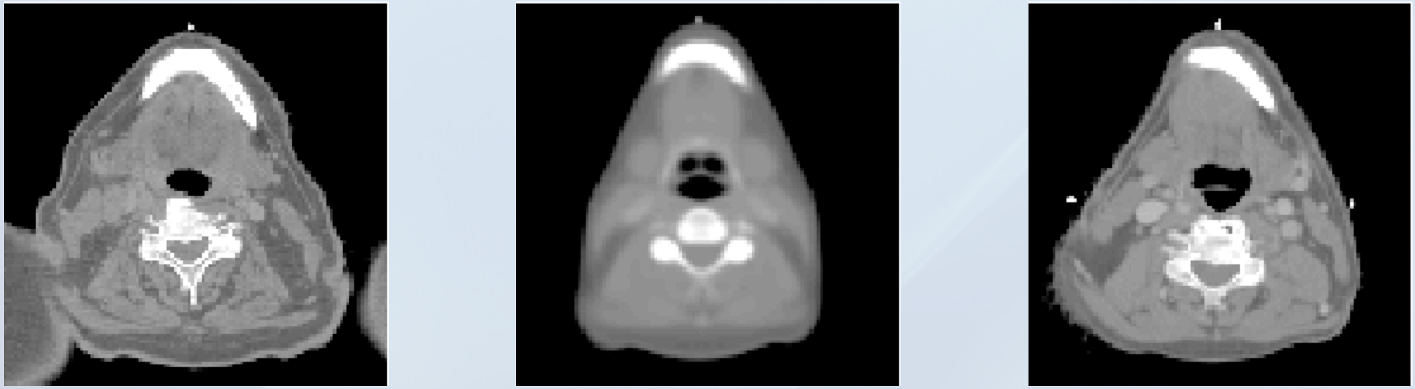
[Warfield et al., 2004] Simultaneous Truth and Performance Level Estimation (STAPLE): an Algorithm for the Validation of Image Segmentation, IEEE TMI, 2004
[Rohlfing et al., 2004] Performance-based classifier combination in atlas-based image segmentation using EM parameter estimation, IEEE TMI, 2004.
[Langerak et al., 2010] Label-fusion in atlas-based segmentation using SIMPLE. IEEE TMI, 2010.

Multi Atlas Segmentation: Summary

- Advantages
  - Potential for better registrations
  - Ability to reject mis-registered images
  - Improved robustness for large anatomy differences
- Disadvantages
  - A posteriori selection of useful images
    - Problem if many errors in individual registrations
  - Computationally expensive (N registrations instead of 1)
    - Difficult to use in clinical context

Most Similar Atlases Based Segmentation

- Assumption
  - Registration accuracy depends on atlas - patient “similarity”



Patient Average atlas Similar image

- Objective
  - Select a priori only a subpart of the database

O. Commowick, G. Malandain. Efficient Selection of the Most Similar Image in a Database for Critical Structures Segmentation. MICCAI, 2007.

Most Similar Atlases

- Key interrogation
  - How to define “similarity” between images?
  - Central to keep meaningful images

- Two main approaches
  - Similarity from intensities: after registration, similar images have similar intensities
    - Similarity measure (eg SSD) as selection criterion
  - Similarity from transformations: the transformation between similar images is very close to identity
    - E.g. : Log-Euclidean distance between transforms

- Choosing the right selection measure is an open problem

Most Similar Multi Atlas Segmentation

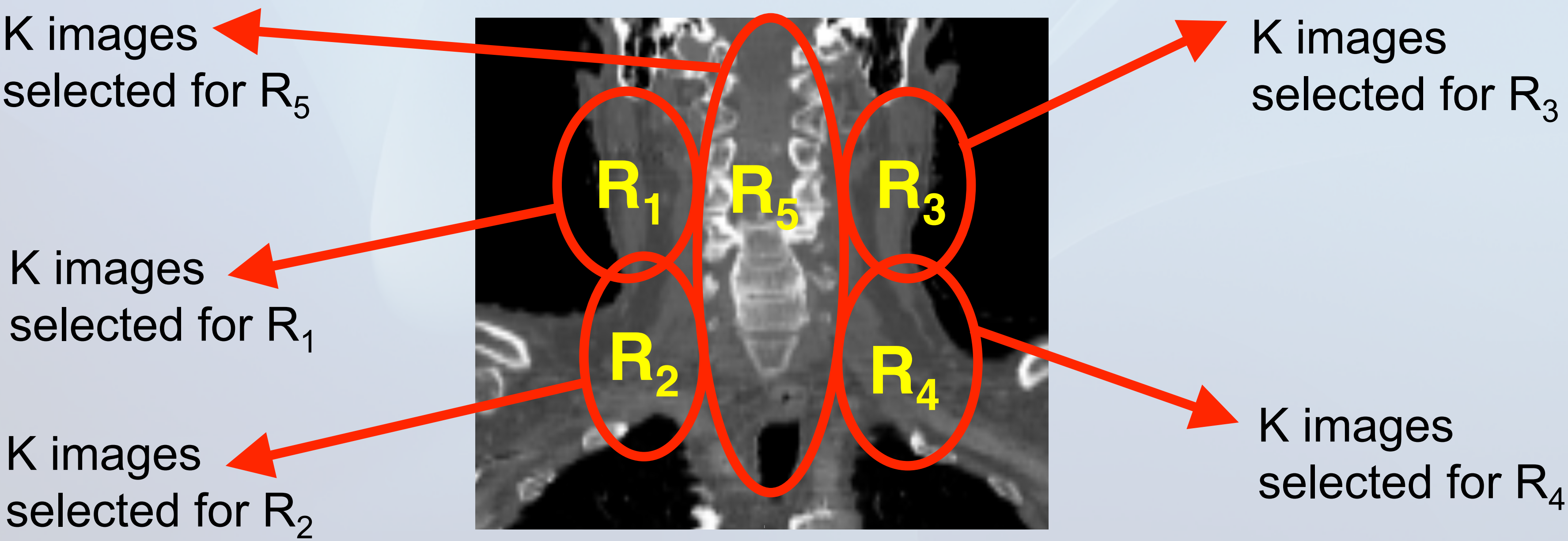
- Method from Aljabar et al
  - Register all atlases on a reference
  - Select the K most similar images at a global scale
    - Selection based on intensity between patient and template image
  - Combine the K most similar segmentations

- Advantage
  - Improved results compared to multi-atlas segmentation
- Disadvantage
  - Selection at a global scale

O. Commowick et al.. Efficient Selection of the Most Similar Image in a Database for Critical Structures Segmentation. MICCAI, 2007.
P. Aljabar et al. Multi-atlas based segmentation of brain images: Atlas selection and its effect on accuracy. Neuroimage, 46(3), 2009.

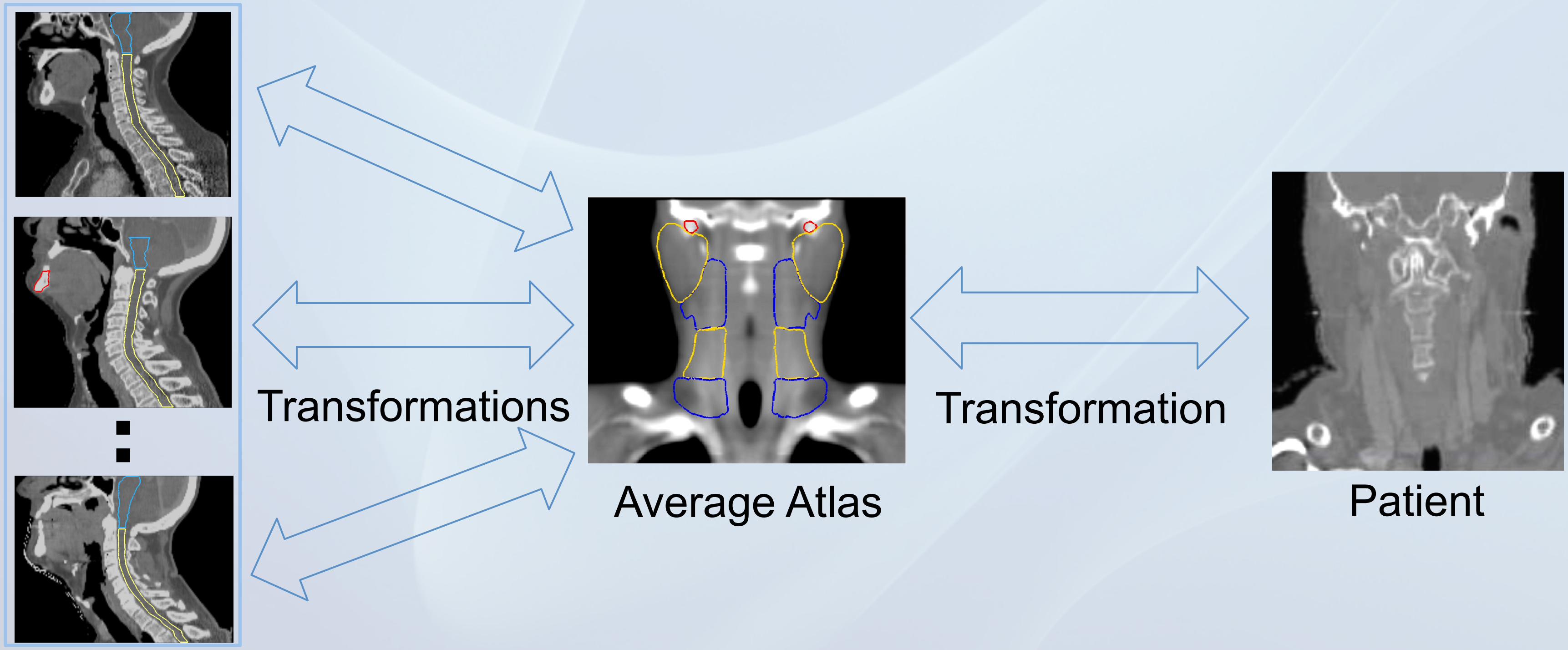
Locally Most Similar Atlas: Frankenstein

- Another approach: the “Frankenstein’s creature”
  - Select K images for several predefined regions of interest
  - Combine them into a patient-specific atlas



L. Ramus, O. Commowick, G. Malandain. Construction of Patient Specific Atlases from Locally Most Similar Anatomical Pieces. In MICCAI, Beijing China, 2010.

Efficient Selection of the Most Similar Images



- Atlas as an intermediate image
  - Regions of interest defined on the average atlas
  - Correspondences database images – atlas precomputed

Efficient Selection of the Most Similar Images

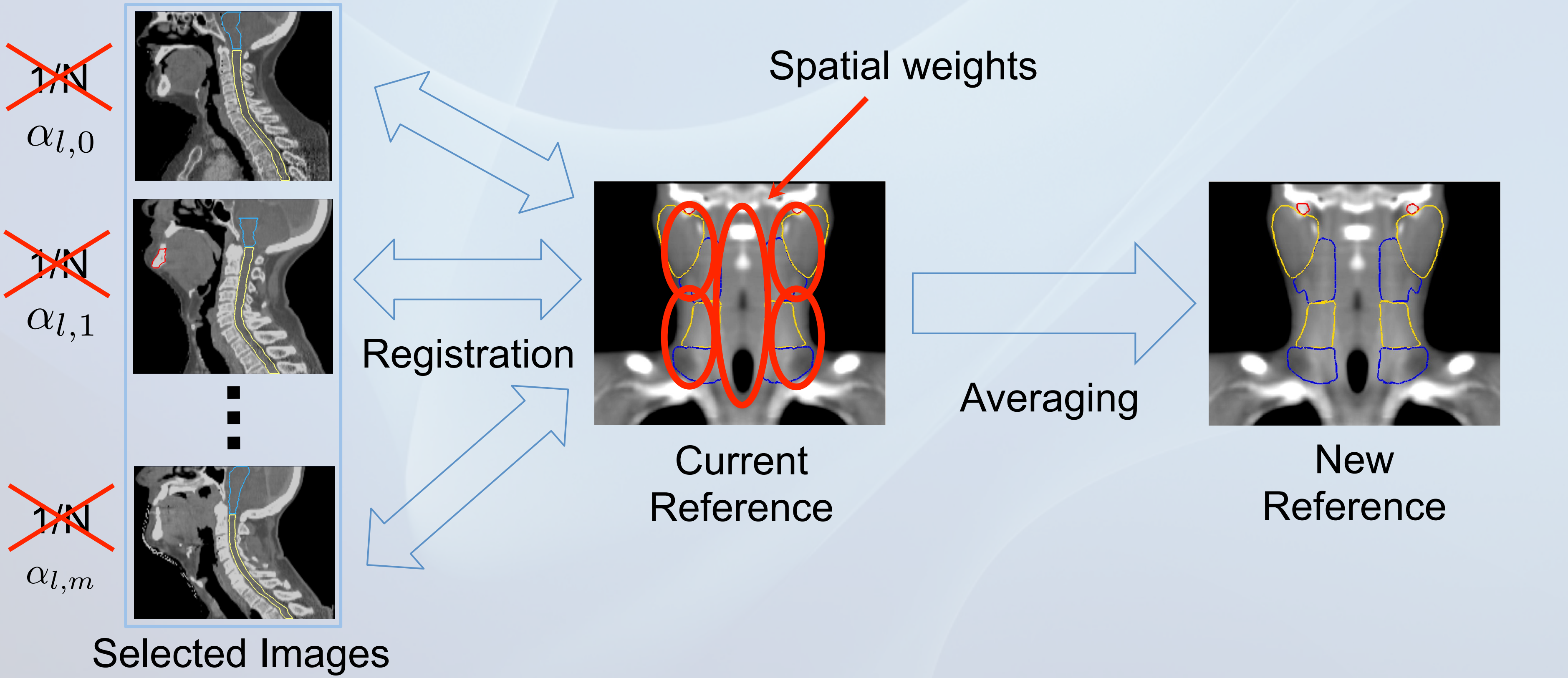
- Selection based on deformations
  - Between database image and average atlas : $T_{I_j \leftarrow M}$
  - Between patient and average atlas : $T_{P \leftarrow M}$

- For each region, rank images according to $d_{R_l}(I_j, P)$
  - Compare average dilation/contraction in the region of interest
  - Utilizes average Jacobians of the deformations $\bar{J}_{R_l}(T)$

$$d_{R_l}(I_j, P) = \|\bar{J}_{R_l}(T_{P \leftarrow M}) - \bar{J}_{R_l}(T_{I_j \leftarrow M})\|$$

- Result : For each R_l , a set of K most similar images $\tilde{I}_{l,k}$

Combining Selected Images into a Template



- Extended Guimond's atlas construction
  - Spatially varying weights for images

Combining Selected Images into a Template

- First step: Average of images weighted by
  - Region of selection : distance to the region R_l
  - Selection metric : $\alpha_{l,m} = G_{\mu,\sigma}(d_{R_l}(\tilde{I}_{l,m}, P))$

$$M_{k+1}(x) = \frac{1}{N}\sum_j I_j \circ T_j(x) \Longrightarrow M_{k+1}(x) = \sum_{l=1}^{L}\left[\underbrace{\boxed{\bar{w}_{l,k}(x)}}_{\text{Spatial weights}}\left(\sum_{n=1}^{K_l}\underbrace{\boxed{\bar{\alpha}_{l,n}}}_{\text{Selection weights}}\left(\tilde{I}_{l,n} \circ T_{\tilde{I}_{l,n}}\right)(x)\right)\right]$$

- Second step: Modified unbiasing step
  - Compute an average transformation (polydiffeomorphism)

$$\bar{T} = \exp(\frac{1}{N}\sum_j \log(T_j)) \Longrightarrow \bar{T} = \exp\left[\sum_{l=1}^{L}\boxed{\bar{w}_{l,k}(x)}\left(\sum_{n=1}^{K_l}\boxed{\bar{\alpha}_{l,n}}\log\left(T_{\tilde{I}_{l,n}}\right)(x)\right)\right]$$

  - Apply $\bar{T}^{-1}$ to the new reference $\tilde{M}_{k+1} = M_{k+1} \circ \bar{T}^{-1}$

Road Map

- Introduction
- Image Registration for Atlas Based Segmentation
  - Challenges and Review
  - One Adapted Technique: Locally Affine Registration
  - Example Results
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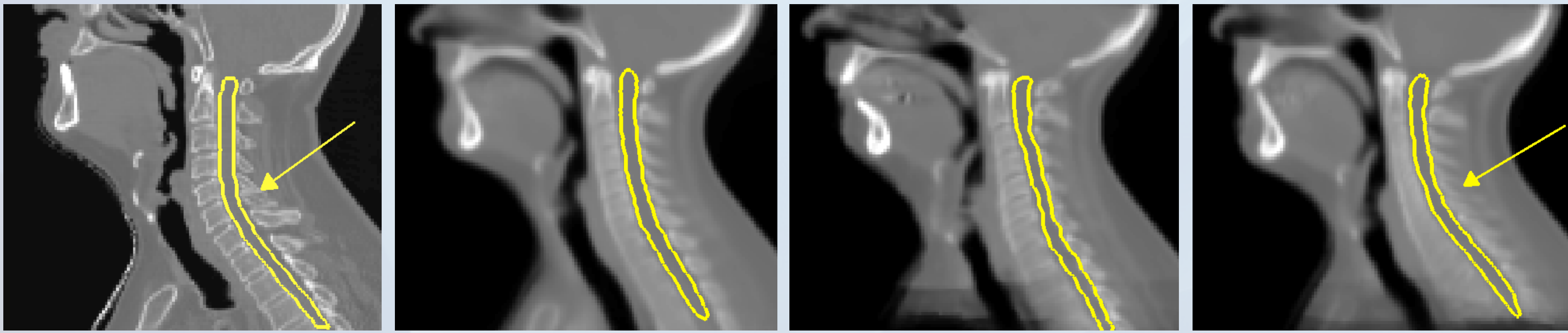
Atlas Comparison

- Adaptation to neck flexion



Patient

Average atlas

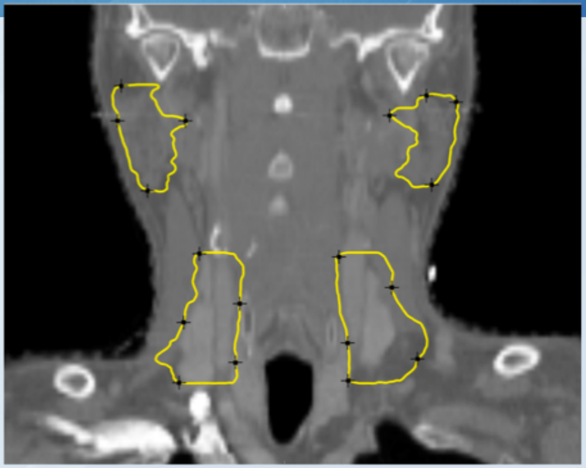
Piecewise most similar atlas built from K=1 image per region

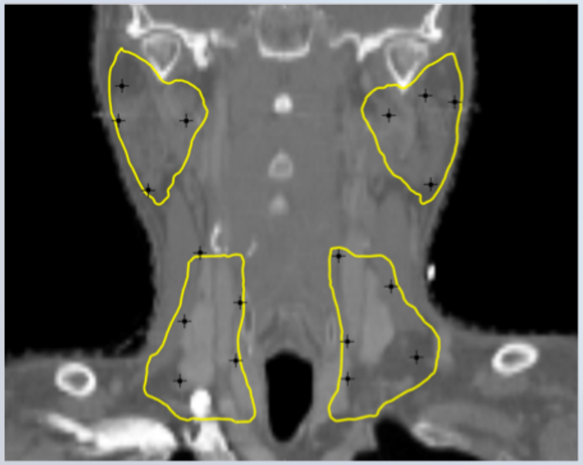
Piecewise most similar atlas built from K=10 images per region

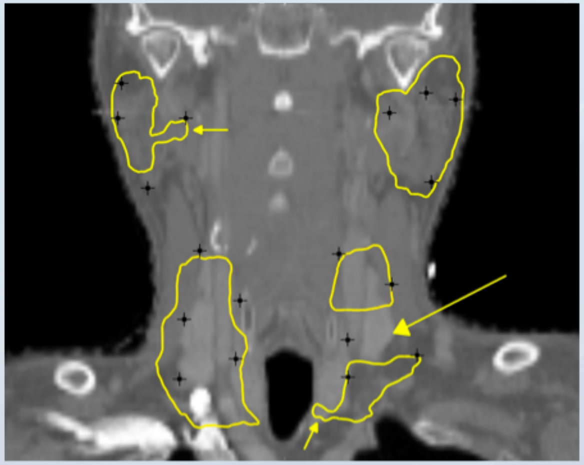
After affine registration on the patient

Segmentation Results

Manual
segmentation







Automatic segmentations obtained with:

Average atlas

Frankenstein with K=1
image per region

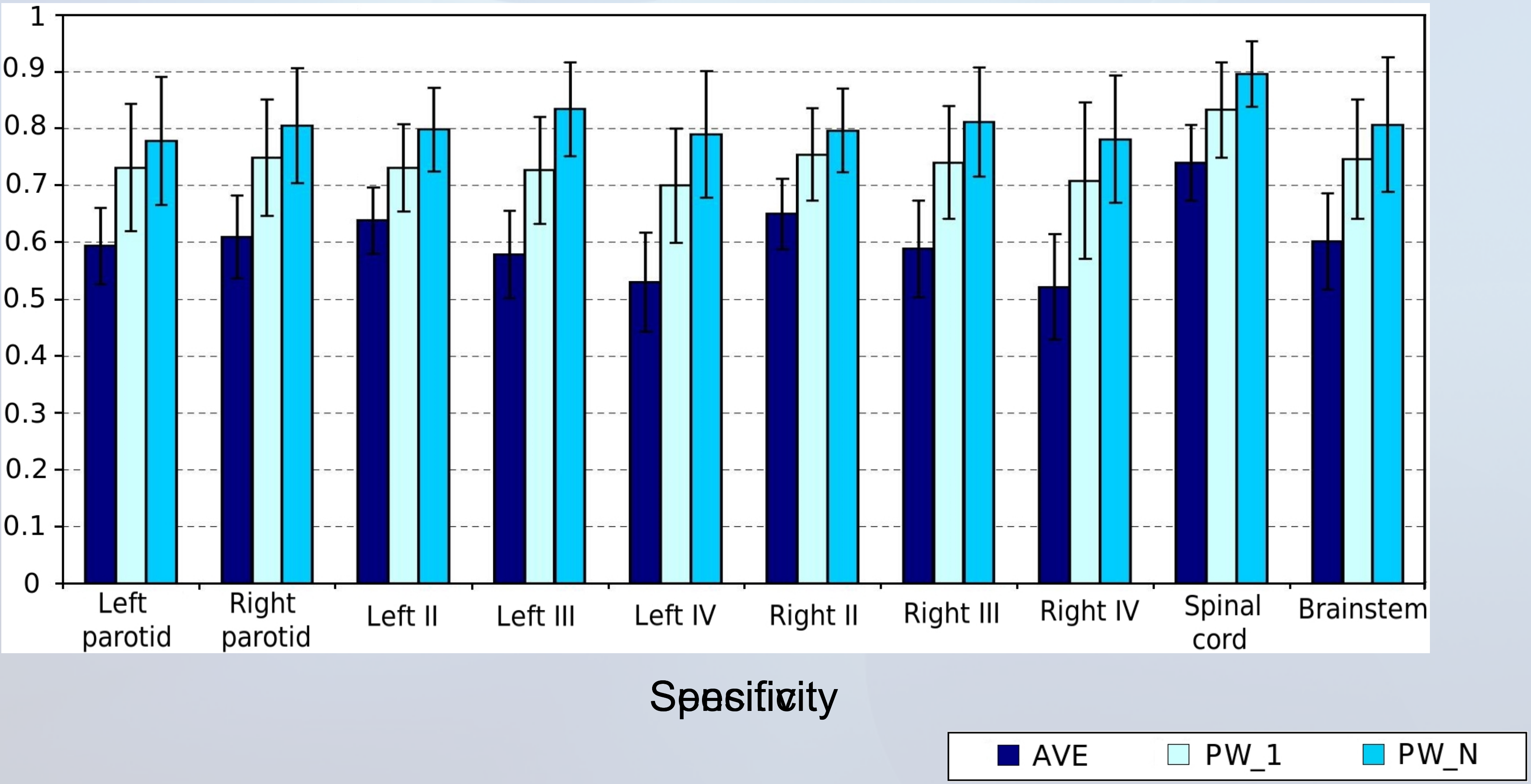
Frankenstein with K=10
images per region

Over-segmentation

- Local specificities
- Discontinuities

Quantitative Results

- Leave-One-Out study on 105 CT images



Specificity

Summary

- Two main approaches to build patient adapted atlases
  - A posteriori selection of useful templates
    - Multi-atlas segmentation
  - A priori selection of most similar images
    - Frankenstein, most similar multi atlas segmentation
- Similarity for selection
  - Open problem
  - Intensity, transformation, segmentations
- Able to handle anatomy variability
  - Often at the cost of multiple registrations

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Conclusion

- Atlas based segmentation
  - Fast and robust technique for segmentation

- Several key points
  - Registration: robust and precise (local affine nice for head and neck)
  - Atlas selection strategy (eg multi atlas, Frankenstein)
    - Keep only images that are close to the patient
    - Local a priori selection
    - A posteriori robust combination of segmentations

- Results
  - Average atlas: good positioning, over-segmentation
  - Adapted atlas: more precise segmentation

Perspectives

- Registration is always perfectible
  - Much research on automatic detection of local affine regions
  - New dense methods may be better adapted to brain cortical structures
- How to define image closeness?
  - No measure is perfect, many choices
  - Utilizing several measures together
    - Segmentation + intensity?
    - Intensity + Deformation?
- Towards more efficient methods: large databases

Contacts & Acknowledgments

- Contacts
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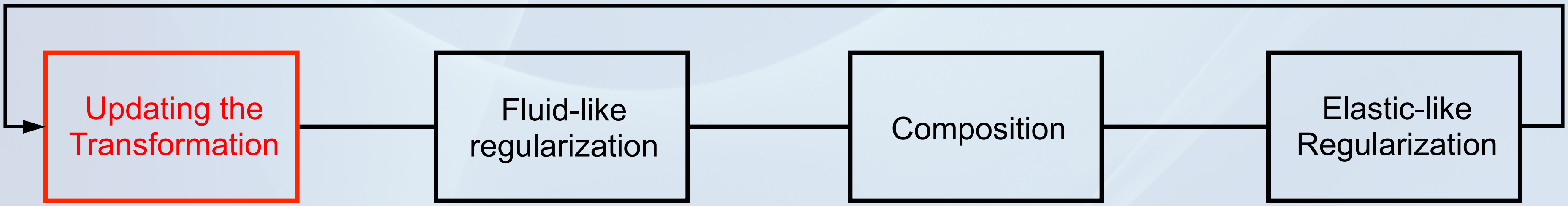
- INRIA
  - Asclepios Team (http://www-sop.inria.fr/asclepios)
  - VisAGeS Team (https://www.irisa.fr/visages)
- CRL, Children's Hospital Boston (http://www.crl.med.harvard.edu)
- DOSIsoft S.A (http://www.dosisoft.com)

LAF: Updating the transformation

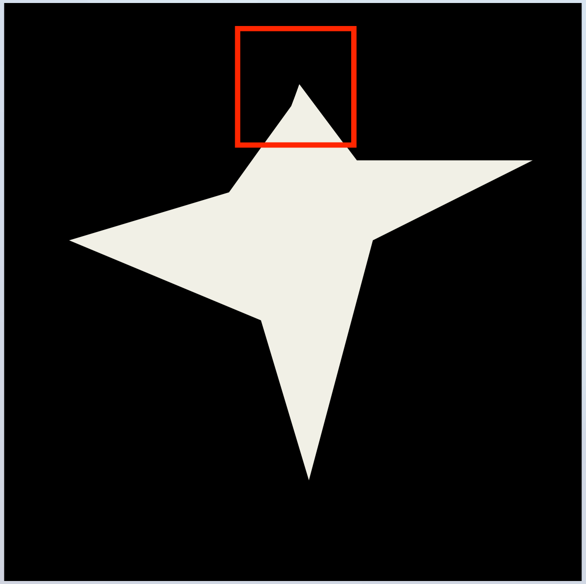


- Local affine correction δA_i estimation
- Block-Matching algorithm [Ourselin et al.]
  - Move blocks in a neighborhood
  - Pairing: chosen according to a similarity value
- Least Trimmed Squares Weighted Estimation
  - Weighted by similarity measure values
  - Weighted by $w_i(x_v)$

[Ourselin et al., 2000]: A General Framework to Improve Robustness of Rigid Registration of Medical Images. MICCAI, 2000.

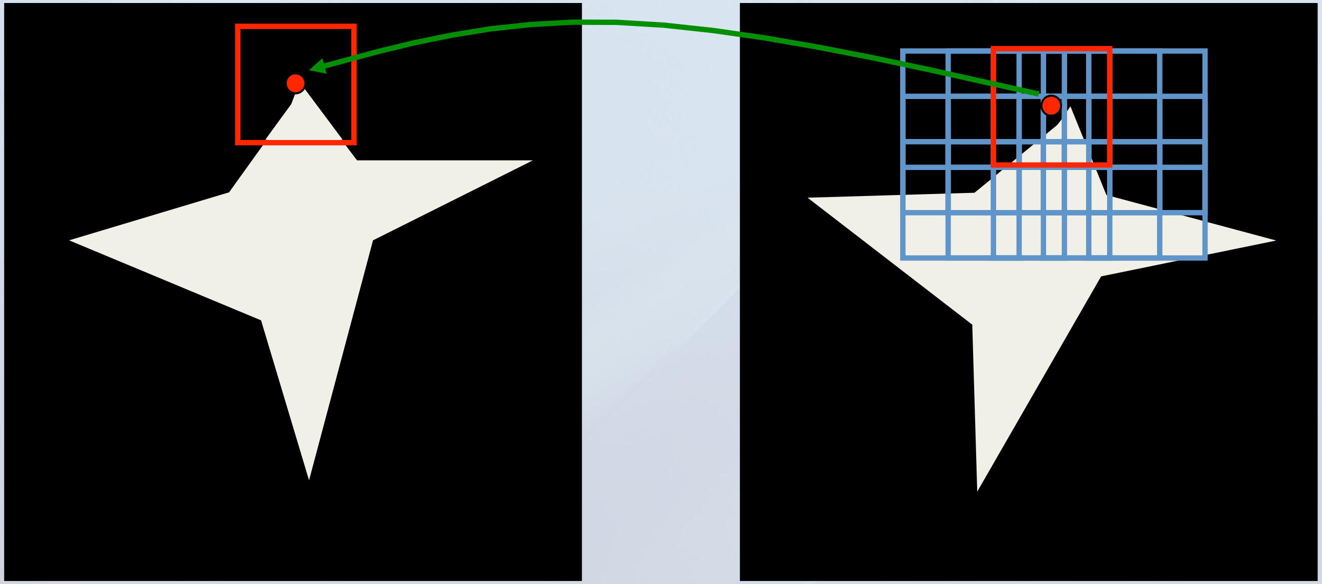
"Block Matching" Technique

- 1. Consider regularly sampled sub-images (or "blocks")



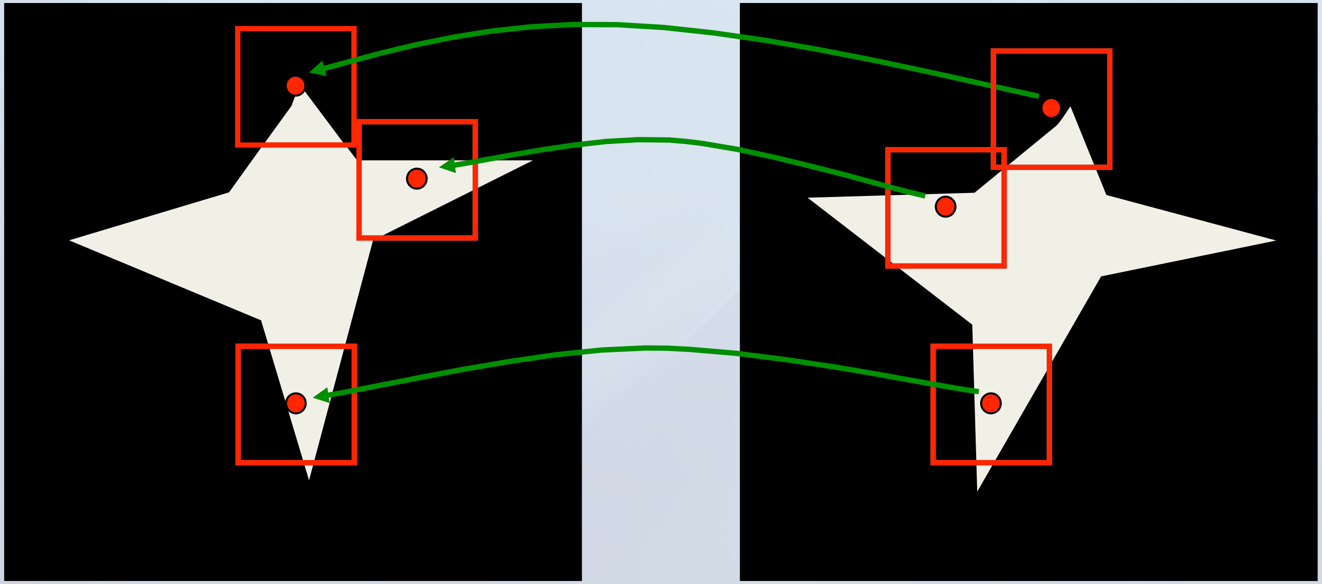
“Block Matching” Technique

- 2. Search the “most similar” block: gives point to point correspondence

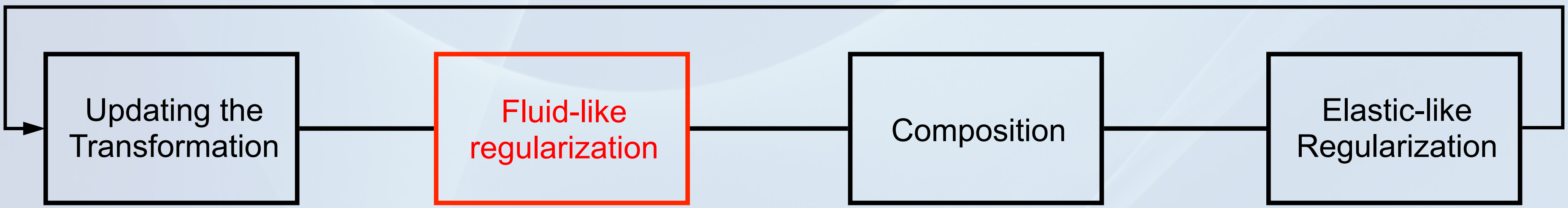


"Block Matching" Technique

- 3. Obtain pairings between regions



LAF: Fluid-like Regularization

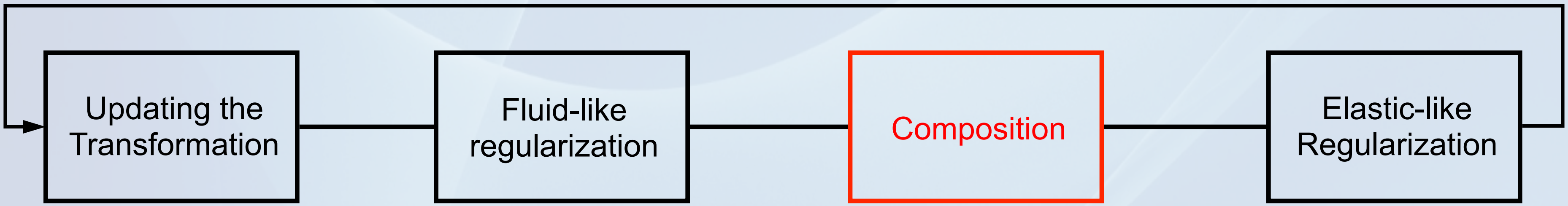


- Fluid-like regularization of local transformation corrections
- Gradient descent on

$$\mathrm{Reg}(\delta A_i, w_i) = \sum_{i=1}^{N} \sum_{j \neq i} p_{i,j} \| \log(\delta A_i) - \log(\delta A_j) \|^2$$

- Log-Euclidean polyaffine framework
  - $\log(A_i)$ belongs to a vector space
  - Generalization of usual regularization energies

LAF: Composition of Corrections

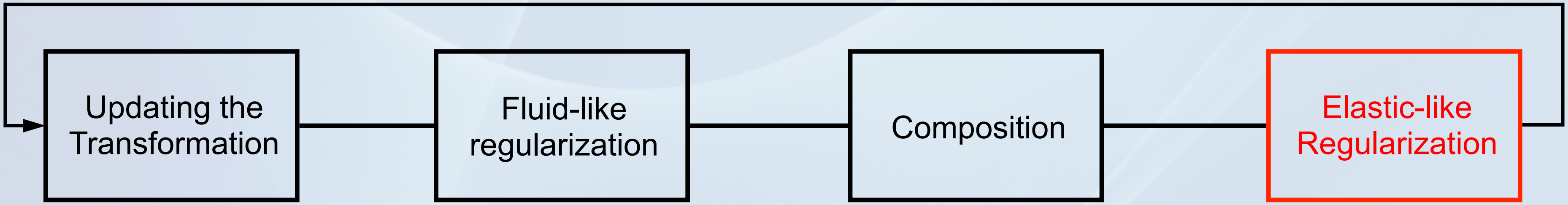


- Regularized corrections: $\delta \tilde{A}_i$

- Composition of corrections with the current transformation

$$A_i^l = A_i^{l-1} \circ \delta \tilde{A}_i$$

LAF: Elastic-like Regularization



- Gradient descent on

$$\mathrm{Reg}(A_i^l, w_i) = \sum_{i=1}^{N} \sum_{j \neq i} p_{i,j} \| \log(A_i^l) - \log(A_j^l) \|^2$$

- Similar to fluid-like regularization
  - Regularization on transformations A_i^l

Measures for Segmentation Validation

- Overlap measures based on a sum over voxels
  - Sensitivity $\mathrm{Sens} = \dfrac{TP}{TP + FN}$
  - Specificity $\mathrm{Spec} = \dfrac{TN}{TN + FP}$