Design and Use of Anatomical Atlases for Radiotherapy

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Jury:

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Road Map

• Introduction
• Incorporating Priors in Non Linear Registration
• Atlas-Based Brain Segmentation
• Head and Neck Atlas-Based Segmentation
• Conclusion and Perspectives
Medical Context

• Different cancer treatments
  • Chemotherapy
    – Drugs killing cells in division
  • Surgery
    – Remove physically the tumor
  • Radiotherapy
    – High irradiation killing cells in division

• Treatment of tumors on two regions
  • Brain
  • Head and Neck
Radiotherapy

- 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
Brain Anatomy

• Many organs at risk
  • Eyes, optic nerves, chiasma
  • Brainstem, cerebellum
  • Grey nuclei

• Different categories [Pontvert, 2004]
  • Very high risk (eyes)
  • High risk (optic nerves, brainstem)
  • Medium risk (grey nuclei)

Head and Neck Anatomy

• Structures of interest
  • Lymph nodes areas
    – Separated using visible landmarks
    – Tumor dissemination regions
  • Parotids
  • Spinal cord
  • Sub-mandibular glands

Radiotherapy planning

• Requires an accurate delineation
  • Head and Neck radiotherapy
    – Only CT image acquired, necessary for dosimetry
  • Brain radiotherapy
    – MRI exam often added
    – Better differentiation of soft tissues

• Segmentation done manually
  • Time consuming (2 to 4 hours)
  • Not reproducible

• Objective: provide fast and automatic segmentation tools
Automatic Segmentation for Radiotherapy

• Goal: automatic segmentation of organs at risk

• Available segmentation methods
  • Intensity based (adaptive thresholding, EM)
    ‒ No prior on shape or position
  • Deformable models, level-sets, active contours
    ‒ Possible priors on structures
  • Atlas based segmentation
    ‒ Atlas: image and its segmentation
    ‒ A priori on respective positions and shapes

Increasing prior knowledge
Atlas Construction

• First approach:
  • One image delineated by an expert
    – Brain atlas (from Dr. Pierre-Yves Bondiau [Bondiau, PhD, 2004])
    – must be representative (possible bias)

Atlas Construction

• Second approach:
  • Average image from a dataset of images
  • Head and neck atlas
    – Images from Pr. Vincent Grégoire (UCL)
Atlas-based Segmentation Principle

First alignment (affine)
Atlas-based Segmentation Principle

Second alignment (non linear)
Non linear transformations

- Tradeoff in non linear registration
  - Able to handle atlas/subject variability
  - Robust and smooth

- Transformations:
  - Parametric
    - Interpolated between control points
    - Arbitrary number of degrees of freedom
    - RBF [Rohde et al., 2003], FFD [Rueckert et al., 1999]
  - Dense
    - One displacement vector per voxel
    - Maximal number of degrees of freedom
    - Pasha [Cachier et al, 2003], …

Challenges in Atlas-Based Segmentation

• Goal: Automatic segmentation of critical structures for radiotherapy

• Requirements:
  • Minimal interaction from user
  • Robust to different acquisition protocols
  • Realistic contours in a minimal time

• Key point of the approach: non linear registration
  • Smooth transformation
  • Able to handle atlas/subject variability
  • Robust registration method
  • Method as fast as possible
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Road Map

• Introduction

• **Incorporating Priors in Non Linear Registration**
  • Existing Registration Method
  • Incorporating Deformability Statistics in Registration
  • Non Linear Registration with Outlier Rejection
  • Locally affine Registration Framework

• Atlas-Based Brain Segmentation

• Head and Neck Atlas-Based Segmentation

• Conclusion and Perspectives
Existing Dense Non Linear Registration

• Method of [Stefanescu et al., 2004]: Runa
  • Spatially inhomogeneous regularization
  • Fluid regularization on highly variable regions
  • More elastic regularization elsewhere

• Iterative process

Runa: Correction Field Computation

- Computation of correction $\delta T$
  - Gradient descent on a similarity measure:

$$\delta T = \nabla SSD(R, F \circ T^{l-1}) = (R - F \circ T^{l-1}) \cdot (F \circ T^{l-1})$$

- SSD: Sum of Squared Differences
- $R$: reference image
- $F$: floating image
- $T^{l-1}$: transformation obtained at iteration $l - 1$
Runa: Fluid Regularization

- Regularization of correction field

\[ \frac{\partial \delta T}{\partial t}(x) = (1 - k(x)) \Delta \delta T(x) \]

- Weighted by a factor \( k(x) = f_i(\|\nabla R\|) \)
  - Spatially dependent
  - Less confidence (more regularization) in homogeneous regions
Runa: Composition of Correction

- Regularized correction field: $\delta\widetilde{T}$

- Composition with transformation at iteration $l-1$

\[ T^l \leftarrow T^{l-1} \circ \delta\widetilde{T} \]
Runa: Elastic Regularization

- Regularization of the transformation

\[ \frac{\partial T^l}{\partial t} = \nabla (D(x) \nabla T^l) \]

- Weighted by \( D(x) = f_2(i(x)) \)
  - Scalar, tissue dependent \( i(x) \), heuristic model
  - White and grey matter: high regularization
  - CSF: low regularization
Segmentation Result (Runa)
Summary

• Advantages
  • Precise deformations
  • Inhomogeneous regularization

• Drawbacks
  • Noisy contours (not realistic)
  • Registration parameters
    – Need to be set for each patient
    – Need to be set for each acquisition protocol

• Solution
  
  Correction field Computation

  Fluid Regularization
    Spatially dependent

  Composition

  Elastic Regularization
    Tissue-dependent
    Spatially dependent
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Statistics Computation Pipeline

Scalar Mean Deformability

- Isotropic measure of deformability

- Determinant of the Jacobian matrix \( |J_i(x)| \)
  - \( |J_i(x)| > 1 \) : local dilation
  - \( |J_i(x)| < 1 \) : local contraction

- Mean deformability:

\[
\overline{\text{Def}}(x) = \frac{1}{N} \sum_i \text{abs}(\log(|J_i(x)|))
\]
Incorporating Statistics in Regularization

Correction field Computation → Fluid Regularization → Composition → Elastic Regularization

\[
\frac{\partial T^i}{\partial t} = \nabla \cdot (D(x)\nabla T^i)
\]

- Inverse mean scalar deformability measure

\[
D(x) = \left(1 + \lambda \overline{Def}(x)\right)^{-1}
\]

- Values of \(D(x)\)
  - Between 0 and 1
  - Close to 1: High regularization
  - Close to 0: Low regularization
Segmentation Result (Runa, Scalar Statistics)
Segmentation Result (Runa)
Tensor-based Mean Deformability

- Based on tensor derived from the Jacobian matrix

\[ W_i(x) = J_i^T(x) \cdot J_i(x) \]

- Mean deformability

\[ \bar{\Sigma}(x) = \frac{1}{N} \sum_i \text{abs}(\log(W_i(x))) \]

- Quantification of anisotropy in deformability

Incorporating Statistics in Regularization

\[ \frac{\partial T^i}{\partial t} = \nabla \cdot (D(x) \nabla T^i) \]

- Inverse mean tensor-based deformability measure
  - Formula analogous to the scalar case

\[ D(x) = (Id + \lambda \overline{\sum}(x))^{-1} \]
Segmentation Result (Runa, Tensor Based Statistics)
Segmentation Result (Runa, Scalar Statistics)
Summary

- Introduction of deformability statistics [Commowick et al., 2005]
  - Reduced dependency to registration parameters
  - Smoother and more precise contours

- Problems:
  - Time consuming: around 40 minutes
  - Still regularity problems (eyes)
  - Parameters to set for each acquisition protocol

=> Objective: Introduce more robustness and regularity

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• Conclusion and Perspectives
Non Linear Registration with Outlier Rejection

- Block-Matching method [Ourselin et al., 2000]
  - Move blocks in a neighborhood
  - Pairing: chosen according to a similarity value

- Pairings Estimation (Block-Matching [Ourselin et al., 2000])
  - Sparse pairings field $C$
  - Associated to confidence field $k$: similarity value of each pairing

“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 sparse field from \((x_v, y_v), C(x_v) = y_v - x_v\)
Baloo: Updating the Transformation

- Transformation correction $\delta T$ estimation
- Interpolated from pairings weighted by confidence field

$$\delta T = \frac{G_\sigma \cdot kC}{G_\sigma \cdot k}$$

- $G_\sigma$: Gaussian kernel of variance $\sigma$
Baloo: Removal of Outliers

- Comparison between pairings and interpolated corrections

- Outlier criterion \( \|C(x_v) - \delta T(x_v)\| > s \)

- \( s \) depends on mean \( e \) and variance of errors \( \sigma_e \)

\[
e = \frac{1}{N} \sum_v \|C(x_v) - \delta T^l(x_v)\| \\
\sigma_e^2 = \frac{1}{N} \sum_v \left(e - \|C(x_v) - \delta T^l(x_v)\|\right)^2
\]
Baloo: Composition of Corrections

- $\delta I$: correction interpolated from pairings minus outliers

- Composition of current transformation $T^{l-1}$

\[ T^{l-1} : T^l \leftarrow T^{l-1} \circ \delta I \]
Segmentation Result (Baloo)
Segmentation Result (Runa)
Summary

• Dense Registration with Outlier Rejection (Baloo)
  • Faster than classical dense registration (20 minutes)
  • Smooth transformation
  • Precise contours

• Problems left:
  • Still depends on images quality (eyes)
  • Larger slice thickness

• Objectives
  • More robustness by constraining the transformation
  • Registration only on regions of interest
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  • Locally Affine Registration Framework

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Locally Affine Framework

- Principle:
  - Register only anatomic areas of interest
  - Interpolate a global transformation from all local transformations
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, PhD, 2006]


LAF: Updating the Transformation

- Local affine correction $\delta A_i$ 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 \[ \text{Reg}(\delta A_i, w_i) = \sum_{i=1}^{N} \sum_{j \neq i} p_{i,j} \| \log(\delta A_i) - \log(\delta A_j) \|^2 \]

• Log-Euclidean polyaffine framework
  • \( \log(A_i) \) belongs to a vector space
  • Generalization of usual regularization energies
LAF: Composition of Corrections

- Regularized corrections: $\delta A_i$

- 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

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

- Similar to fluid-like regularization
  - Regularization on transformations \( A_i^l \)
Locally Affine Registration

• Final global transformation computation
  • Solution 1 (weighted interpolation): Fast but not always invertible
  • Solution 2 (polyaffine): Slower but always invertible
Segmentation Result (Locally Affine)
Segmentation Result (Baloo)
Conclusion

• Locally Affine Registration [Commowick et al., 2006a], [Commowick et al., 2006b]
  • Smooth transformation
  • Robust registration
    – One parameter set for all tested acquisition protocols
  • Fast computation time (10 minutes)

• Registration method able to recover large displacements
  • Ideal for articulated structures (head and neck)


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Evaluation Methodology

- Three evaluation methods
  - Visual inspection
  - Semi-quantitative validation
    - Visual inspection by a clinician
    - Graduation between 0 and 5
  - Quantitative validation
    - Experts manual segmentations
    - Two steps:
      - Ground truth computation using STAPLE [Warfield et al., 2004]
      - A posteriori computation of sensitivity/specificity

Brain Evaluation

- Database of MRI from CAL Nice (Dr. P.-Y. Bondiau)
  - 2mm slice thickness

- Use of manual expert segmentations
  - Brainstem: 7 experts, 6 patients
Quantitative Evaluation (II): Runa, Baloo, LAF

![Graph showing sensitivity and specificity for different methods.]

- Experts
- Runa
- Baloo
- Multi-Affine
Evaluation in Clinical Conditions (Runa)
Evaluation in Clinical Conditions (Baloo)
Evaluation in Clinical Conditions (LAF)
Semi-Quantitative Evaluation in Clinical Conditions

• Evaluation in clinical conditions [Isambert et al., 2005]
  • Done at Institut Gustave Roussy
  • In the frame of MAESTRO European project

[Isambert et al., 2005]: Requirements for the use of an atlas-based automatic segmentation for delineation of Organs at Risk (OAR) in conformal radiotherapy (CRT): quality assurance (QA) and preliminary results for 22 adult patients with primary brain tumors. ESTRO, 2005.
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    • Atlas Construction Method
    • Atlas Evaluation
    • Results
• Conclusion and Perspectives
Head and Neck Atlas Construction

• Atlas construction
  • From a dataset of delineated images
  • Needs to be representative of all patients
    – Symmetric atlas construction method
  • Other possible method: [Grabner et al., 2006]

• Three steps construction method
  • Mean image construction
  • Mean segmentations
  • Atlas symmetrization

[Grabner et al., 2006]: Symmetric Atlassing and Model Based Segmentation: an Application to the Hippocampus in Older Adults. MICCAI, 2006.
Atlas Construction Method

Images and manual delineations database → Mean Image Construction (not symmetric) → Mean Image Symmetrization → Symmetric Atlas

Images → Transformations → Mean Segmentations Construction (not symmetric) → Transformation
Mean Image Construction

• Unbiased atlas construction [Guimond et al., 2000]:
  • Iterate the following process

  - Take the average model as new reference image

Mean Segmentations

• One transformation for each patient
  • All segmentations in the mean image referential

• Mean segmentation using STAPLE [Warfield et al., 2004]:
  • Estimation of mean segmentations
  • Computation of performance parameters

• Probability maps for each class (including background)
  • A posteriori classification into structures

[Warfield et al., 2004]: Simultaneous Truth and Performance Level Estimation (STAPLE): an Algorithm for the Validation of Image Segmentation, IEEE TMI, 2004
Atlas Symmetrization

• Method of [Prima et al., 2002]
  • Obtain transformation $R$ bringing $I$ on its mid-sagittal plane
  • Principle: registration between $I$ and the mirrored image $I \circ S$
  • $R$ satisfies the relation $I \circ R = I \circ R \circ S$

• Mean symmetric image obtained from $\tilde{M}$

$$\tilde{M}_S = \frac{\tilde{M} \circ R + \tilde{M} \circ R \circ S}{2}$$

• Mean symmetric segmentations obtained in two steps
  • Symmetrization of the probability maps from STAPLE
  • A posteriori classification into structures

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  - Atlas Construction Method
  - Atlas Evaluation Strategy
  - Results
- Conclusion and Perspectives
Atlas Evaluation Strategy

• Leave-One-Out method
Evaluation protocol

• Image database:
  - 45 patient CT-scan images (Pr. V. Grégoire, MAESTRO)
  - Different tumors shapes at different localizations
  - Small tumors not deforming the surrounding anatomy (N0 grade)
  - Various patient position and anatomy

• Three registration methods compared:
  - $M_1$: Block-Matching based dense registration method
  - $M_2$: Locally-affine registration method
  - $M_3$: $M_2$ followed by $M_1$
Image Database Examples
Road Map

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Obtained Atlases

$M_3 \cap M_2 \cap (M_1 \cup M_0)$
Qualitative Results

Manual Segmentation

M2 Atlas Segmentation
Quantitative Atlas Evaluation

• Use of Leave-One-Out method:
  • Mean over 12 patients completely delineated (13 structures)

• $M_3$ Atlas performs better for atlas construction
Conclusion

• Symmetric atlas construction method
  • From existing techniques

• Atlas Evaluation method [Commowick et al., 2006c]
  • Registration method to build the atlas
  • Registration method to register the atlas

• Application to Head and Neck
  • Hierarchical registration (M₃): well adapted in this context
  • Promising results
  • Many perspectives on atlas construction

[Commowick et al., 2006c]: Evaluation of Atlas Construction Strategies in the Context of Radiotherapy Planning. SA2PM Workshop, held in conjunction with MICCAI. 2006.
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Contributions

• Registration
  • Introduction of deformability statistics in registration
  • Dense registration with outlier rejection
  • Locally affine framework
    – Good results without changing parameters

• Head and neck atlas
  • Atlas construction method from a dataset of CT images
  • Evaluation via leave one out method

• Other contributions (not presented here)
  • Taking pathology into account in registration process
  • Ad-Hoc method for optic nerves segmentation
Software Integration

- Integration in DOSIsoft radiotherapy planning system
  - Atlas-based segmentation module
  - Both brain and head and neck atlases

- Validation in clinical conditions at IGR
  - MAESTRO European project
Discussion on Head and Neck Atlas

• Problem: Over-segmentation of the lymph nodes areas

• First reason: inside the atlas
  • Contours dispersion
    – Large inter-patient variation
  • STAPLE for generating mean segmentations
    – Influence of the background class

• Possible solutions
  • Cluster dataset in several groups
  • Use of new methods [Warfield et al., 2006]
    – No background class

Discussion on Head and Neck Atlas

• Second reason: when registering the atlas
  • Large atlas/patient differences
    – Corpulence
    – Neck flexion

⇒ Results in local discrepancies

• Possible solutions
  • Build several atlases from one database
    • Clustering of the dataset
  • Choose the closest image among the dataset images
    • Definition of distance
Perspectives

• Registration methods
  • Computation of statistics of deformability
    – Several registration methods to build unbiased statistics
  • Locally affine framework
    – Refining local affine regions

• Study of robustness of registration methods
  • With respect to registration parameters
  • Other type of validation

• Measure of quality of registration
  • Based only on images
  • Is a region well registered or not?
Perspectives

• Further validation
  • on more structures and more patients
  • Other quantitative measures
  • Fully quantitative validation in clinical conditions

• Taking into account pathology
  • Model the deformation caused by the tumor
Questions