Deformable Image Registration in Image Guided Therapy

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• IMPAC Physics Advisory Board
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Objectives

• Techniques for Deformable Registration
  – SSD, MI, CC, contour mapping
  – B-spline, Optical Flow, linear elastic
• Validation & QA
  – Phantoms
  – Clinical Data
  – Mathematics
• Clinical Implementation & Caveats
  – Radiobiology
  – Changing volume
  – Paradigm shift and clinical knowledge
Uses of Deformable Registration for IGRT

- Contour propagation
  - ‘Surface’ deformation
  - Mapping the target for image guidance
  - Re-planning
- Volumetric propagation
  - Full deformation
  - Tissue Tracking
- Dose accumulation
  - Reference state
  - Accounting

Techniques

Deformable Registration Algorithms How do they work?

- Match something
  - Intensity, gradients, boundaries, features
- Constrain by a function
  - Geometric, physical, biomechanical

Deformable Registration Algorithms How do they work?

- Match something
  - Intensity, gradients, boundaries, features
- What happens when the intensity correspondence varies?
- What happens when the gradient isn’t there?
- What happens when the boundaries aren’t well defined?
- What happens with the features aren’t visible?
- Constrain by a function
  - Geometric, physical, biomechanical
  - Can you rely on this model when the match above is missing?
**How is Registration Performed?**

<table>
<thead>
<tr>
<th>Metric</th>
<th>Regularization</th>
<th>Optimization</th>
</tr>
</thead>
<tbody>
<tr>
<td>Your Eye</td>
<td>Translation</td>
<td>Brain-power</td>
</tr>
<tr>
<td>Least Squares (Points)</td>
<td>Translation + Rotation</td>
<td>Simplex</td>
</tr>
<tr>
<td>Chamfer Matching (surface matching)</td>
<td>Affine (Translation + Rotation + scaling + shearing)</td>
<td>Gradient descent</td>
</tr>
<tr>
<td>Contour matching</td>
<td>Spline (B-spline, Thin plate spline)</td>
<td>etc…</td>
</tr>
<tr>
<td>Mean Square Difference</td>
<td>Physical (optical/liquid flow, elastic body)</td>
<td></td>
</tr>
<tr>
<td>Correlation Coefficient</td>
<td>Biomechanical</td>
<td></td>
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<tr>
<td>Mutual Information</td>
<td></td>
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</tr>
</tbody>
</table>

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**Thin-Plate Splines**

\[ T(P) = a_0 + a_2 x + a_3 y + a_4 z + \sum_{i=1}^{n} w_i (P - P_i) \]

**Transformation is built up using a set of weighted basis splines**

\[ \Delta X = \sum w_i \beta(X-k_i) \]

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**Deformable ROI Propagation: CT to kV CBCT**

- **Motivation**: adaptive IGRT
  - Challenging CBCT image quality for automation → robustness needed
- **Salient points as 3D anchor points of the deformation**
  - Sharply prominent and distinctive image features

1. Extract a patient-specific salient point model
2. Retrieve it via template-matching
3. Propagate ROIs using point correspondences

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* Courtesy of Stéphane Allaire, Princess Margaret Hospital - Allaire et al., IEEE MMBIA 2008
B-Splines

Transformation is built up using a set of weighted basis splines

\[ X' = X + \Delta X = X + \sum w_i \beta(X-k_i) \]

B-Splines

Basis function has finite range

\[ X' = X + \Delta X = X + \sum w_i \beta(X-k_i) \]

This seems a lot like intensity modulation!

Feature Matching + Min of Elastic E

- M Söhn et al., Med Phys 35(3) 2008
- NMI, constrained by min elastic E, combined with B-spline
- CBCT to Planning CT
- 5200 featurelets (15x15x5 voxels)
- CT to MR
- 1800 featurelets (10x10x8 voxels)
- Qualitative results
- 14 min on 8 CPUs

Multi-Scale Demons Registration

Next Multi-Scale Level

Last Multi-Scale Level?

Converged?

Image 1 (moving)

Image 2 (fixed)

Demons Registration Iteration

Force Calculation

Gaussian kernel

*Courtesy S Nithiananthan, JHU
Iterative Intensity Match

Faster Convergence With Symmetric Force

ABAS Adaptive Algorithm Process

Automatic re-contouring result-ABAS adapt
Biomechanical Models

- Al-Mayah, PMB 2011
- Boundary Conditions:
  - Rigid registration on each VB
  - Rigid Registration on mandible
- Parotid glands and tumor
  - Linear elastic FEA
- Multi-organ encased in body contour
- Validation based on surface comparison
- Initial (Rigid Reg at Tx)
- $5.4 \pm 0.3$ (GTV) mm $4.1 \pm 0.4$ (LPG) mm $3.1 \pm 0.7$ (RPG) mm
- $0.7 \pm 0.2$ (GTV) mm $0.7 \pm 0.2$ (LPG) mm $1.7 \pm 0.4$ (RPG) mm

Validation and QA

Validation for Deformable Registration

- **Goal**: Identification of boundary, internal structures, volume change, dose accumulation...
- **Issues**: What are the boundaries? How are the internal structures/volume changing? What is the ‘true’ accumulated dose?
- **Potential Solutions**: Indistinguishable boundaries from observer, visual validation, phantoms, matching of naturally occurring and implanted fiducials, mathematical criteria, similarity index, deformable dosimetry...

Visual Verification

M Söhn et. al., Med Phys 35(3) 2008
S. Nithiananthan et. al., Med Phys 2010
Indistinguishable Boundaries from Observer

- Series of experts contour a series of structures on a series of patients
  - Hope they are somewhat consistent!
- Perform deformable registration to map structures
- Compare auto-segmentation to observers
  - DCE similarity metric, statistical tests to prove if indistinguishable, etc
- Says nothing about the internal volume of the anatomy!

Is Contour Matching Enough?

- Error
  - DCE similarity metric, statistical tests to prove if indistinguishable, etc

Digital or Physical Phantoms

- NCAT Phantom (Segars)
- U of Mich lung phantom
- McGill lung phantom
- Can know the true motion of all points
- Doesn’t include anatomical noise and variation, likely not as complex as true anatomical motion
- Does give a ‘best case’ scenario for similarity/geometric defm reg algorithms

Natural/Implanted Fiducials

- Reproducibility of point identification is sub-voxel
  - Gross errors
  - Quantification of local accuracy within the target
  - Increasing the number increases the overall volume quantification
- Manual technique
- Can identify max errors
MIDRAS Results

- max error > 5 mm SI, N = 14
- max error > 10 mm, N = 2
- NO max error > 5mm, N = 3

- Implementation matters
  - 3 Demons algorithms (Liver): $\mu = 2.3, 3.3, 4.8$ mm
  - 3 Thin Plate Spline (Liver): $\mu = 2.1, 2.9, 7.8$ mm
  - 4 B-Spline (Lung): $\mu = 1.6, 2.0, 2.5, 3.0$ mm
- Time: 100s – 100,000s!

Mathematical and Similarity Metrics

- Jacobian: identifies volume change and inversion
  - Inversion = physical violation
  - Volume change – what is right?
- Similarity Metric (SSD, MI, NCC)
  - Must be independent of technique
  - Only MI for multi-modality

Shrinking Volume

- How do we model the reduction?
- Does it have dosimetric consequences?
- What volume to we use for the DVH?

Modeling Volume Reduction

- Tumor with ‘core’
- Heterogeneous plan
- Variation in volume reduction
  - Homogeneous
  - Dissolving rim
  - Necrotic Core
Modeling Volume Reduction Dosimetric Effect

Homogeneous Necrotic Core Dissolving Rim Plan

Clinical Application: Accuracy of Dose Accumulation

- How do we QA dose accumulation?
- What is the 'gold' standard?
  - Ion chambers/TLDs/Film can’t deform
  - Put them in a deforming phantom?
- How accurate does it need to be?
  - Every voxel exactly right?
  - Isodose line comparison (2%/2mm)?

Use of Deformable Gel Dosimeter

- Deform gel cyclically by 1 cm
- Deliver 4 Gy in 8 beam plan
- Defm Acc: < 2 mm
- Gel readout in MR
- Calibration using control gel
- Difference:
  - Mean: 1% ± 13%
- 95% Isodose within 2.5 mm
- 92% of voxels within SD of reference

Implementation
Technical Motivation

- Improve target definition
  - Integration of MR (w/ERC) images
- Reduce uncertainty in targeting
  - Understand the limitations of surrogates (seeds)
- Provide the opportunity for novel Tx development
  - Intra-prostatic boost

Improve Image Integration

- Integrating multi-modality and multi-instance images
- Resolving geometric discrepancies between images
- Tracking tissue throughout Tx

Deformable Modeling: Accurate tumor targeting
### Accuracy: Multi-Organ Prostate

<table>
<thead>
<tr>
<th></th>
<th>dx</th>
<th>dy</th>
<th>dz</th>
<th>dV</th>
</tr>
</thead>
<tbody>
<tr>
<td>All Patients (N=19)</td>
<td>0.01 ± 0.09</td>
<td>0.03 ± 0.16</td>
<td>-0.03 ± 0.16</td>
<td>0.22 ± 0.09</td>
</tr>
<tr>
<td>All Markers (N=57)</td>
<td>0.07 ± 0.06</td>
<td>0.13 ± 0.09</td>
<td>0.13 ± 0.09</td>
<td>0.22 ± 0.09</td>
</tr>
</tbody>
</table>

- **Mean Relative Error ± SD [cm]**
  - All Patients: 0.01 ± 0.09
  - All Markers: 0.07 ± 0.06

- **Mean Absolute Error ± SD [cm]**
  - All Patients: 0.07 ± 0.06
  - All Markers: 0.13 ± 0.09

- **Min Error [cm]**
  - All Patients: -0.26
  - All Markers: -0.35

- **Max Error [cm]**
  - All Patients: 0.28
  - All Markers: 0.29

- **Mean Residual Surface Deformation ± SD [cm]**
  - All Patients: 0.00 ± 0.06
  - All Markers: 0.01 ± 0.07

### Technical Motivation

- **Improve target definition**
  - Integration of MR (w/ERC) images

- **Reduce uncertainty in targeting**
  - Understand the limitations of surrogates (seeds)

- **Provide the opportunity for novel Tx development**
  - Intra-prostatic boost

### Prostate Motion & Deformation

- **Tx setup:** gold markers and a COM translation to align
- **Including rotations may help**
  - Residual deformation may remain!
- **Translation+Rotation**: 
  - Residual Seed Error: 1.2 mm (SD: 0.6 mm)
  - 48% of pts had > 3 mm defm in 10% of surface
- **Transln+ Rotn+ Defm?**

*Nichol et. al. IJROBP 2006*

### Establishing Correlation with Surrogates

- **Biomechanical Modeling**

[Diagrams showing prostate motion and deformation with contour and displacement maps]
Organ Specific Modeling: Prostate

- Investigation 1: align seeds and evaluate residual deformation
- 3 of 29 (10%) of patients had >50% of the prostate deformed by >3mm under conditions of translation or translation and rotation.
- Worst case patient: 74% with >3mm discrepancy (with rotation included)

Accuracy: Single Organ Prostate

- Investigation 2: Perform deformable registration of the prostate and use the seeds to validate the deformation
- Seeds: AVG ABS error:
  - LR = 0.08 cm
  - AP = 0.13 cm
  - SI = 0.11 cm
- >85% of patients had an expected error of <2 mm in LR, AP, and SI
- Boundary Points: AVG ABS (SD):
  - 0.10 (0.07), 0.15 (0.12), and 0.12 (0.09) cm LR, AP, SI

Technical Motivation

- Improve target definition
  - Integration of MR (w/ERC) images
- Reduce uncertainty in targeting
  - Understand the limitations of surrogates (seeds)
- Provide the opportunity for novel Tx development
  - Intra-prostatic boost

Multi-Organ Modeling: Prostate
Salvage MRI-Guided and Tumor-Targeted Prostate Brachytherapy

- Prospective clinical trial
- Suspected local recurrence
  - MRI-guided mapping biopsy
  - 15 patients
    - Median age 72, PSA 4, 6 yrs after
    - 12 recurrences -11 focal -10 single
- Confirmed focal recurrence
  - HDR Salvage – 2 implants 7-14 d.
    - PTV (GTV) 11Gy (V100>98%)
    - PTV (CTV) 8Gy (V95>95%)
  - 6 patients
    - 5 single focus
    - 1 two foci, same sextant

GTV – Histologically Referenced MRI

Needles
Cores
GTV map

Study Purpose: Develop / validate technique for deformable registration

Method - MORFEUS

Biomechanical model-based
1. 3D meshes from contours
2. Prescribes displacement boundary condition on surface
3. Interior deforms according to biomechanical properties of tissue

<table>
<thead>
<tr>
<th>Young’s Modulus</th>
<th>Poisson’s Ratio</th>
</tr>
</thead>
<tbody>
<tr>
<td>Prostate</td>
<td>21 kPa</td>
</tr>
<tr>
<td>Tumor</td>
<td>78 kPa</td>
</tr>
</tbody>
</table>
**Method - Geometric Comparison**

- Proportion of registered GTV missed by estimated (purple)
  \[
  \frac{|R| - |E|}{|E|}
  \]
- Proportion of excess GTV in estimated (blue)
  \[
  \frac{|E| - |R|}{|E|}
  \]

**Results - Geometry**

- % of Registered GTV Missed by Estimated
- % of Excess GTV in Estimated

**Method - Dosimetric Impact**

**Results - Dosimetric Impact of Planning on Estimated GTV**
Conclusions

• Advancing Prostate treatment techniques require deformable registration
  – Integration of MR
  – Caution when shrinking margins when alignment is based on seeds
• Potential benefit of specific dose targeting to small tumors hinges on technical accuracy
• Prostate deformation between diagnostic and therapeutic procedures - inadequacy of commercial rigid registration tools

Summary

• Many different deformable registration options
• Validation is a must prior to clinical integration
• Visual validation is not enough! (for initial validation)
• Boundary matching is enough ONLY for auto-segmentation
• Phantoms are useful for benchmarking, but likely do not include the complexities of true clinical imaging
• Implanted and naturally occurring fiducials give us a ‘spot check’
• Mathematical/Similarity metrics are easy automated checks
• Validation using dosimetric techniques can give us a clinical perspective for IGRT/Dose Accumulation studies

Words of Caution

• Visual validation should only be used as a qualitative, spot check test after you have quantitatively validated the algorithm on your data
• Understand how the algorithm behaves when limited information/uncertainties are presented
• Matching the organ boundary does not guarantee accurate modeling of internal volume
• Manually adjusting auto-segmentation is fine, manually adjusting deformable registration is not

Conclusions

• Deformable registration is a promising tool for understanding tissue response to radiation
  – Must understand HOW it works and HOW ACCURATE it is
• Validation of dose accumulation is challenging but possible
• Use for dose accumulation is very promising…
• However, we must work to understand how the tumor and normal tissues are responding over the course of radiation and be thoughtful in clinical implementation