Is deformable image registration a solved problem?

Marcel van Herk
On behalf of the imaging group of the RT department of NKI/AVL
Amsterdam, the Netherlands
Image registration

• Find translation….deformation to align two 2D..4D data sets (2 .. 1000000 degrees of freedom)

• Allows combination of scans on a point by point basis

• Applications:
  • Complementary data
  • Motion tracking and compensation (imaging)
  • Image guidance
  • Adaptive radiotherapy
  • Response monitoring
  • Dose accumulation
  • Data mining

Delineation: CT versus CT + PET
reduce observer variations

11 observers from 5 institutions
delineated 22 patients (stage I to IIIB)
Estimate pattern of spread from response to incidental dose in clinical trial data (high risk prostate patients)

Average dose no failures – average dose failures ≈ 7 Gy

p = 0.02

Time (months)
72
60
48
36
24
12
0
Free from any failure
1.0
0.8
0.6
0.4
0.2
0.0
< median (53.1 Gy)

Treatment group IV, Hospital A (n=67)

= median

≥ median

p = 0.000

0%
3
6 Y
80%
60%
40%
20%
0%

PSA controls
PSA failures

Witte et al, IJROBP2009; Chen et al, ICCR2010

Deformable image registration is considered a cornerstone of 4D and adaptive RT
But, does it actually work?

- Christian Graeff used forced breath-hold and contrast to correctly deform inside of a pig heart CT - CT
  - Totally different DVF with and without contrast
  - Plastimatch

- Mayyas et al (Med Phys 2014) claim that they can precisely register the inside of the prostate between CT and CBCT
  - Velocity

Christian Graeff - GSI

- Cardiac-gated 4DCTs - native and contrast enhanced
  - Native for treatment planning
  - Contrast needed for motion maps
Overconfidence in commercial systems

FIG. 1. An example of the registration process in the coronal plane. The rectangular box is the region of interest, which includes the entire CBCT. The contour structure is the CTV. In (a), CBCT and f executive markers. In (c), CBCT is deformed fiducial markers were used to evaluate the registration for each case. The error in the prostate alignment was defined as the average distance between the markers on CBCT and the corresponding SimCT datasets. Alignment error less than 2 mm was considered acceptable. Figure 2 illustrates the workflow with regard to image registration and data analysis. As shown, out of 200 CBCT-to-CT deformable registrations, 107 showed alignment agreement within 2 mm.
Under the hood

General Framework for Image Registration

- **Fixed image**
- **Floating image**
- **Metric**
  - Similarity
  - Mapped Image
- **Interpolator**
  - Geometric Transformation
- **Optimizer**
  - Adjusted Parameters
- **Transformer**
Grey Value / Intensity matching
Uses all pixel values in ROI: e.g., sum of squared differences

Somewhat slower to process all voxels: depends on the size of the ROI

Root Mean Square Difference

\[ H(I_{MRI}) \]

\[ H(I_{CT}) \]

\[ H(I_{MRI-CT}) \]
The Mutual Information of 2 images is the information that is common to both images. The Mutual Information of 2 images is maximized when they are registered.

\[
MI(I_{MRI}, I_{CT}) = \sum_{I_{MRI}, I_{CT}} p(I_{MRI}, I_{CT}) \log \frac{p(I_{MRI}, I_{CT})}{p(I_{MRI})p(I_{CT})}
\]

The Mutual Information of 2 images is

\[
H(I_{MRI-CT}) = \sum_{I_{MRI}, I_{CT}} p(I_{MRI}, I_{CT}) \log p(I_{MRI}, I_{CT})
\]

Mutual Information

2D joint intensity histogram

MI = .99

Aligned!
Mutual Information

Not so Aligned!

2D joint intensity histogram

\[ p(I_{\text{CT}}, I_{\text{MR}}) \]

\[ \text{MI} = .62 \]

General Framework for Image Registration

Fixed image \rightarrow Metric \rightarrow Optimizer

Floating image

Mapped Image

Geometric Transformation

Adjusted Parameters

Transformer

Interpolator

Similarity
Degrees of Freedom

PET/CT  MR - CT  4D CT

0?  3 to 6  3 x N

None?  Few  Many

By enforcing smoothness the optimization becomes tractable

Example thin-plate spline deformations (manual)
General Framework for Image Registration

- Fixed Image
- Metric
  - Similarity
  - Optimizer
  - Adjusted Parameters
- Mapped Image
- Interpolator
  - Geometric Transformation
- Transformer
- Floating Image

Deformable Registration Movie
Visual verification

sliding window

Overlay

Checker

Subtract

The power of 4D animation
Different DVF provide same visual registration result

• Descriptive: it must look good
  • e.g. contour propagation

• Quantitative: it must be an anatomically correct, also inside homogeneous organ
  • e.g. dose accumulation
The bladder is a balloon in a box with stuff – it expands isotropically constrained in by the organs around it. You get the contours right, but not the tissue cells \( \rightarrow \) danger for dose accumulation.

### Penalty terms

- Several penalty terms can be implemented\(^1\):
  - Smoothness penalty
  - Rigidity penalty
  - Volume penalty

\[ J_T(x) = \begin{pmatrix} \frac{\partial T_x(x)}{\partial x} & \frac{\partial T_x(x)}{\partial y} & \frac{\partial T_x(x)}{\partial z} \\ \frac{\partial T_y(x)}{\partial x} & \frac{\partial T_y(x)}{\partial y} & \frac{\partial T_y(x)}{\partial z} \\ \frac{\partial T_z(x)}{\partial x} & \frac{\partial T_z(x)}{\partial y} & \frac{\partial T_z(x)}{\partial z} \end{pmatrix} \]

\(^1\text{(Rueckert, 1999), (Rohlfing, 2003), (Loeckx, 2006), (Staring, 2007)}\)

There is a great need for biomechanical penalties.
General Framework for Image Registration

- Fixed image
- Floating image
- Metric
- Similarity
- Optimizer
- Constraint
- Mapped Image
- Interpolator
- Transformer
- Geometric Transformation
- Adjusted Parameters
- Prostate MRI w/wo Endo Rectal Coil

Prostate MRI w/wo Endo Rectal Coil

Global smoothness penalty
CBCT – Planning CT Registration

Planning CT  CBCT

Constraint Deformable b-Spline Deformable b-Spline Registration

Validation
Accuracy of the observers $O_1$, $O_2$, $O_3$

$O_1$ : First human observer
$O_2$ : Second human observer
$O_3$ : Registration method

\[
\begin{align*}
\sigma^2_1 &= \left(\sigma^2_{2-1} + \sigma^2_{3-1} - \sigma^2_{3-2}\right) / 2 \\
\sigma^2_2 &= \left(\sigma^2_{3-2} + \sigma^2_{2-1} - \sigma^2_{3-1}\right) / 2 \\
\sigma^2_3 &= \left(\sigma^2_{3-1} + \sigma^2_{3-2} - \sigma^2_{2-1}\right) / 2
\end{align*}
\]
Analysis of variance

- Landmark validation
- 7 patients, 7 – 8 fractions
- 23 landmarks per CBCT, two human observers
- B-spline deformable registration for landmark propagation
- Use of ANOVA method to correct for observer variation

Results

<table>
<thead>
<tr>
<th>Method</th>
<th>Accuracy (1SD mm)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>$\text{SD}_{\text{LR}}$</td>
</tr>
<tr>
<td>Rigid registration</td>
<td>1.8</td>
</tr>
<tr>
<td>B-spline No penalties</td>
<td>1.4</td>
</tr>
<tr>
<td>B-spline + penalties</td>
<td>0.9</td>
</tr>
</tbody>
</table>
Applications

Image Enhancement

4DCT → Full 3D DVF

Motion corrected 4DCT @ mean pos.

Average frames

Mid-position CT
Mid-ventilation method versus mid-position reconstruction (motion compensated 4DCT) using deformable registration

Motion compensated CBCT
PET-CT motion compensation

2.5 cm motion
Compensated

Lung DIR easy?
Repetitive 4D CT:
treatment response

Modes of Tumor Regression

‘elastic’

‘erosion’
Generate intermediate contours for plan selection approaches

Interpolation of cervix motion
Adaptive replanning on average anatomy

Summary

- Deformable image registration plays an important role in target definition, advanced treatment planning and image guidance
- Validation of registration accuracy is essential for each clinical problem
- Visual verification remain essential as automatic algorithms are never perfect
- Work towards faster and more robust deformable images registration continues
- In our clinic, rigid registration is still a cornerstone, e.g. for tumor contour propagation
Summary 2

• Image registration does not know about biology and biomechanics
  • Sliding tissue
  • Tumor growth and regression
  • Weight loss
• This is OK to make pretty pictures and propagate HU and OAR contours
• The best deformable registration between image A and B: copy A B
• In strongly believe DIR is not a solved problem!