Validation

Biomedical Image Analysis

Prof. Dr. Philippe Cattin

MIAC, University of Basel

Apr 12th, 2016

Contents

- Abstract 2
- 1 Validation
  - 1.1 General Concepts
    - Validation of Registration 5
    - Validation of Registration (2) 6
    - Robustness 7
    - Consistency 8
    - Consistency (2) 9
    - Consistency (3) 10
    - Consistency (4) 11
    - Visual Assessment 12
    - Visual Assessment 13
    - Visual Assessment (2) 14
    - Visual Assessment (3) 15
    - Visual Assessment (4) 16
    - Visual Assessment (5) 17
  - 1.2 Quantitative Validation for Rigid Registration
    - Gold Standard for Rigid Registration 19
    - Registration Error Measures 20
    - FLE vs FRE vs TRE 21
Abstract

For medical doctors a quantitative evaluation of the image registration result is essential. However, this is difficult to produce in particular for elastic registration techniques. This section explains the difficulties one is facing when trying to quantify the registration errors.
Validation

General Concepts

Validation of Registration (5)

Before an image registration method can enter clinical practice, it must undergo thorough validation

- Technical validation
  - Speed, robustness, accuracy, reliability,...
- Clinical validation
  - usefulness, improved clinical diagnosis and patient management in health care
- FDA approval, incorporation into commercial system
  - Liability

The biggest problem to evaluate registration methods is the lack of ground truth (in particular for multi-modal methods)

Validation of Registration (6)

(2)

Prior to deployment several important properties must be analysed:

1. Robustness
   - Measurement precision
2. Consistency
   - Circular (invertible) transformations
3. Visual assessment
   - Subtraction images, overlays, landmarks, contours,...
4. Quantitative analysis
   - Rigid registration: Implanted/attached markers, landmarks
   - Non-rigid registration: Simulation of deformation followed by a motion recovery
Robustness (7)

Robustness can be measured as the discrepancy of registration transformations if different starting estimates are given or the images are perturbed.

1. How is the registration affected by external factors
   - Misregistration of an image by a known amount, e.g. by up to ±30 mm or ±30°
   - Adding noise, inhomogeneity, artefacts
   - Adding error to landmark or feature estimates

2. Deviation from identity transformation which forms the ground truth
   - Individual deviations of DOFs (tx, ty, tθ, and the Euler angles)
   - Target registration error (TRE) at landmarks or within volume overlap

→ try to workout a range of working conditions.

Consistency (8)

- Involves registration of an image triple, A to B, B to C, and C to A
- Ideally, the resulting transformations form a circular registration
  \[ T_{AB}(T_{BC}(T_{CA}(x))) = I(x) = x \] (8.1)
- Can be tested for robustness via individual transformation parameters or via TRE
- Consistency is not a measure for registration accuracy!
Consistency (2)

Can individual registrations be composed?

Fig 8.2: Consistency test (2)

Consistency (3)

Scan/Rescan consistency

A true measure of reproducibility for a particular scanner/acquisition method.

Fig 8.3: Consistency test (3)
**Consistency (4) (11)**

Forward/reverse registration consistency.

Some registration methods enforce this consistency property.

**Visual Assessment (12)**

The simplest validation can be performed by visually comparing the image pair before and after registration. Several approaches are used:

- Subtraction mode (only for mono-modal images)
- Overlay mode
  - Iso-contours or colour coded (red/green)
  - Checkerboard, morphing
  - Horizontal or vertical shutters

Reformatting (interpolation) of the images might be required to show the same anatomical location.

*Visual assessment is only a qualitative validation method*
Visual Assessment (13)

Image subtraction is a widely spread method for mono-modal images.

Fig 8.5: CT of a leg
Fig 8.6: Pre-registration image subtraction
Fig 8.7: Post-registration image subtraction

Visual Assessment (2) (14)

Checkerboard visualisation

Fig 8.8: Registered retina fundus and fluo image shown in a checkerboard fashion
Visual Assessment (3) (15)
Displaying contours of important structures in the other modality are not only applicable for mono-modal but also for multi-modal images.

Fig 8.9: CT, unregistered MR contour
Fig 8.10: CT, registered MR contour

Visual Assessment (4) (16)
Parts of the MR and CT image are displayed with a moveable shutter.
Visual Assessment (5) (17)

The MR (red) and CT (green) data set are displayed simultaneously. Their respective intensity can be adapted dynamically.
Quantitative Validation for Rigid Registration

Fig 8.12: Visual assessment using colour coding (red = MR, green = CT)
Gold Standard for Rigid Registration

The theory behind accuracy establishment for rigid registration is well understood.

- The gold standard method uses either physical markers or well-defined natural landmarks
- It allows to determine the registration accuracy
- It can be obtained from known marker positions from which ground truth transformation can be obtained
- Given a transformation of points from space $X$ of the first view to space $Y$ of the second view
  - Goal: make $x' = T(x) \approx y$
  - Target Registration Error ($TRE$): $T(x) - y$

The remaining $TRE$ might stem from registration mismatches or because the rigid body assumption is not accurate.

Registration Error Measures

**Def:** *Fiducials* are either attached or implanted markers (such as a gold sphere) used for rigid registration validation and targeting.

- Fiducial localisation error ($FLE$)
  - Error of localisation fiducials
- Fiducial registration error ($FRE$)
  - Distance between points (fiducials) used for registration
  - Minimum value of cost function
- Target registration error ($TRE$)
  - Distance between points (targets) not used for registration
  - This is the clinically relevant error
FLE vs FRE vs TRE (21)

![Diagram showing FLE vs FRE vs TRE](image)

**Point-Based Registration Error: Theory**

The expected value of $FRE$ and $TRE$ can be estimated from $FLE$ using perturbation theory.

- The fiducial registration error $FRE$ is a function of $FLE$, $N$ and given by
  \[
  \langle FRE^2 \rangle = \frac{N - 2}{N} \langle FLE^2 \rangle \tag{8.2}
  \]
- The target registration error is a function of $FLE$, $N$, fiducial configuration, and the target position. It is defined by
  \[
  \langle TRE^2(r) \rangle \approx \frac{\langle FLE^2 \rangle}{N} \left( 1 + \frac{1}{3} \sum_{k=1}^{3} \frac{d_k^2}{f_k^2} \right) \tag{8.3}
  \]

where $\langle \cdot \rangle$ is the expected value, $d_k$ is the distance of the target from the principal axis $k$, and $f_k$ is the RMS distance of the fiducials from the principal axis $k$. 

Fig 8.13: Visualisation of $FLE$, $FRE$, and $TRE$
Point-Based Registration (23)

Error: Characteristics of TRE

- $TRE$ proportional to $FLE$
- $TRE$ inversely proportional to $\sqrt{N}$
- $TRE$ depends on target position $r$
- $TRE$ has its minimum value at the fiducial configuration centroid (translational component)
- $TRE$ increases as the distance of the target point from the principal axis increases
- Iso-error $TRE$ contours are ellipsoidal
Validation of Non-Rigid Registration

- Robustness
  - *Difficult to find different valid initial starting estimates*
- Consistency
  - Non-rigid transformation must be invertible
- Visual assessment
  - *Small localised misregistrations difficult to see*
- Gold standard
  - *Landmarks too sparse to give dense deformation map, markers need to be attached on/implanted to deformable tissue*
- Simulation of a ground truth
  - Deformation simulations are *often not of a plausible nature, and often the same motion model is used for simulation and registration*, introducing a *bias*
A possible solution for intra-subject registration

- Application: Motion compensation in contrast-enhanced MR mammography
- Objective: Assessment of TRE with the region of suspected lesions
- Validation strategy: Simulation using FEMs
  - Modelling of interrelation of different tissue types
  - Applied forces or displacements can predict physically plausible motion
  - Simulation of a range of typical, physically plausible motion

- Registration of post-contrast volume $I_2$ to its FEM deformed version $I_2'$ → beware of correlated noise!!!
- The gold standard transformation from the FEM model maps every point $p$ in $I_2$ to $I_2'$
- TRE can be calculated over all voxels within the deformed breast volume

Fig 8.14: Non-rigid registration validation scheme using FEM models
A possible solution for intra-subject registration (3)

- Registration of the pre-contrast $I_1$ to the deformed post-contrast $I_2' \rightarrow D_1$
- Calculating the TRE from $D_1$ would be subject to a small residual, as the motion between $I_1$ and $I_2$ was neglected
- Solution:
  - Estimate the transformation $D_{12}$ which maps $I_2$ to $I_1$
  - Subtract $D_{12}$ from $D_1$ and calculate the residual corrected TRE called consistency registration error (CRE)

Fig 8.15: Non-rigid registration validation scheme using FEM models
A Better Solution for Multi-Modal Intra-Subject Registration Validation

Take simultaneously acquired T1- and T2-weighted breathhold MR images. Their contrast difference is very similar to real multi-modal images such as MR/CT.

- No problems with correlated noise
- Transformation $D_{12}$ is close to the identity, as the two images were captured at the same time
- $TRE$ can be easily calculated

Conclusions

Set-up of generic validation tool for non-rigid registration

- Applicable to other non-rigid registration methods and medical applications
- Useful for improving the registration method
- Helps to compare the performance of different methods
Discussion

- Validation of image registration is essential, if not vital
- The ground truth is hardly ever available
- Rigid registration accuracy can be assessed using a gold standard (e.g. markers)
- Non-rigid registration accuracy can be only assessed using simulations of a gold standard (e.g. FEMs)

However, the validation methodology should always be independent of registration methodology!

The Holy Grail

The Holy Grail of image registration would be an on line self-diagnosing registration method

Fig 8.17: Holy Grail of the Monastery of Xenophontos