# A Practical Review on Medical Image Registration: from Rigid to Deep Learning based Approaches


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SIBGRAPI'18

# Summary

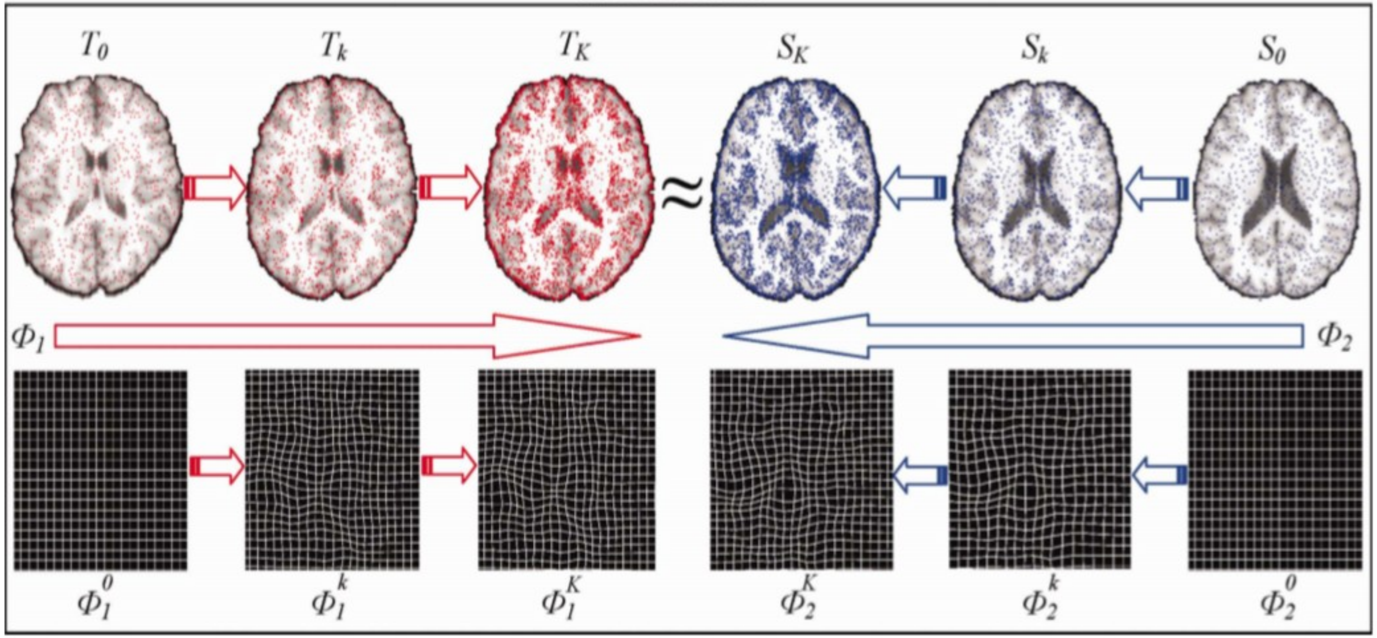
1. Medical image registration definition and applications (Cappabianco)
2. Registration description (Cappabianco)
3. Classical methods (Natan)
4. Concepts of deep learning (Faria)
5. Deep learning applied to medical image registration (Faria)

# Introduction

- Definition
- Applications
- Preprocessing
- Main concepts

# Medical Image Registration

- **Definition:** process of estimating an optimal transformation between two images.



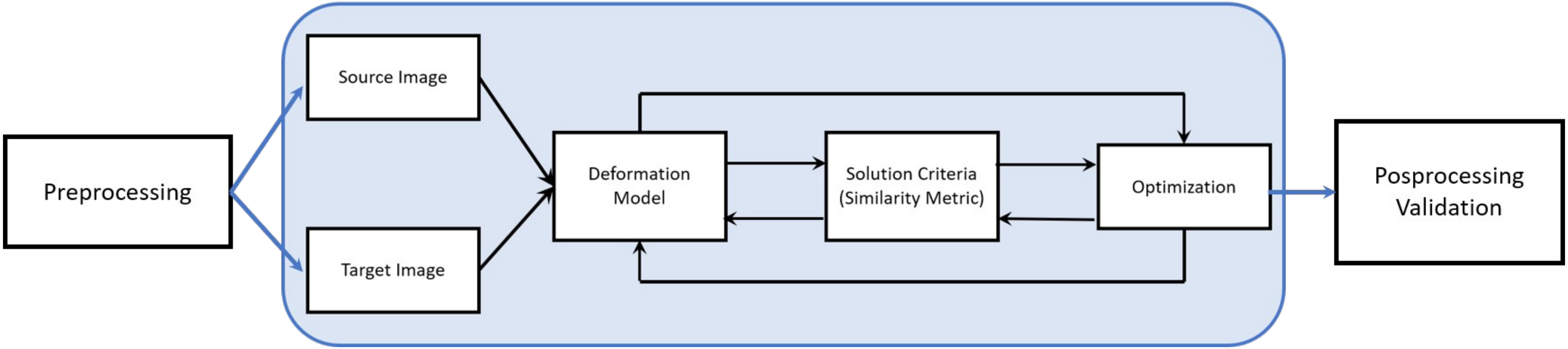

Wu et al., 2013

# Related Applications

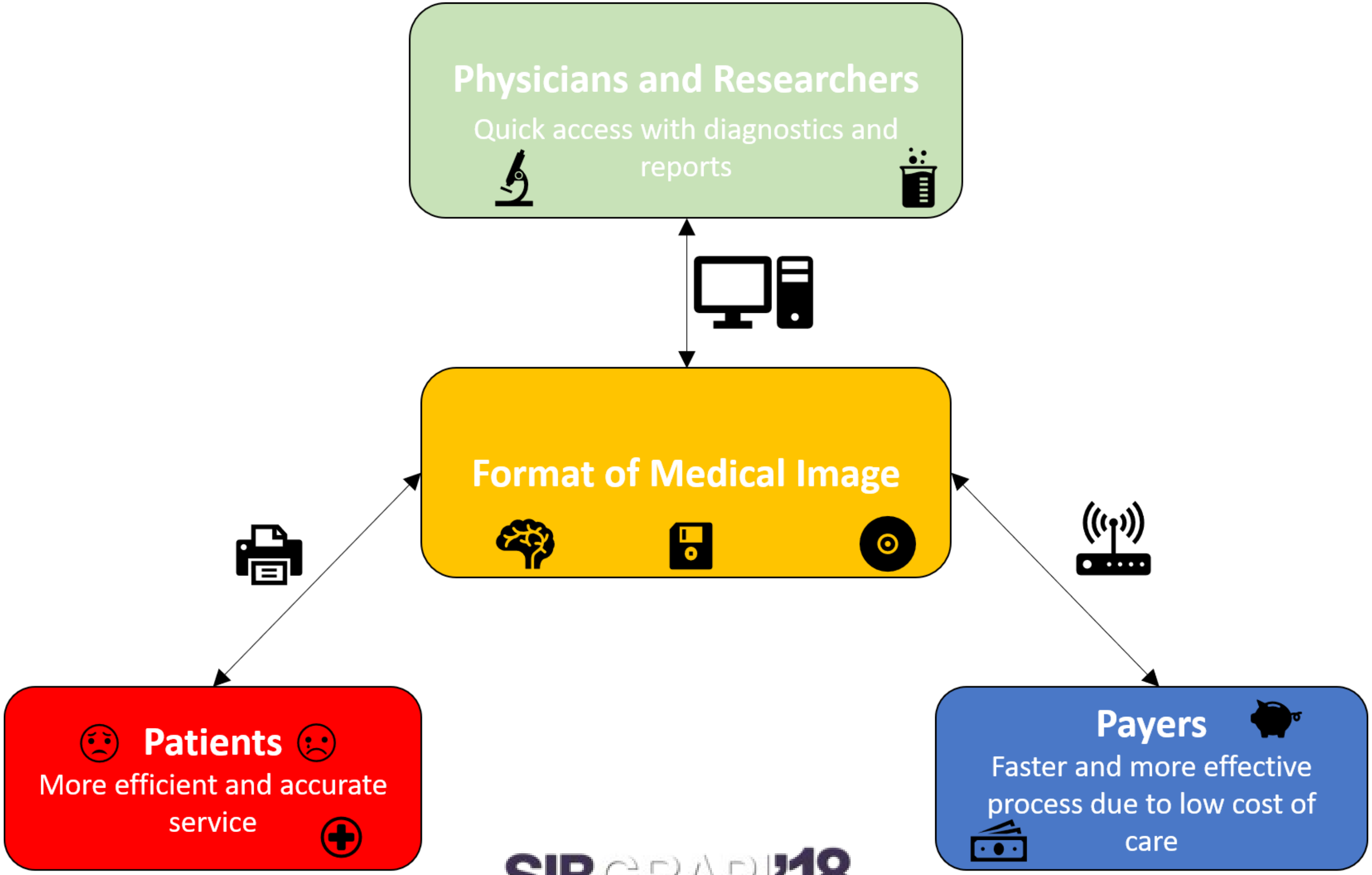
- Fusion of Multi-modal images;
  - TC/MRI/PET
- Longitudinal Studies;
  - Desease development
- Populational Studies;
  - Etiology studies
- Functional studies;
  - fMRI

# Overview

Medical Image Registration



# Medical Imaging Acquisition



# Format of Medical Images

- **DICOM** (Digital Imaging Communications in Medicine)
  - American College of Radiology (ACR) and National Electrical Manufacturers Association (NEMA)
  - 1990s several terms for access, usability, diagnoses, protocol communication
  - Header: image acquisition protocol, patient information, other information
  - Data: image description
- Purpose: interoperability issues in medical imaging.
  - Not a framework or architecture for clinical workflow

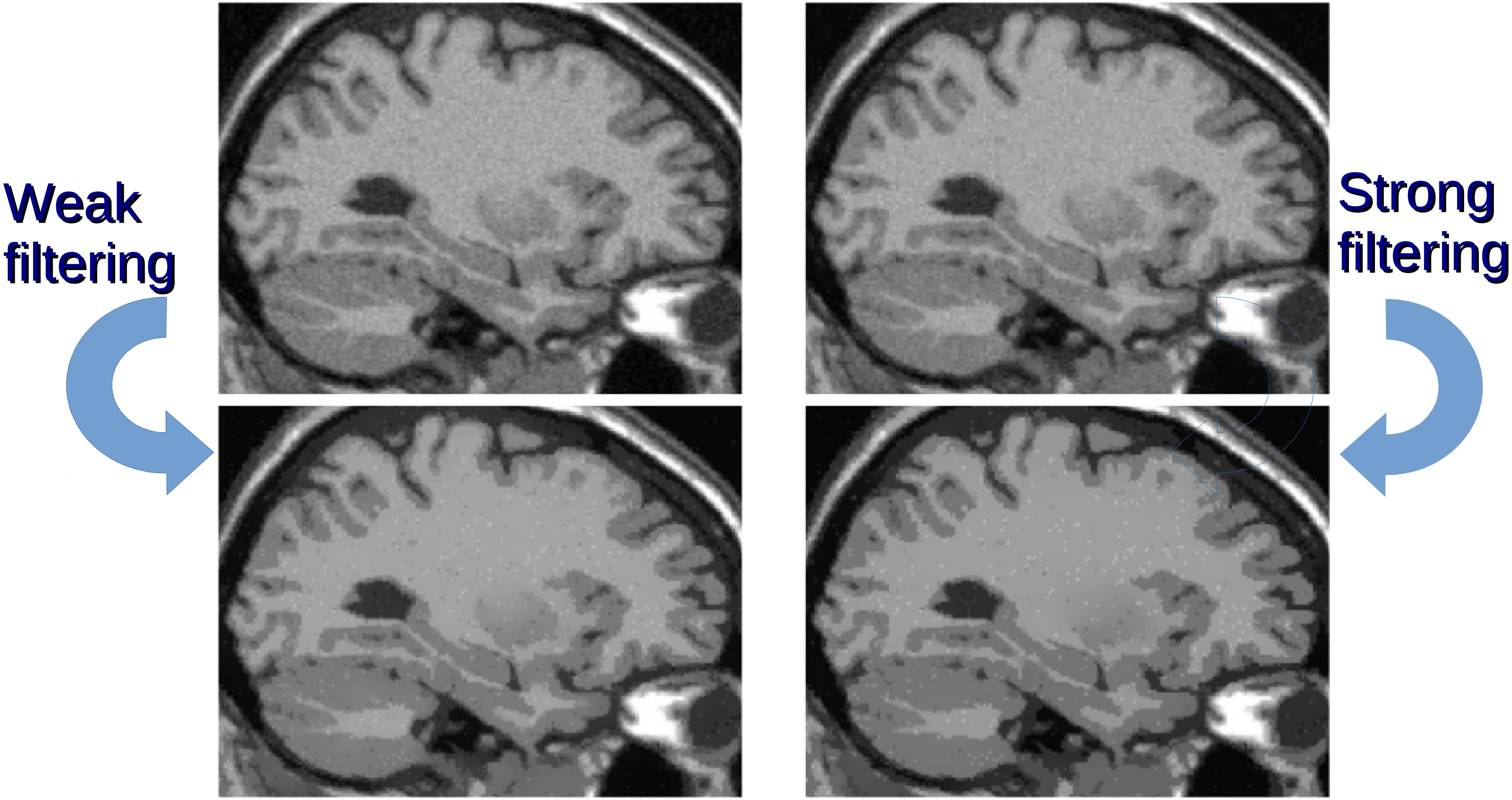
# Format of Medical Images

- **ANALYZE**
  - .img file: voxel intensities
  - .hdr file: data description
- **NIfTI** (Neuroimaging Informatics Technology Initiative)
  - National Institute of Mental Health
  - National Institute of Neurological Disorders and Stroke
  - .nii file: data and header together.
  - Progress of neuroinformatics tools
  - Intelectual properties rights.

# Preprocessing

- Noise/Artifact correction
- Intensity normalization
- Inhomogeneity correction
- Region of Interest delineation
  - Mask segmentation

# Noise/Artifact Correction

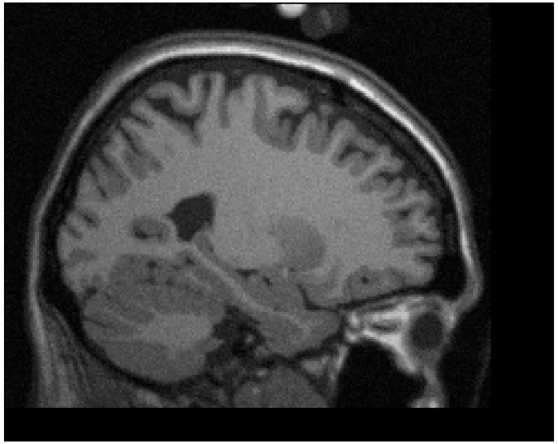


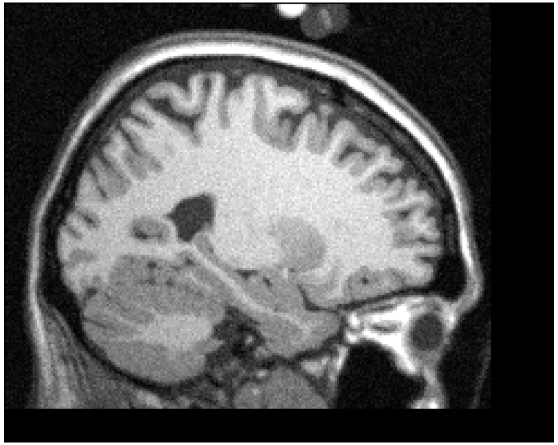
# High-frequency Noise Filtering

- 1st generation of filters: isotropics
  - e.g. Mean, median, gaussian
- 2nd generation of filters: local anisotropics
  - e.g. diffusion, bilateral [Smith 1997]
- 3rd generation of filters: non-local anisotropics
  - e.g. non-local means [Tristan-Vega 2012], BM3D, PLOW

# Intensity Normalization

- Used to standardize intensity range and distribution of a set of images.
- Based on landmarks.
  - Normally, just mean and quartiles are enough.
  - [Zhuge 2006]





# Intensity Normalization

- Two steps method
  - 1st – training: find landmarks in the histogram of input image.
  - 2nd – transformation: find landmarks in target images and map them to the ones of the training image.
- Consequences:
  - Improves inhomogeneity correction.
  - Improve registration. (around 15%)

# Inhomogeneity Correction

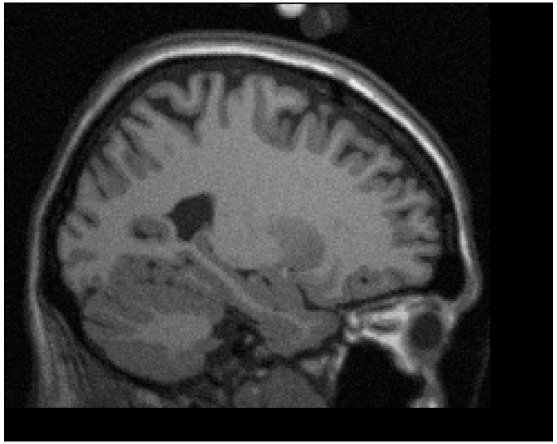
- Consists of a multiplicative low-frequency noise.
  - $I(s) = \hat{I}(s) * B(s) + \eta(s)$
- Depends on:
  - Magnetic field or scanner features
  - Scanned subject

# Inhomogeneity Correction

- General methods:
  - N3 [Sled 1998], N4 [Tustison 2010]
    - Used over any kind of images.
- Brain specific methods:
  - BFC, FAST (also segments tissues)
    - Used over skull stripped brain images.

# Region of Interest

- Improves overall registration quality.
- Focus on more important region.



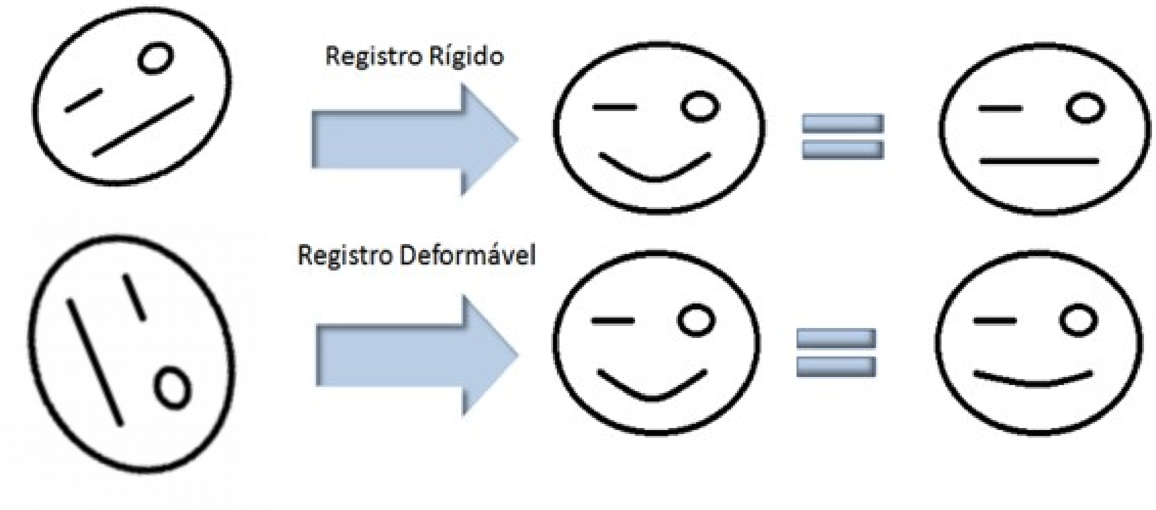
# Strutucture of Registration

1. *Deformation Model*
   I. Computational efficiency vs flexibility
   II. Transformation nature

2. *Matching Criteria*
   I. Measurement of (dis)similarity
   II. Geometric (landmarks) vs Iconic (pixels)

3. *Optimization Method*
   I. Continuous vs discrete
   II. Criteria and regularization

# Deformation Model




(Avants, 2011)

Affine Registration with ANTS

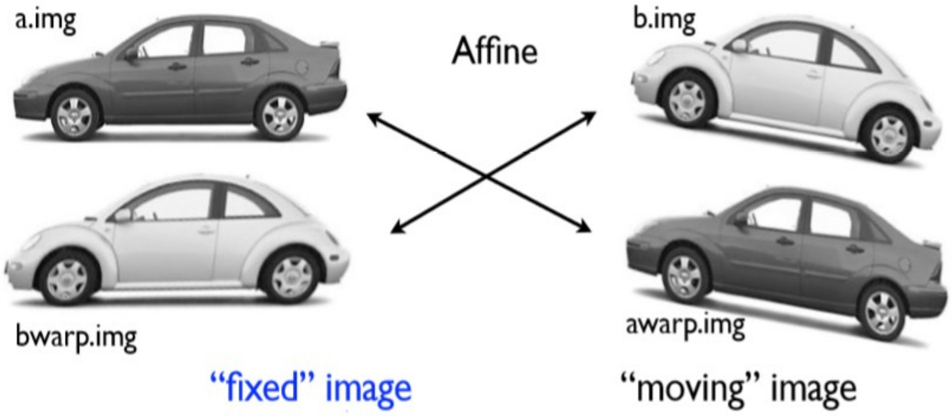
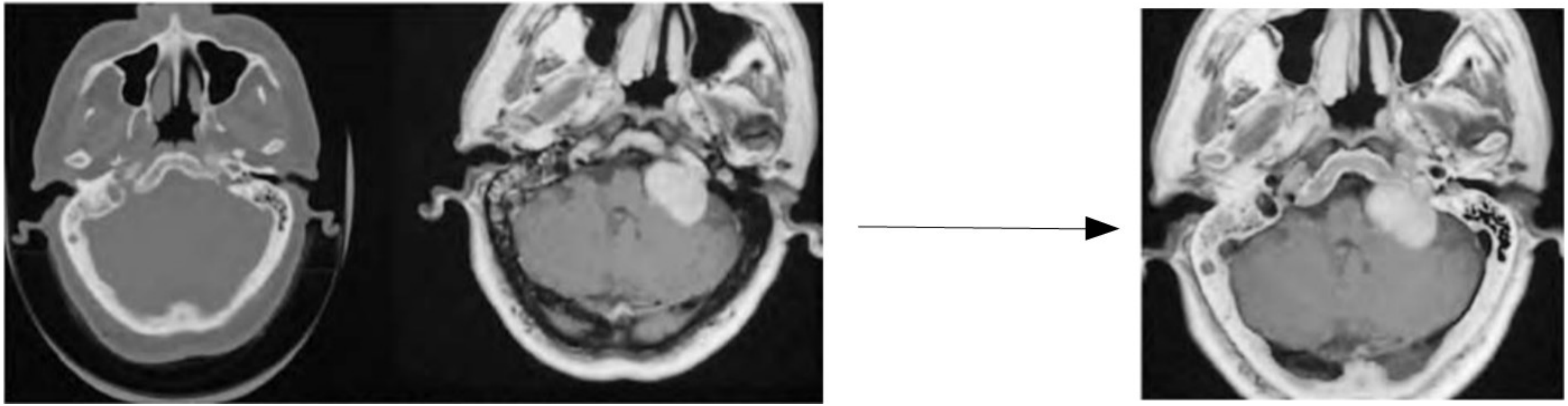



Figure 4: The anatomy of an ANTs optimization and application of the resulting warping.

# Deformation Model

- Deformation model selection:
  - Depends on application
  - Depends on time requirements
  - Depends on image quality

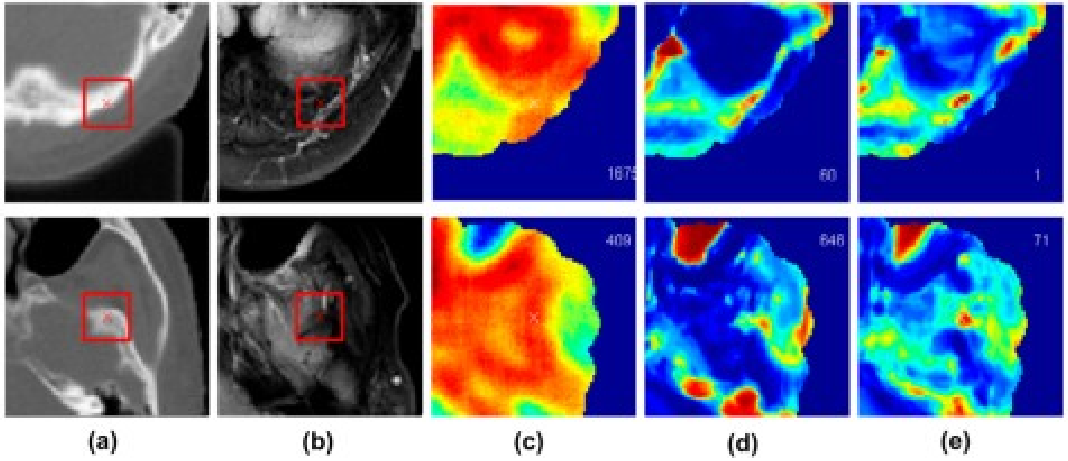


# Deformation Model

- Rigid
- Volume/topolgy preservation
- Affine
- Flow/Diffusion
- Elastic
- Viscous
- Free-form

# Matching Criteria

- Geometric
  - Feature distance
  - Geometric distance
- Iconic
  - Sum of square distances
    - Unimodal
  - Mutual Information
    - Multi-modal



# Examples of Metrics

| MEASURE | ACRONYM | TYPE | USAGE | FORMULA |
|---|---|---|---|---|
| SUM OF SQUARED DIFFERENCES | SSD | DIST. | SINGLE-MOD | $D_{SSD}(I,J) = \sum_{x\in\Omega}\left(I(x) - J(x)\right)^2$ |
| SUM OF ABSOLUTE DIFFERENCES | SAD | DIST. | SINGLE-MOD | $D_{SAD}(I,J) = \sum_{x\in\Omega} I(x) - J(x)$ |
| CORRELATION COEFFICIENT | CC | SIM. | SINGLE-MOD | $S_{CC}(I,J) = \sum_{x\in\Omega}\frac{(I(x) - E[I(x)])(J(x) - E[J(x)])}{\sigma(I)\sigma(J)}$ |
| MUTUAL INFORMATION | MI | SIM. | MULTI-MOD | $S_{MI}(I,J) = \sum_{i}\sum_{j}\rho_{IJ}(i,j)\log(\frac{\rho_{IJ}(i,j)}{\rho_I(i)\rho_J(j)})$ |
| CORRELATION RATIO | CR | SIM. | MULTI-MOD | $S_{CR}(I,J) = \frac{\sigma^2(E[\,J \mid I\,])}{\sigma^2(I)}$ |

# Optimization Method

- Non-exaustive search method

| METHOD | CLASSIFICATION | | |
|---|---|---|---|
| POWELL [12] | GRADIENT FREE | LOCAL | SERIAL |
| SIMPLEX [13] | GRADIENT FREE | LOCAL | PARTIALLY PARALLELIZABLE |
| SOBLEX[1] [14] | GRADIENT FREE | COMBINED | PARTIALLY PARALLELIZABLE |
| MDS[1,2] [15] | GRADIENT FREE | LOCAL | PARTIALLY PARALLELIZABLE |
| GRADIENT DESCENT [12] | GRADIENT BASED | LOCAL | PARTIALLY PARALLELIZABLE |
| QUASI-NEWTON [12] | GRADIENT BASED | LOCAL | PARTIALLY PARALLELIZABLE |
| LEVENBERG-MARQUARDT [12] | GRADIENT BASED | LOCAL | PARTIALLY PARALLELIZABLE |
| SIMULATED ANNEALING [12] | GRADIENT FREE | COMBINED | PARTIALLY PARALLELIZABLE |
| DIRECT[3] [16] | GRADIENT FREE | GLOBAL | FULLY PARALLELIZABLE |
| GENETIC [17] | GRADIENT FREE | GLOBAL | FULLY PARALLELIZABLE |

[1] A simplex variant, [2] multidirectional search, [3] dividing rectangles.

http://users.cecs.anu.edu.au/~ramtin/papers/2010/SPM_2010.pdf

# Basic Mathematics of Registration

The images are intensities $I, J: \Omega \subset R^d \rightarrow R^d$ in which *d* means dimensionality. If the transformation denoted by $I \circ T$, considering $T: R^d \rightarrow R^d$ as a spatial mapping..

$$T(x) = x + S(x)$$

In which $x$ is a point that belongs to $\Omega$ and $S(x)$ is a vector of $d$-dimensional deformation.

$$\epsilon = M + R$$

Measurable criterion $M$ to match the images. R is the regularization term. This parameter aims to impose constraints between the registration processes

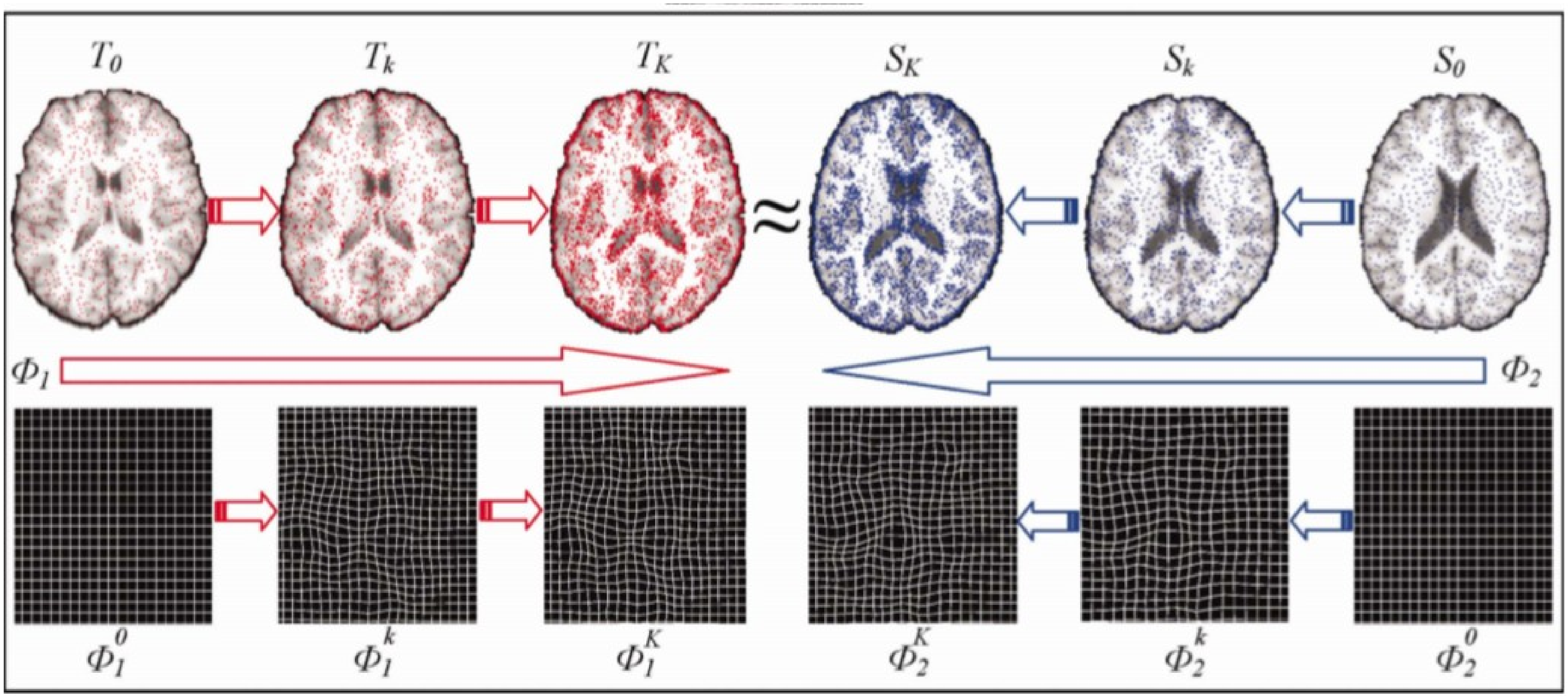
$$\hat{T} = arg\ min_T \epsilon(T)$$

The final transformation of the process will be indicated in this case by minimizing the energy

# Desirable Features

- Consistent inverse transform
  - Penalize distinct inverse transform
- Symmetry
  - Must produce symmetric transformations
- Topology preservation / Diffeomorphism
  - Internal and external structures

# Consistency and Symmetry




Wu et al., 2013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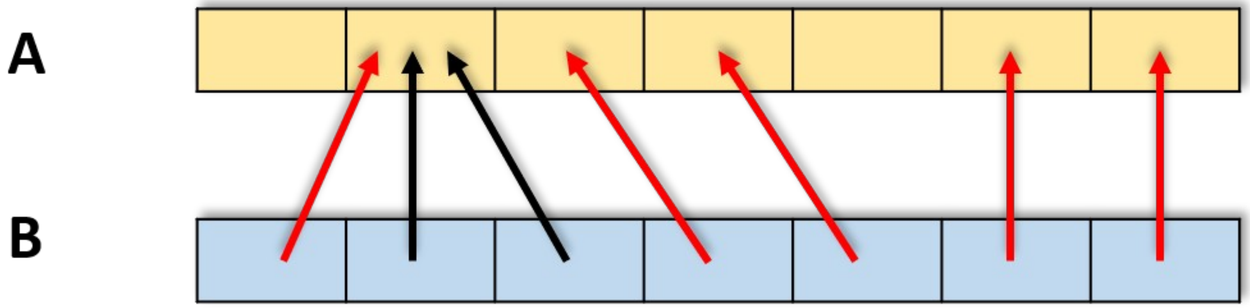
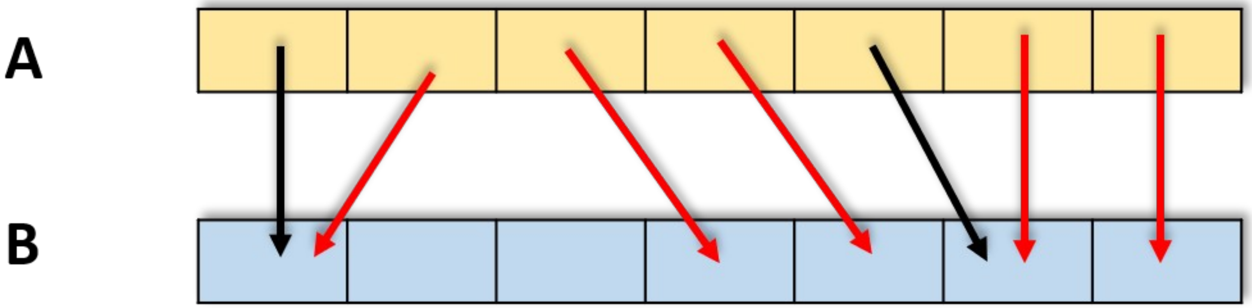
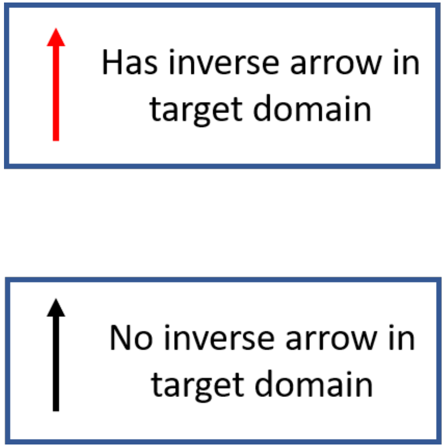
# Topology Preservation / Diffeomorphicity

InverseWarp pulls A into space of B, but is not dense in A




Warp pulls B into space of A, but is not dense in B




( Inspired in Avants et al., 2011)

| Algorithm | Deformation | Similarity | Regularization | Optimization | Applications |
|---|---|---|---|---|---|
| AIR (1992) | Third Order Polynomial | RIU, SSD, SLS | Increase of order | Continuos (Newton-Raphson with Muti-Resolution) | Brain MRI, PET |
| SYN (2008) | Diffeomorphic | CC, JHCT, MI, MSD, NCC, PSE | Gaussian filter | Discrete (Euler Lagrange with Muti-Resolution) | MRI, brain image, thorax CT |
| DARTEL (2007) | Diffeomorphic | Multinomial model | Linear-elasticity; | Continuous (Levenberg–Marquardt strategy with Muti-Resolution) | Brain |
| DRAMMS (2009) | Cubic B-splines | CC, SSD | Bending energy | Discrete (Gradient Descent with Muti-Resolution) | Prostate, brain MR, Cardiac |
| DEMONS DF (2009) | Diffeomorphic | SSD | Gaussian filter | Continuos (Gauss-Newton with Muti-Resolution) | Brain MRI |
| DEMONS MU (2009) | Non-parametric | MI | Gaussian filter | Continuos (Broyden-Fletcher-Goldfarb-Shanno*) | Brain MRI, CT |
| DROP (2011) | Free form deformation | SAD, SADG, SSD, NCC, NMI, CR, CCGIP, HD, JRD, MI, JE, GRAD | Pott's regularization | Discrete (FastPD) | Thorax CT; brain MRI |
| FLIRT (2001) | Linear, Rigid Body | NMI, MI, CR, NCC | - | Continuos (Powell based) | Brain |
| FNIRT (2007) | Cubic B-splines | SSD | Membrane energy | Continuos (Levenberg-Marquardt minimisation) | Brain MRI |
| S-HAMMER (2014) | Diffeomorphic | GMI | Bending energy | Miscellaenous | Brain MRI |

RIU: Ratio Image Uniformity, SSD: Sum of Squared Differences, SLS: Scaled Least-Squared difference image, CC: Cross-Correlation, JHCT: Jensen-Havrda-Charvat-Tsallis divergence, MI: Mutual Information, MSD: Mean Squared Difference, NCC: Normalized Correlation, PSE: Point-Set Expectation, SAD: Sum of Absolute Differences, SADG: Sum of Absolute Differences plus Sum of Gradient Inner Products, NMI: Normalized Mutual Information, CR: Correlation Ratio, CCGIP: Normalized Correlation Coefficient plus Sum of Gradient Inner Products, HD: Hellinger Distance, JRD: Jensen-Renyi Divergence, JE: Joint Entropy, GRAD: Sum of Gradient Inner Products and GMI: Geometric Moment Invariants.

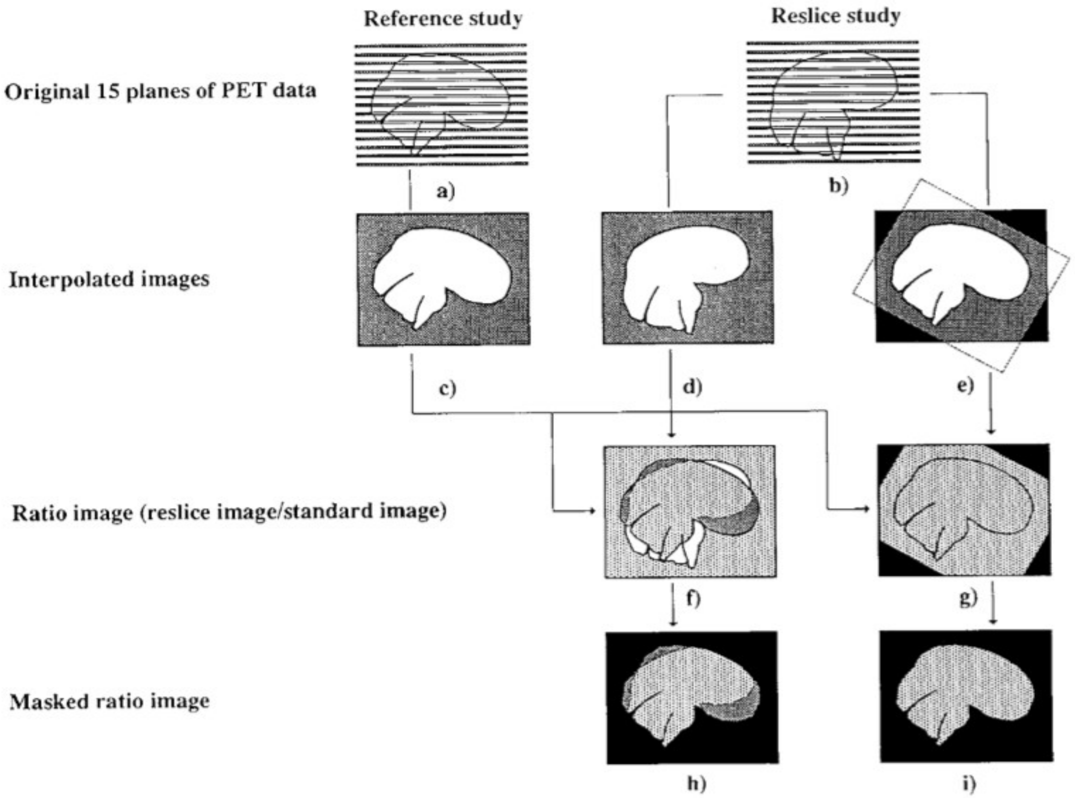
# *AIR – Woods et al.(1998)*

Automated Image Registration

- Automated Image Registration (AIR)

- It is a tool that brought several contributions to the registry area mainly in the field of deformation models using polynomials of various orders.

- Thee Similarity Metrics
  - Sum of Square Difference
  - Ratio Image Uniformity (RIU)
  - Variant RIU

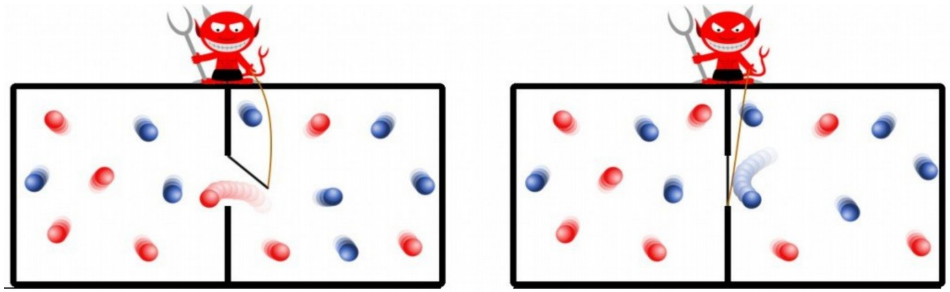


# *Demons – THIRION et al.(1998)*

- The method developed by Thiron is based on the idea of using the Maxwell demon problem.

- Applying this idea, the "demon" will determine to which place the voxel should go and so find their correspondence.

- The similarity metric used corresponds to a difference between the intensities, and this force comes from the calculation of the optical flow that will guide interactively adding the deformation to the total displacement that is initially zero



# *Demons – THIRION et al.(1998)*

➔ **Example of the registration process utilizing Demons**

I. Select all elements of the image as Demon
II. Calculate the force of the demon considering the general restriction by optical flow
III. Assume a non-parametric deformation model that is regularized by applying a filter to each iteration.
IV. Use a trilinear interpolation.
V. Applying the Gaussian filter to each estimated field deformation in an interaction.

# Demons Diffeomorphic – Vercauteren et., (2008)

- Several theoretical explanations about Thirion method.
- It used the strain exponentiation field to ensure the diffeomorphic mapping.
- Representation of log-domain transformations enabled forward and backward forces separately.

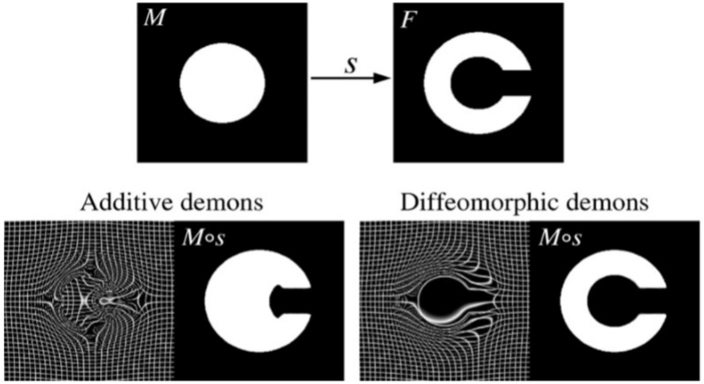


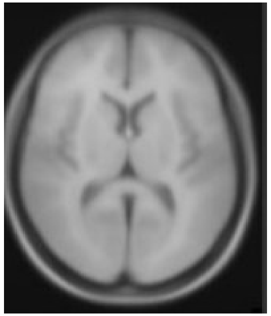

**Fig. 6.** Classical Circle to C registration example. With the same set of parameters the additive demons fails to converge and shows foldings in the registration results whereas the diffeomorphic demons converges with a smooth invertible transformation.

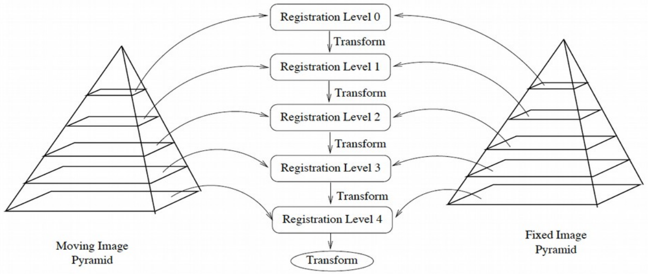
# FSL – FMRIB Software Library (2001)

- FLIRT: FMRIB's Linear Image Registration Tool

- A global, multi-start and multi-resolution optimization strategy specifically for affine image registration problems was proposed.

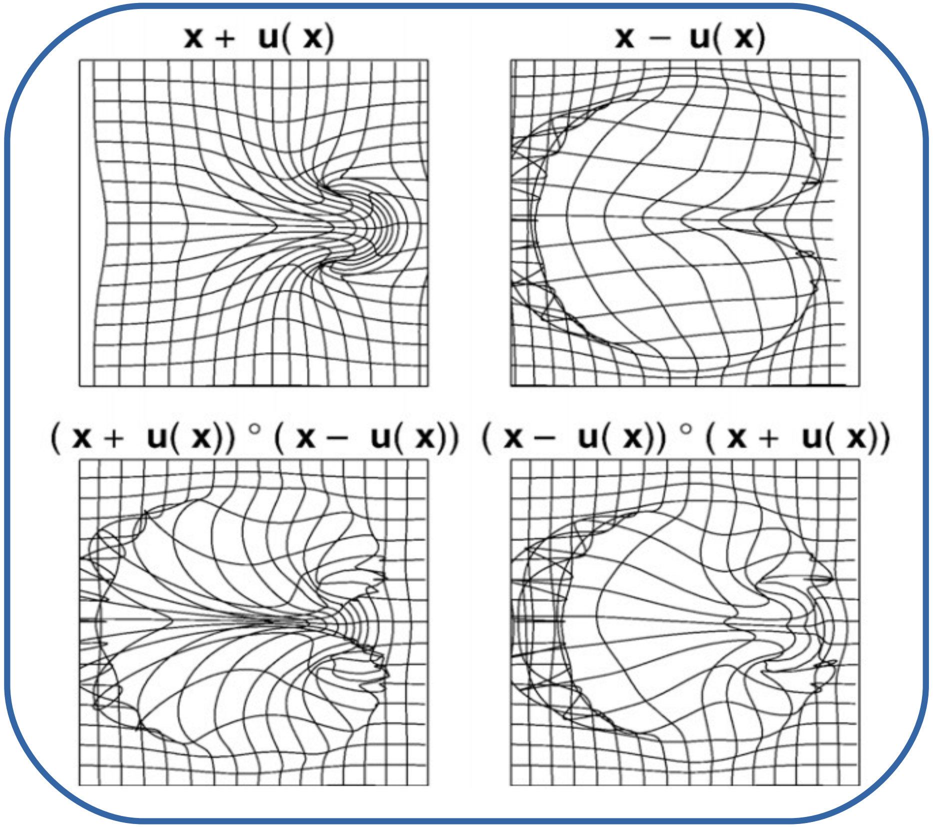
- FNIRT: FMRIB's Non Linear Image Registration Tool

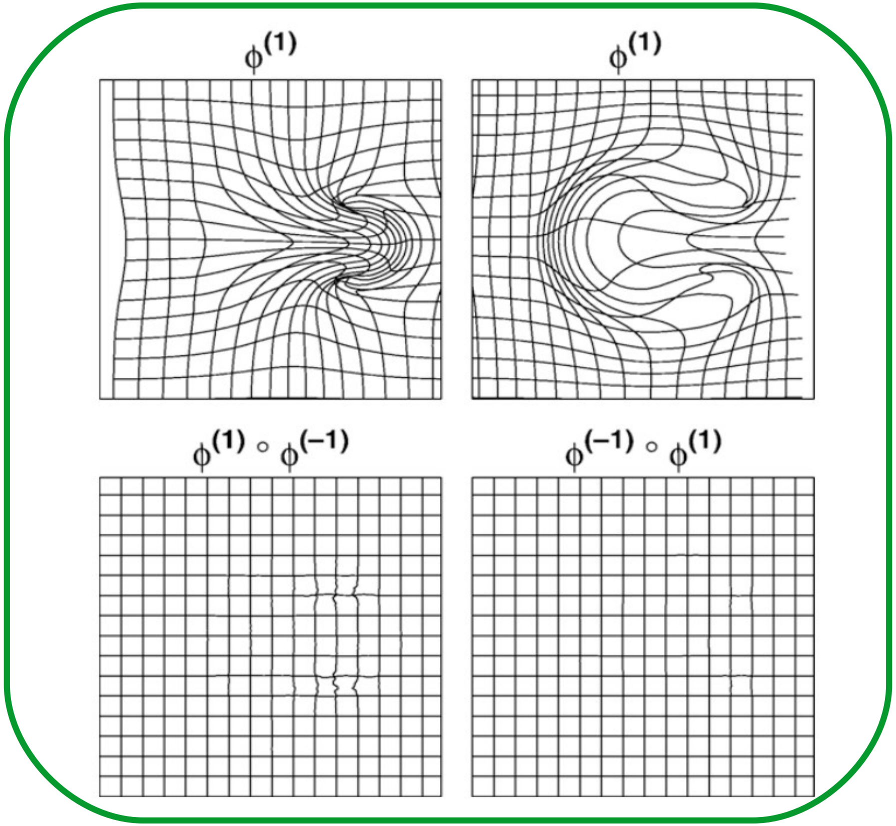




# *Dartel – Ashburner et al.,(2007)*

- Diffeomorphic Anatomical Registration using Exponentiated Lie Algebra



# *DRAMMS – Ou et al., (2009)*

- Deformable Registration via Attribute Matching and Mutual-Saliency Weighting

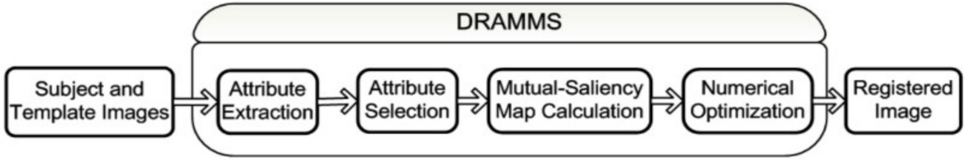
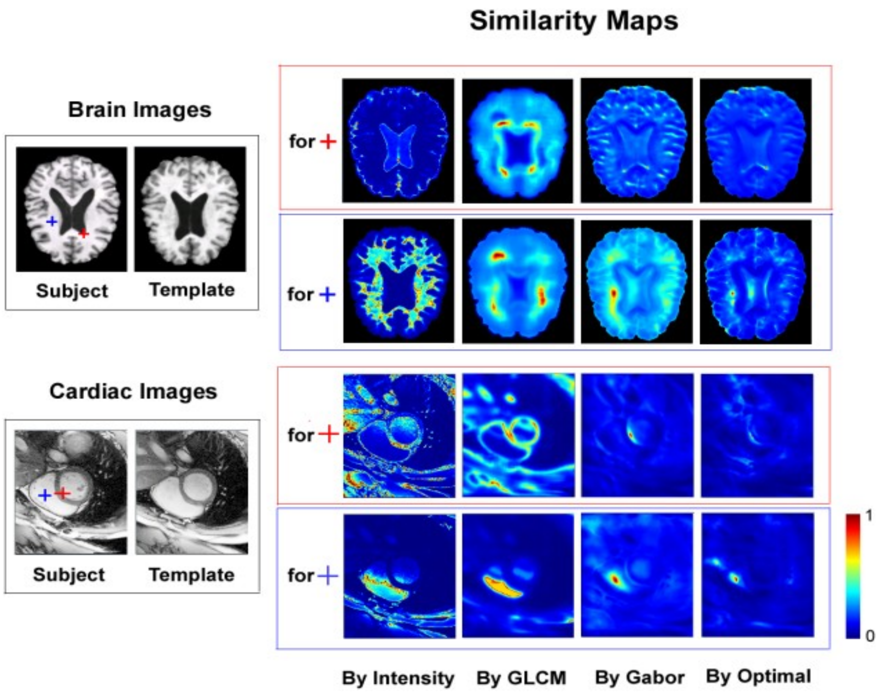
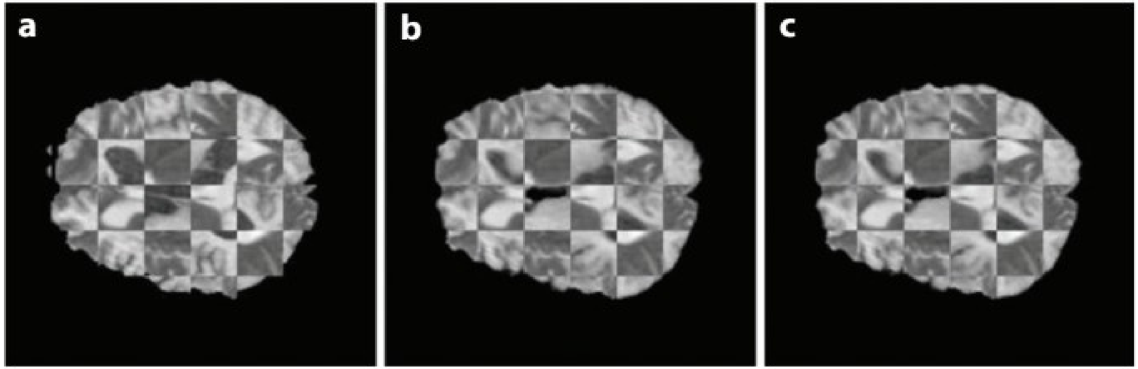



**Fig. 2.** The components of DRAMMS



# *DROP – Glocker et al.,(2011)*

- DROP is a deformable registry that has a great contribution in the field of numerical optimization.
- The processing time of the registry has dropped considerably
- Minimizing the energy of a discrete Markov Random Field (MRF).




Before Iconic approach Hybrid approach

# *SyN – Avants et al.,(2011)*

- Advanced Normalization Tools
- ANTsR, ANTsPy, ANTsRNet.

Transformation Model | Appearance/Similarity Metrics

$$\int_0^1 < Lv(x,t), v(x,t) > dt + w_1 SSD(I,J) + w_2 MI(I,J) + w_3 \sum_i LM_i(I,J)$$

Diffeomorphic Regularization + Intensity Difference + Mutual information + Landmark Guidance

ANTS -t Syn[0.5] –m MSQ(I,J,w1,0) –m MI(I,J,w2,#bins) –m PSE(I,J,w3)

Note: the choice of *L* above relates to the -r (regularization) parameter in ANTS, which would be part of the blue above.

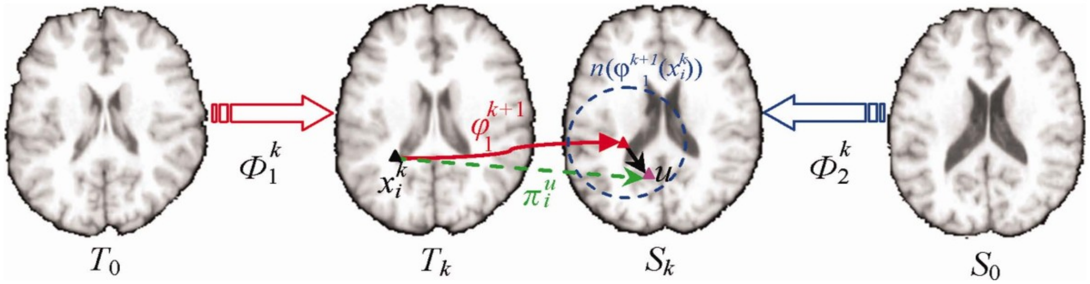
# *SyN – Avants et al.,(2011)*

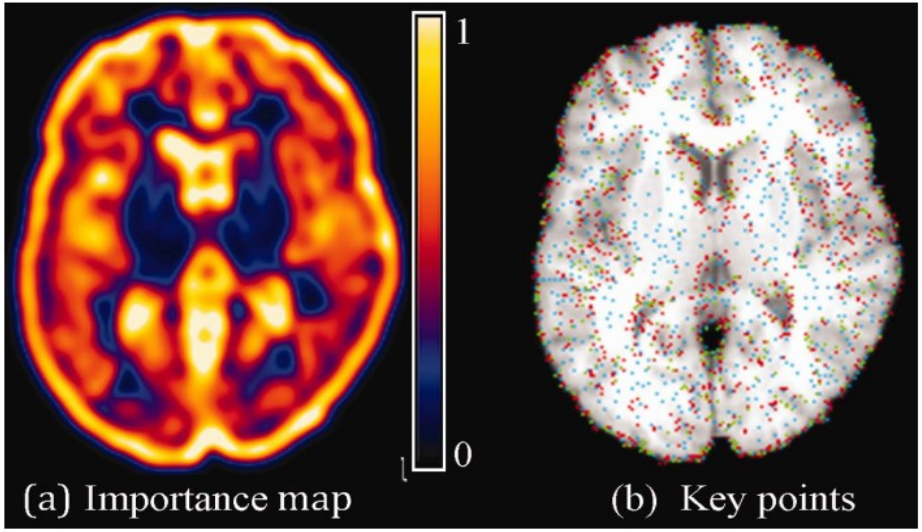
- Advanced Normalization Tools
- ANTsR, ANTsPy, ANTsRNet.

| Category | Transformation, $\phi$ | Similarity Measures | Brief Description |
|---|---|---|---|
| **Linear** | Rigid$^\dagger$ | MI, MeanSquares, GC | Rigid registration. |
| | Similarity$^\dagger$ | MI, MeanSquares, GC | Rotation + uniform scaling. |
| | Affine$^\dagger$ | MI, MeanSquares, GC | Affine registration. |
| **Elastic** | GaussianDisplacementField | CC, MI, MeanSquares, Demons | Demons-like algorithm. |
| | BSplineDisplacementField | CC, MI, MeanSquares, Demons | FFD variant. |
| **Diffeo.** | Exponential$^\dagger$ | CC, MI, MeanSquares, Demons | min $v(\mathbf{x})$ |
| | SyN$^\dagger$ | CC, MI, MeanSquares, Demons | locally in time min $v(\mathbf{x},t)$ |
| | BSplineSyN$^\dagger$ | CC, MI, MeanSquares, Demons | locally in time min $v(\mathbf{x},t)$ |
| | TimeVaryingVelocityField$^\dagger$ | CC, MI, MeanSquares, Demons | min $v(\mathbf{x},t)$ over all time |

# S-Hammer – Wu et al.,(2013)

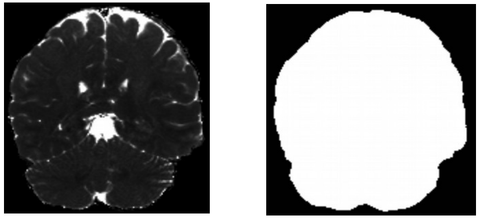
- Hierarchical Attribute-Guided Symmetric Diffeomorphic Registration for MR Brain Image



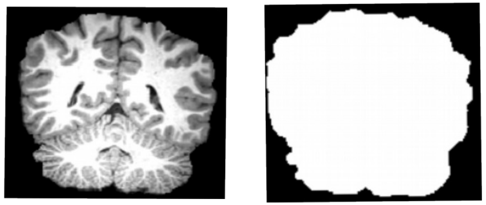



# Evaluate of Registration

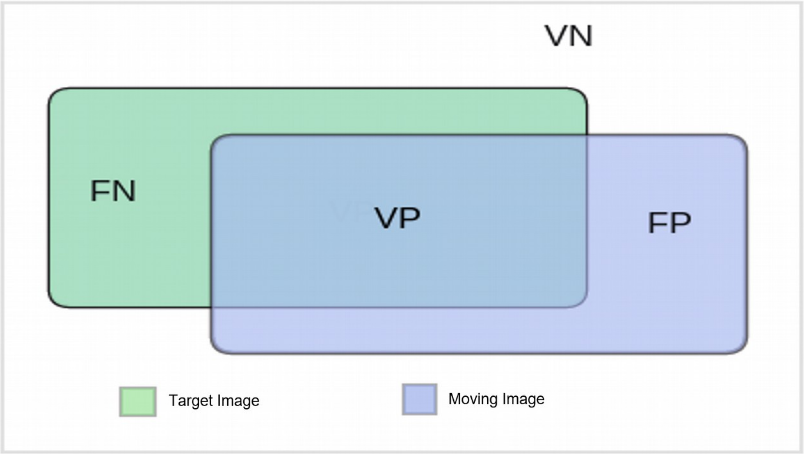
Moving Image



Target Image



Overlap Image




| | FLIRT | AIR | ANIMAL | ART | D. Demons | FNIRT | IRTK | JRD-fluid | ROMEO | SICLE | SyN | SPM_N* | SPM_N | SPM_US | SPM_D | S-HAMMER |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| *L&R post. ventral sup. Temporal sulcus* | 26.7 | 29.0 | 41.5 | 46.1 | 37.9 | 37.3 | 46.9 | 38.9 | 36.0 | 30.0 | 50.3 | 34.8 | 31.8 | 33.8 | 47.1 | 54.5 |
| *L&R ventral somatosensory ctx* | 47.2 | 50.0 | 53.4 | 59.2 | 53.5 | 51.8 | 57.3 | 53.6 | 53.4 | 50.1 | 60.8 | 52.8 | 43.7 | 52.1 | 58.3 | 67.5 |
| *L&R post. central operculum* | 41.5 | 46.8 | 47.1 | 54.5 | 48.9 | 47.2 | 51.1 | 48.3 | 47.3 | 43.4 | 53.4 | 47.2 | 47.6 | 47.6 | 54.7 | 65.8 |
| *L&R dorsal somatosensory ctx* | 42.2 | 43.5 | 48.0 | 53.4 | 48.2 | 46.3 | 51.4 | 49.4 | 47.4 | 44.5 | 55.3 | 47.8 | 32.8 | 45.4 | 53.9 | 45.3 |
| *L&R post. middle frontal gyrus* | 54.5 | 55.5 | 57.9 | 64.0 | 59.2 | 49.8 | 63.1 | 60.2 | 59.8 | 56.5 | 66.1 | 57.1 | 45.5 | 54.5 | 65.7 | 70.5 |