Deep learning for medical imaging

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Master 2 - MVA

Course website: http://www.aramislab.fr/teaching/DLMI-2019-2020/
Piazza (for registered students): https://piazza.com/centralesupelec/spring2020/mvadlmi/

Part 8 – Registration

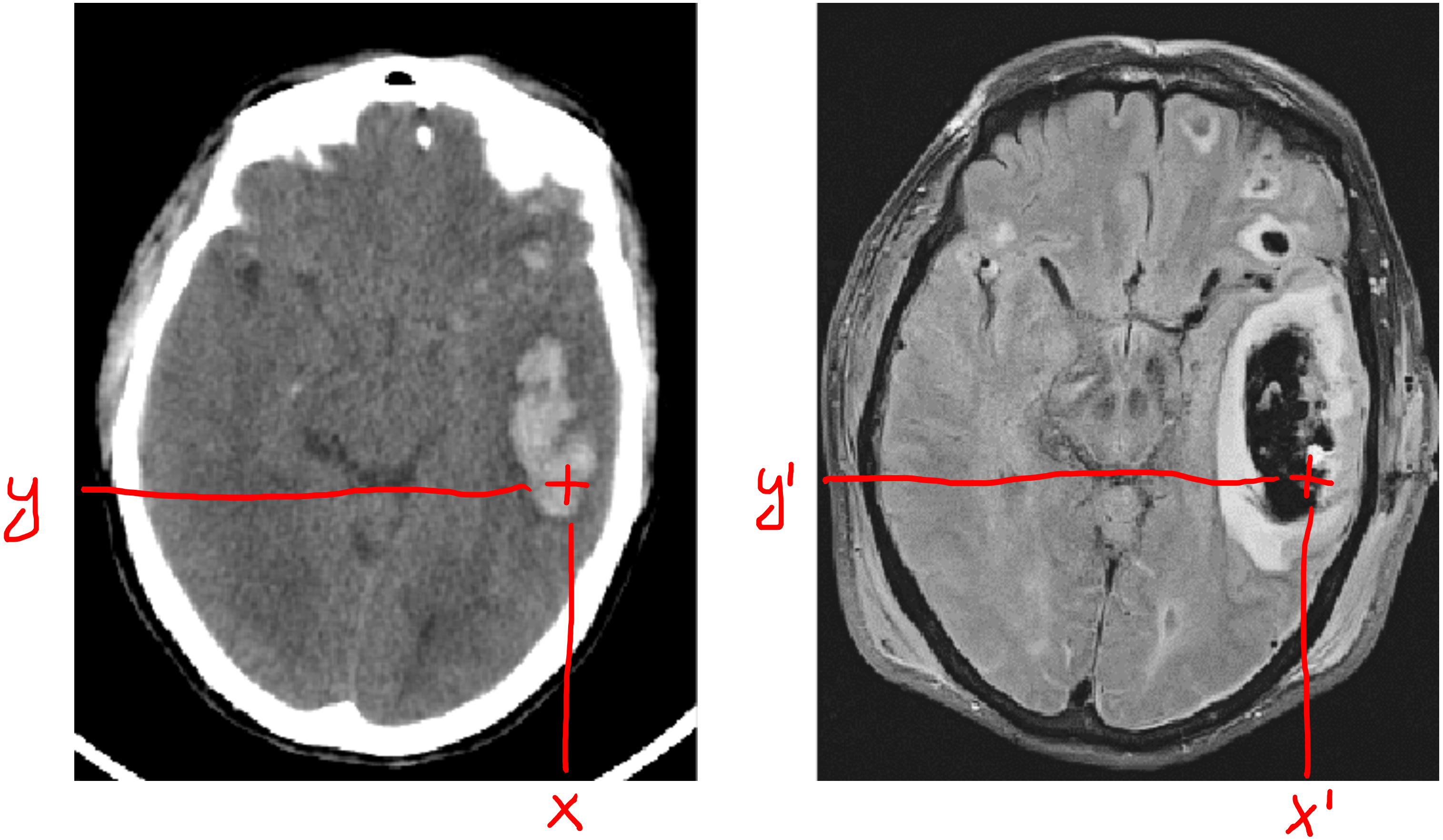
("*Recalage*" in French)

Part 8 – Registration

8.1 Introduction

What is image registration?

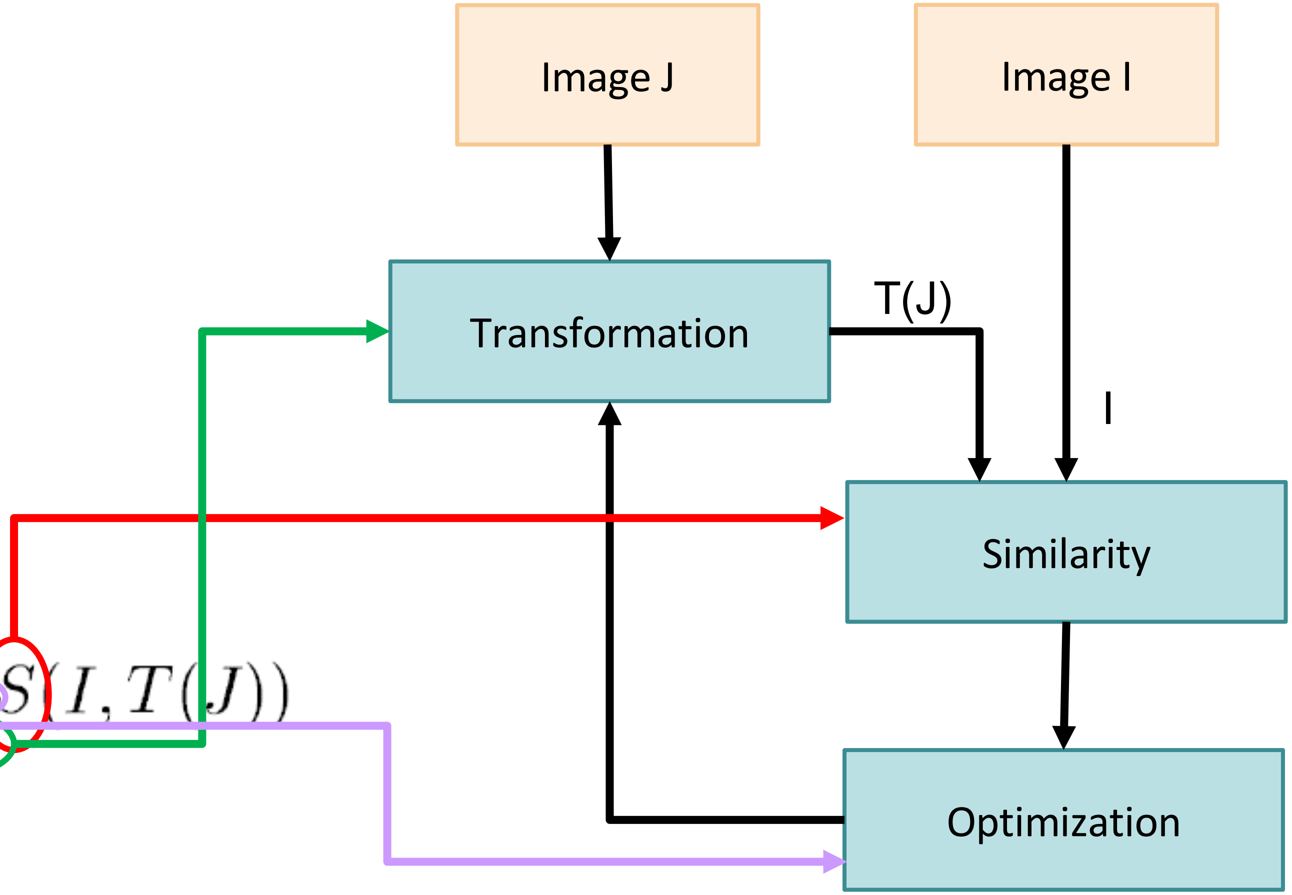
Registration=Establish spatial correspondences between images



$$\begin{pmatrix} x' \\ y' \end{pmatrix} = T \begin{pmatrix} x \\ y \end{pmatrix}$$

Source: B. Glocker/D. Rueckert – Course on Machine Learning for Imaging – Imperial College London

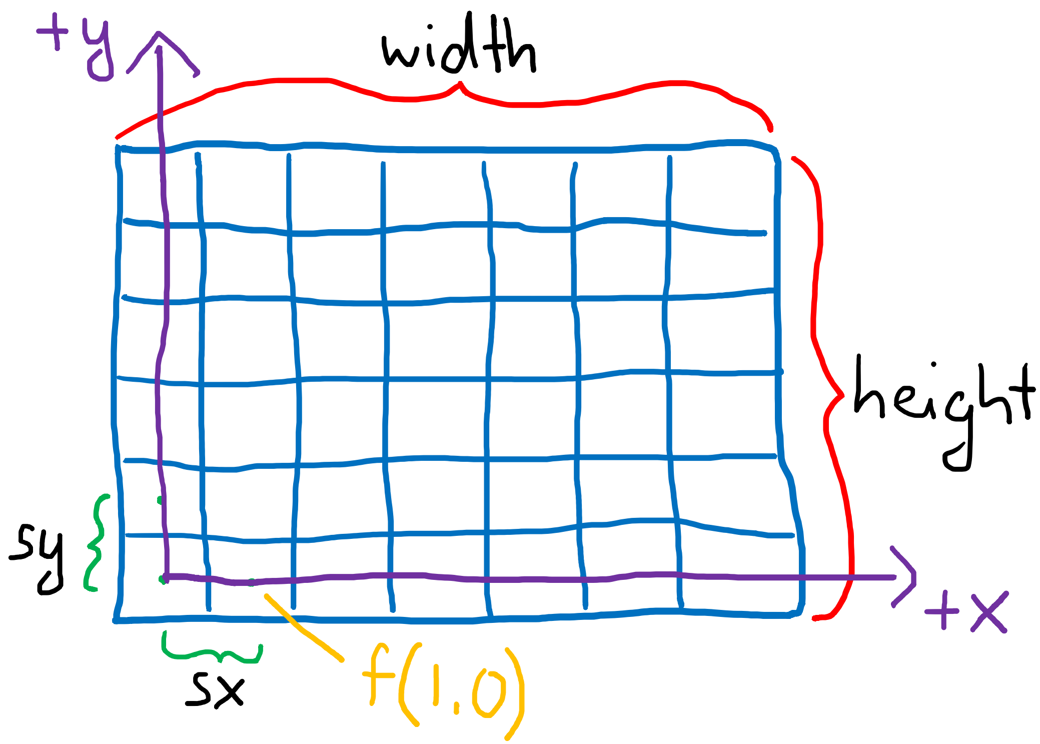
What is image registration?



$$\hat{T} = \arg\max_{T \in E} S(I, T(J))$$

Coordinate systems

Image coordinate system



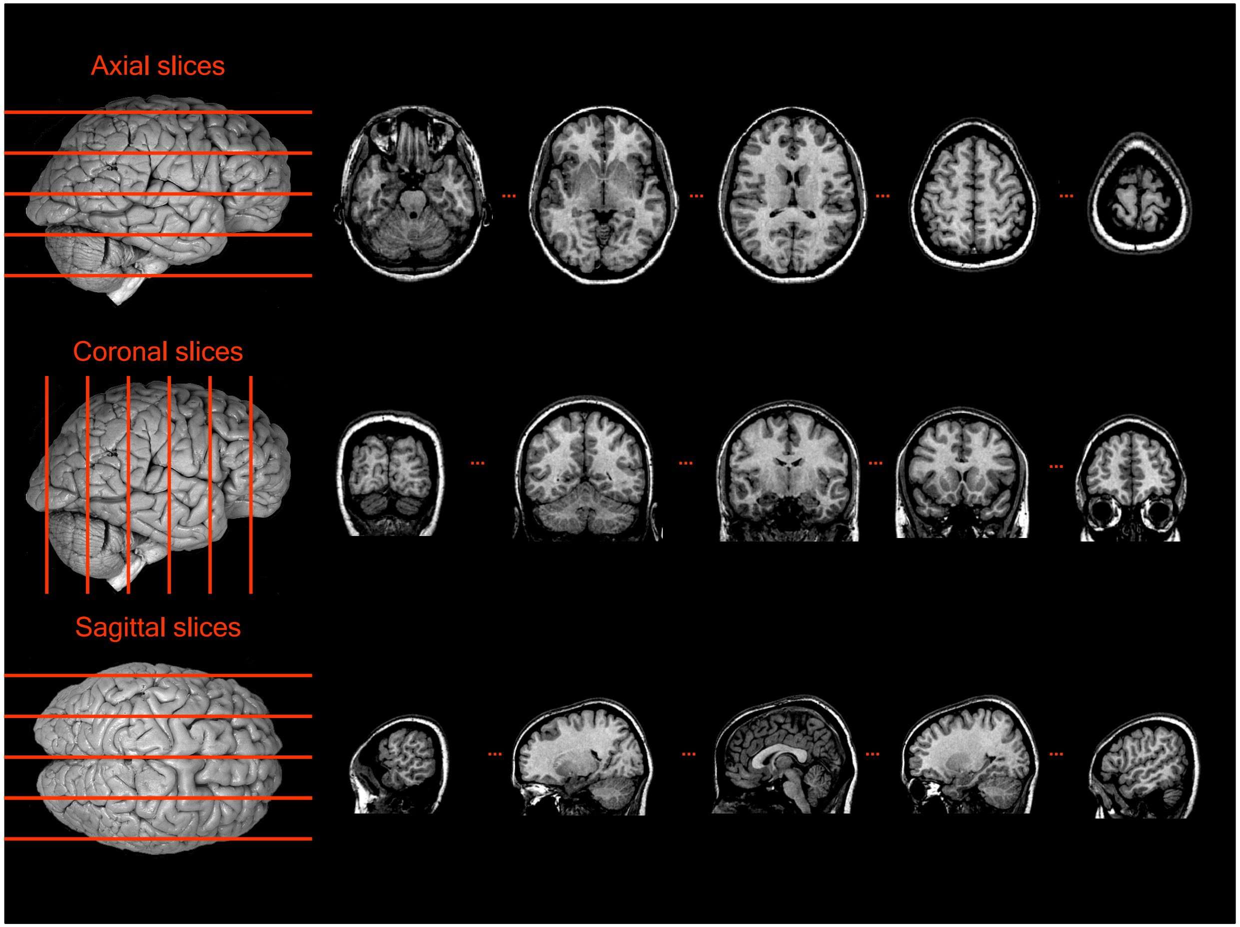
s_x, s_y, s_z : voxel size (in millimeters)

Medical often have non-isotropic voxels/pixels

$s_x \neq s_y \neq s_z$

Source: B. Glocker/D. Rueckert – Course on Machine Learning for Imaging – Imperial College London

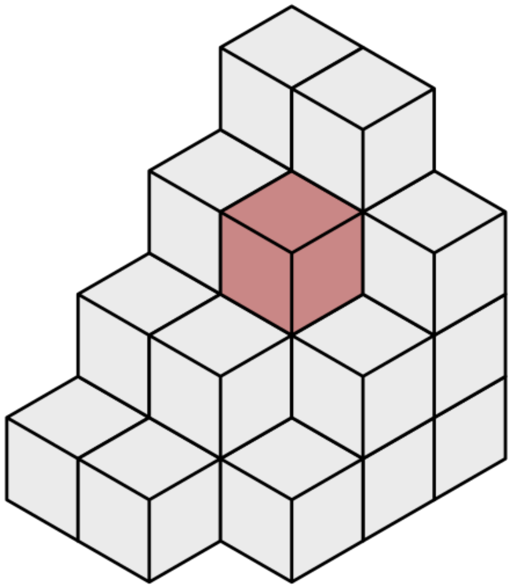
3D images

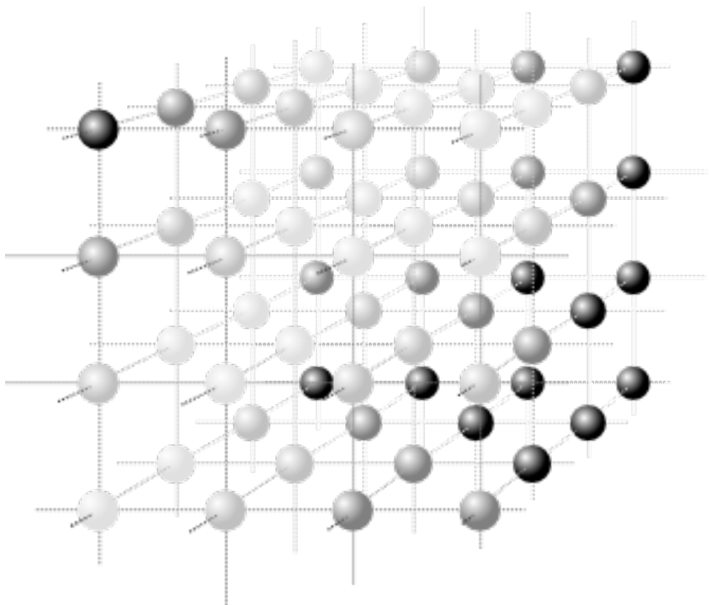


Remember: many medical images are 3D

Some of the course's equations will be given in 2D but real applications are most often in 3D

3D images





Voxel=volume element

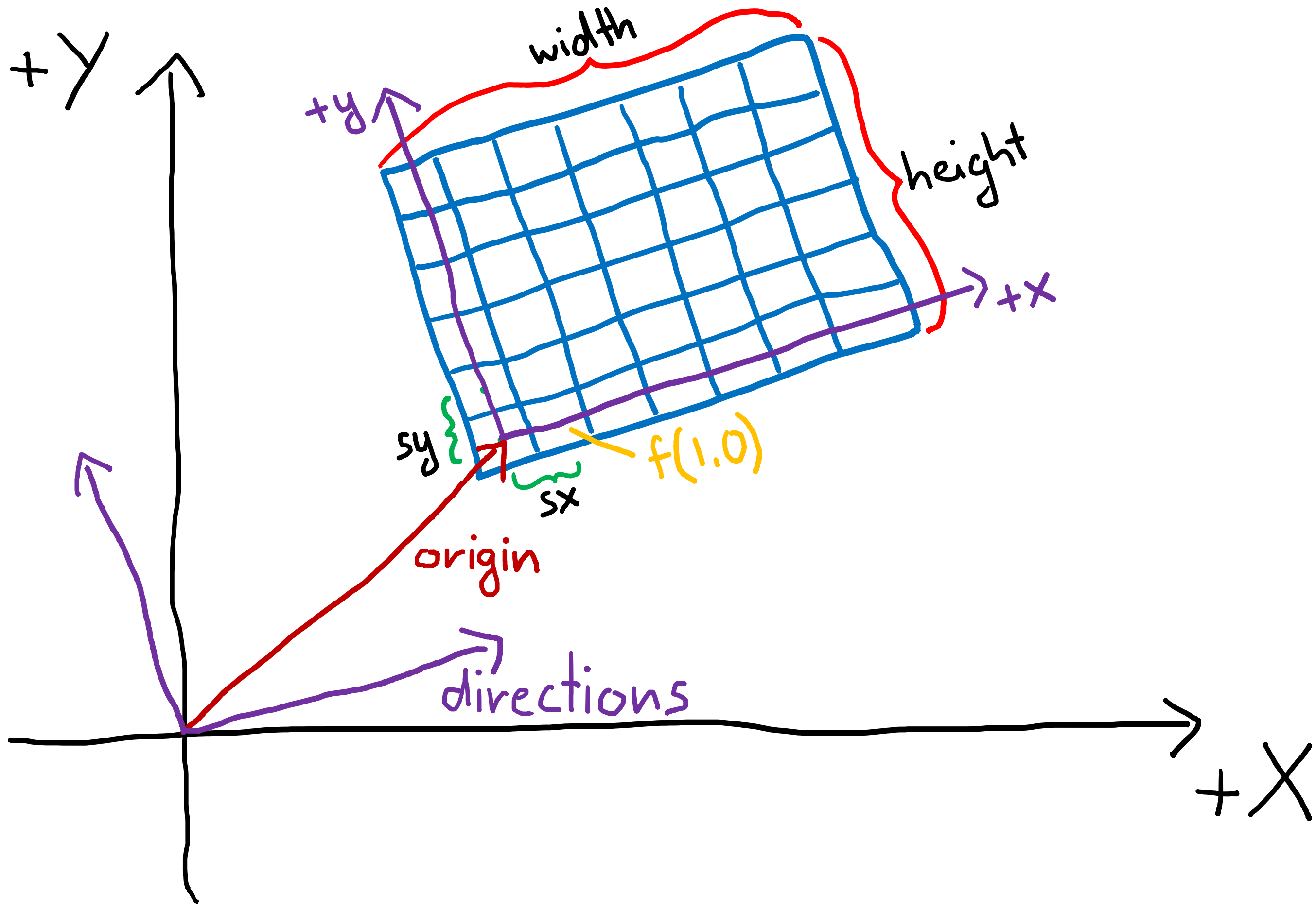
Image source: https://en.wikipedia.org/wiki/Voxel

Remember: many medical images are 3D

Some of the course’s equations will be given in 2D but real applications are most often in 3D

Coordinate systems

World coordinate system



Source: B. Glocker/D. Rueckert – Course on Machine Learning for Imaging – Imperial College London

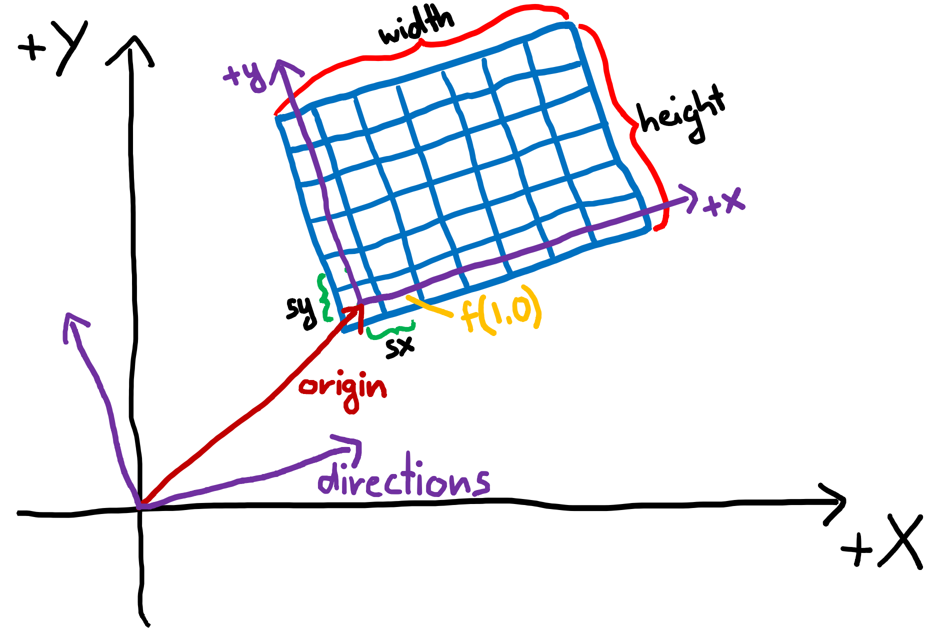
Coordinate systems

Image to world

$$\begin{pmatrix} X \\ Y \\ 1 \end{pmatrix} = \underbrace{\begin{bmatrix} 1 & 0 & ox \\ 0 & 1 & oy \\ 0 & 0 & 1 \end{bmatrix} \begin{bmatrix} dxx & dyx & 0 \\ dxy & dyy & 0 \\ 0 & 0 & 1 \end{bmatrix} \begin{bmatrix} sx & 0 & 0 \\ 0 & sy & 0 \\ 0 & 0 & 1 \end{bmatrix}}_{T_{ItW}} \begin{pmatrix} x \\ y \\ 1 \end{pmatrix}$$

World to image

$$\begin{pmatrix} x \\ y \\ 1 \end{pmatrix} = T_{ItW}^{-1} \begin{pmatrix} X \\ Y \\ 1 \end{pmatrix}$$



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Introduction

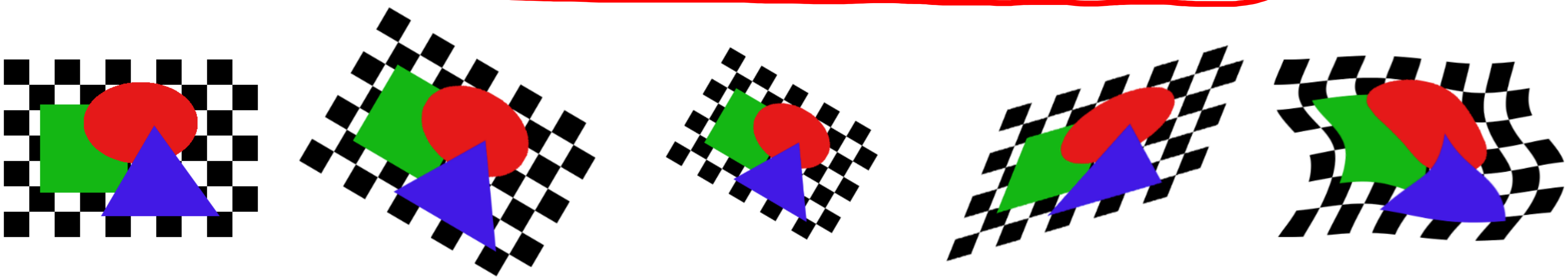
Although deep learning based registration methods have been developed, **they are not (yet) the standard** for this task (unlike, for example, for segmentation)

Part 8 – Registration

8.2 Transformation models

Transformation models

linear				nonlinear
identity	rigid	similarity	affine	deformable
	rotation+translation	rigid+uniform scaling	rigid+nonuniform scaling+shear



degrees of freedom / parameters

0 — 3/6 — 4/7 — 6/12 — thousands/millions

2D 3D

poly-affine
parameterised deformation

Source: B. Glocker/D. Rueckert – Course on Machine Learning for Imaging – Imperial College London

Part 8 – Registration

8.2 Transformation models
8.2.1 Linear transformations

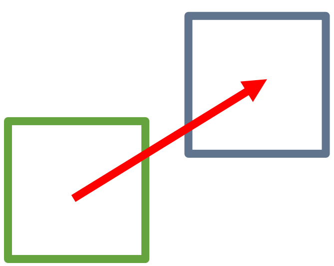
Linear transformations

Parameterisation of linear transformation (using homogeneous coordinates)

2D affine: translation (2), rotation (1), scaling (2), shear(1) = 6 DOF

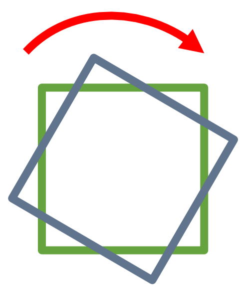
Translation

$$T = \begin{bmatrix} 1 & 0 & t_x \\ 0 & 1 & t_y \\ 0 & 0 & 1 \end{bmatrix}$$



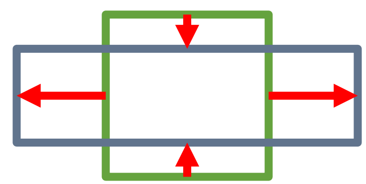
Rotation

$$R = \begin{bmatrix} \cos\theta & \sin\theta & 0 \\ -\sin\theta & \cos\theta & 0 \\ 0 & 0 & 1 \end{bmatrix}$$



Scaling

$$S = \begin{bmatrix} s_x & 0 & 0 \\ 0 & s_y & 0 \\ 0 & 0 & 1 \end{bmatrix}$$



Shearing

$$H = \begin{bmatrix} \cos\omega & \sin\omega & 0 \\ -\sin\omega & \cos\omega & 0 \\ 0 & 0 & 1 \end{bmatrix}$$

?

Source: B. Glocker/D. Rueckert – Course on Machine Learning for Imaging – Imperial College London

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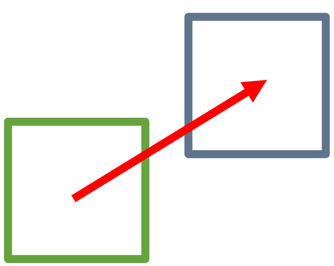

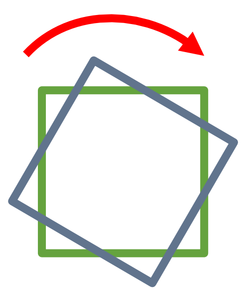

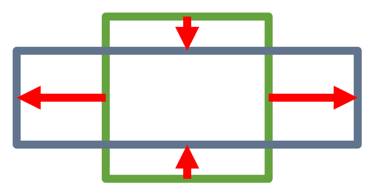

$$H\,S\,H^{-1}$$

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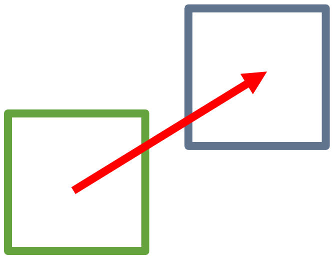

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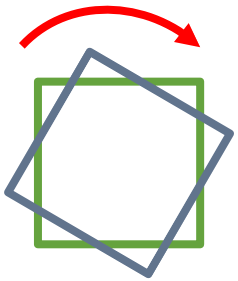

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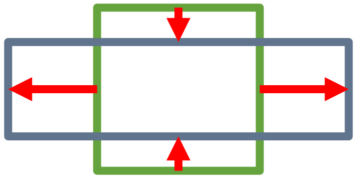

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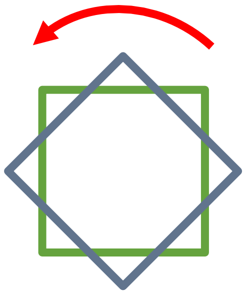

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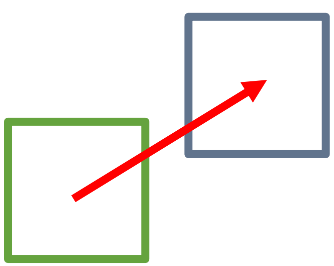

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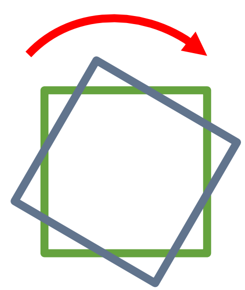

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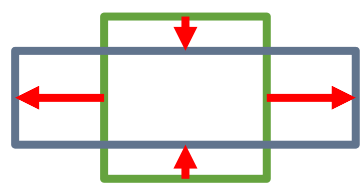

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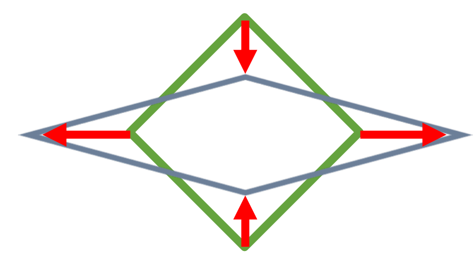

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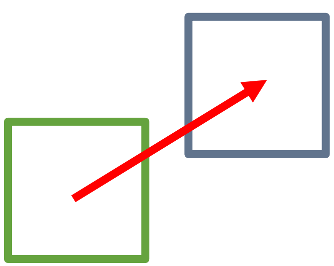

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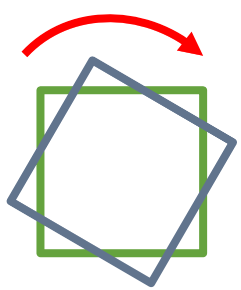

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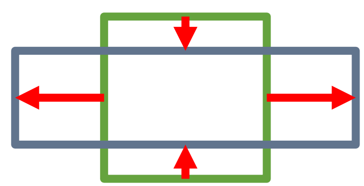

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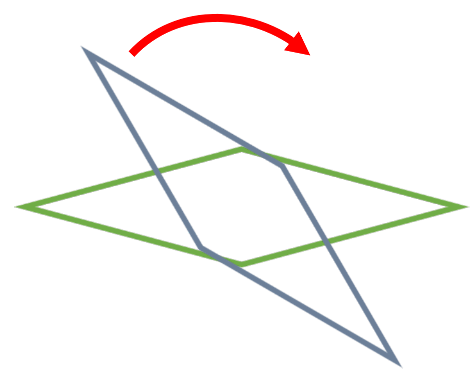

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Shearing

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$$A = H\,S\,H^{-1}R\,T = \begin{bmatrix} a_{11} & a_{12} & a_{13} \\ a_{21} & a_{22} & a_{23} \\ 0 & 0 & 1 \end{bmatrix}$$

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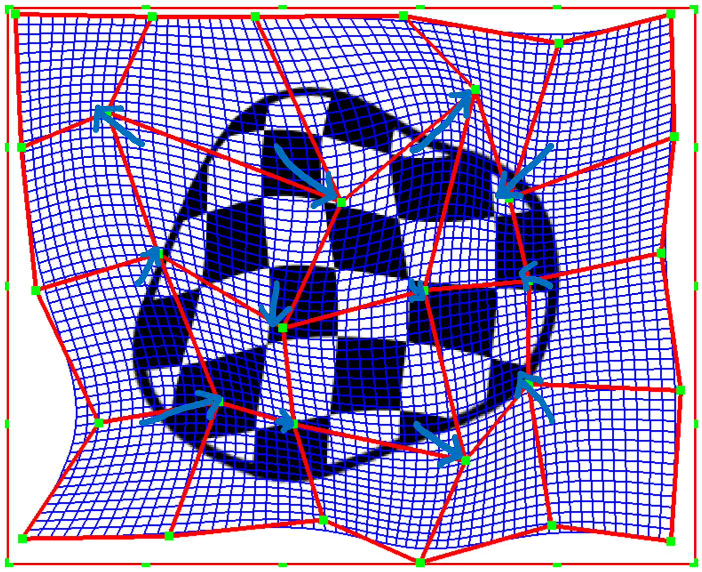
Part 8 – Registration

8.2 Transformation models
8.2.2 Non-linear transformations

Free-form deformations (FFD)



Principle:
Deform an object by manipulating an underlying mesh of control points

Source: B. Glocker/D. Rueckert – Course on Machine Learning for Imaging – Imperial College London

Reference: Rueckert et al, IEEE TMI, 1999

Free-form deformations (FFD)

The deformation is defined with **B-splines**

Let Φ denote a $n_x \times n_y \times n_z$ mesh of control points $\phi_{i,j,k}$ with uniform spacing δ. Then, the FFD can be written as the 3 -D tensor product of the familiar 1 -D cubic B-splines

$$\begin{aligned} &\mathbf{T}_{\text{local}}(x, y, z) \\ &\quad = \sum_{l=0}^{3} \sum_{m=0}^{3} \sum_{n=0}^{3} B_l(u) B_m(v) B_n(w) \phi_{i+l, j+m, k+n} \end{aligned}$$

where $i = \lfloor x/n_x \rfloor - 1, j = \lfloor y/n_y \rfloor - 1, k = \lfloor z/n_z \rfloor - 1$

$$u = x/n_x - \lfloor x/n_x \rfloor, v = y/n_y - \lfloor y/n_y \rfloor, w = z/n_z - \lfloor z/n_z \rfloor$$

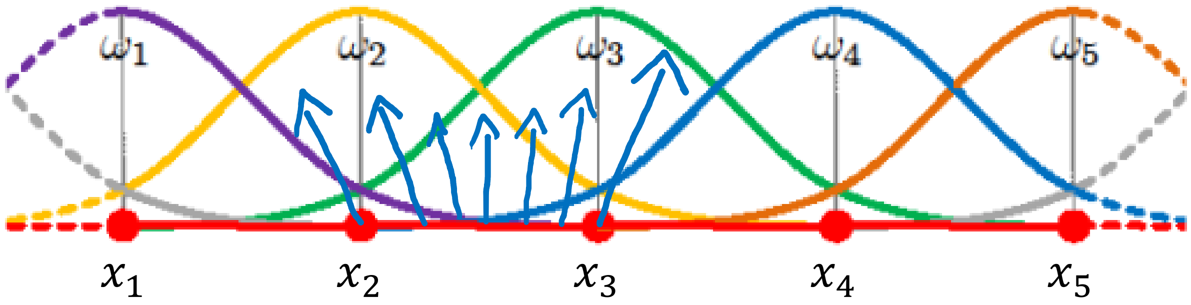
and where B_l represents the l th basis function of the B-spline

$$\begin{aligned} B_0(u) &= (1-u)^3/6 \\ B_1(u) &= \left(3u^3 - 6u^2 + 4\right)/6 \\ B_2(u) &= \left(-3u^3 + 3u^2 + 3u + 1\right)/6 \\ B_3(u) &= u^3/6 \end{aligned}$$

Reference: Rueckert et al, IEEE TMI, 1999

Free-form deformations (FFD)

Low-dimensional deformation model



Source: B. Glocker/D. Rueckert – Course on Machine Learning for Imaging – Imperial College London

Reference: Rueckert et al, IEEE TMI, 1999

Free-form deformations (FFD)

Number of control points

More control points means a more flexible transformation

Reference: Rueckert et al, IEEE TMI, 1999

Free-form deformations (FFD)

In order to produce reasonably realistic deformations, one needs to **add a smoothness constraint** on the transformation

$$\begin{aligned}\mathcal{C}_{\text{smooth}} = \frac{1}{V}\int_0^X\int_0^Y\int_0^Z\Bigg[&\left(\frac{\partial^2\mathbf{T}}{\partial x^2}\right)^2+\left(\frac{\partial^2\mathbf{T}}{\partial y^2}\right)^2\\ &+\left(\frac{\partial^2\mathbf{T}}{\partial z^2}\right)^2+2\left(\frac{\partial^2\mathbf{T}}{\partial xy}\right)^2+2\left(\frac{\partial^2\mathbf{T}}{\partial xz}\right)^2\\ &+2\left(\frac{\partial^2\mathbf{T}}{\partial yz}\right)^2\Bigg]dxdydz\end{aligned}$$

The **objective function** is a compromise between similarity of images and smoothness of the transformation

$$\mathcal{C}_{\text{similarity}}\left(I,\mathbf{T}(I)\right)+\lambda\mathcal{C}_{\text{smooth}}\left(\mathbf{T}\right)$$

Reference: Rueckert et al, IEEE TMI, 1999

Elastic deformations

The transformation is defined by a displacement field u over the whole image

$$\phi_u(x) = x + u(x)$$

where x is a point in $\mathbb{R}^2$ (or $\mathbb{R}^3$ for a 3D image)

The registration problem is then

$$\hat{u} = \arg\max_{u \in H} S(I, \phi_u(J)) + Reg(u)$$

Problem: no garantee that the transformation is invertible. In particular, invertibility would be only obtained for very small displacement fields

LDDMM (Large Deformation Diffeomorphic Metric Mapping)

Diffeomorphisms: invertible, differentiable deformations which inverse is also differentiable

LDDMM: mathematical framework for diffeomorphic registration

- principled approach
- can be used for morphometry through analysis of the computed deformations

References: Trouvé, IJCV, 1998; Dupuis et al, 1998; Beg et al, IJCV, 2005

LDDMM (Large Deformation Diffeomorphic Metric Mapping)

Intution: One can consider ϕ as the concatenation of small deformations ϕ_{u_i}.

$\phi = \Phi_n$ where the Φ_k are recursively defined by $\Phi_0 = Id$ and $\Phi_{k+1} = \phi_{u_{k+1}} \circ \Phi_k$

LDDMM: The deformation ϕ is defined as the integration of a time-dependent velocity vector field $v(.,t)$:

$$\begin{cases} \frac{\partial \phi_v}{\partial t}(x,t) = v(\phi_v(x,t),t) & \forall t \in [0,1] \\ \phi_v(x,0) = x & \forall x \in \mathbb{R}^3 \end{cases}$$

Position of x at time t

The resulting transformation is $\phi = \phi_v(x,1)$

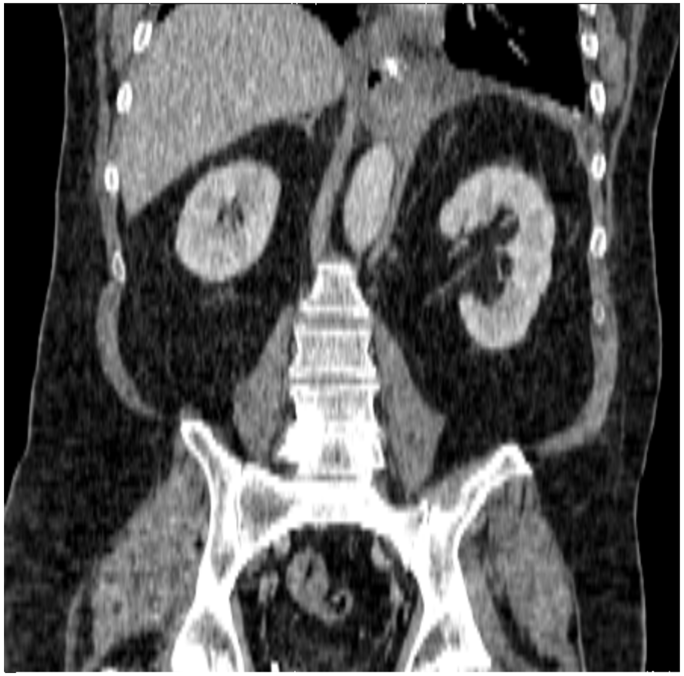
One can define a right-invariant distance on the group of diffeomorphisms: $D(Id,\phi) = \inf\left\{ \int_0^1 \|v(\cdot,t)\|_V dt; v \in L^2([0,1],V), \phi_v = \phi \right\}$

References: Trouvé, IJCV, 1998; Dupuis et al, 1998; Beg et al, IJCV, 2005

Part 8 – Registration

8.3 (Dis)similarity measures

(Dis)similarity measures



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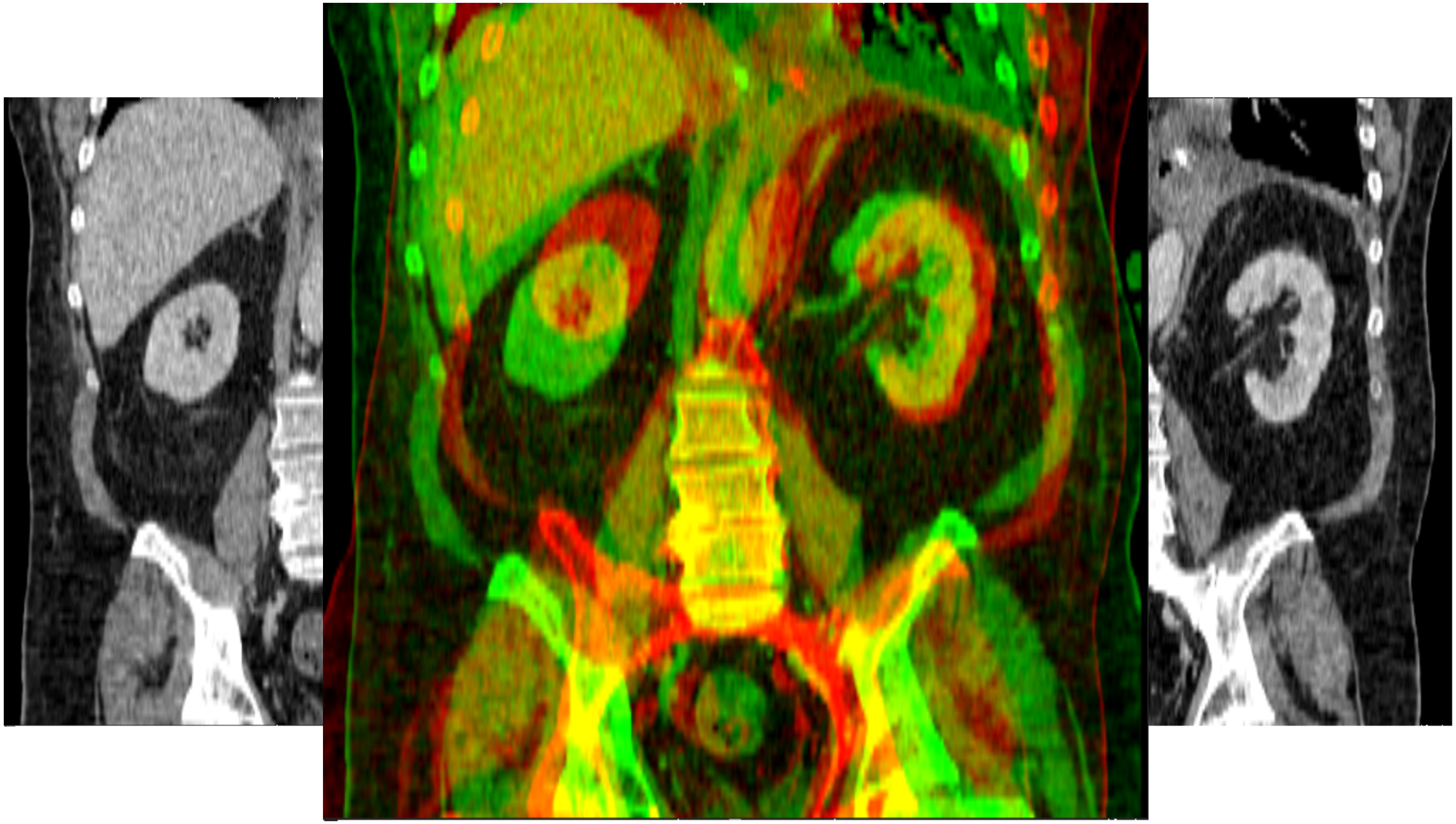
(Dis)similarity measures



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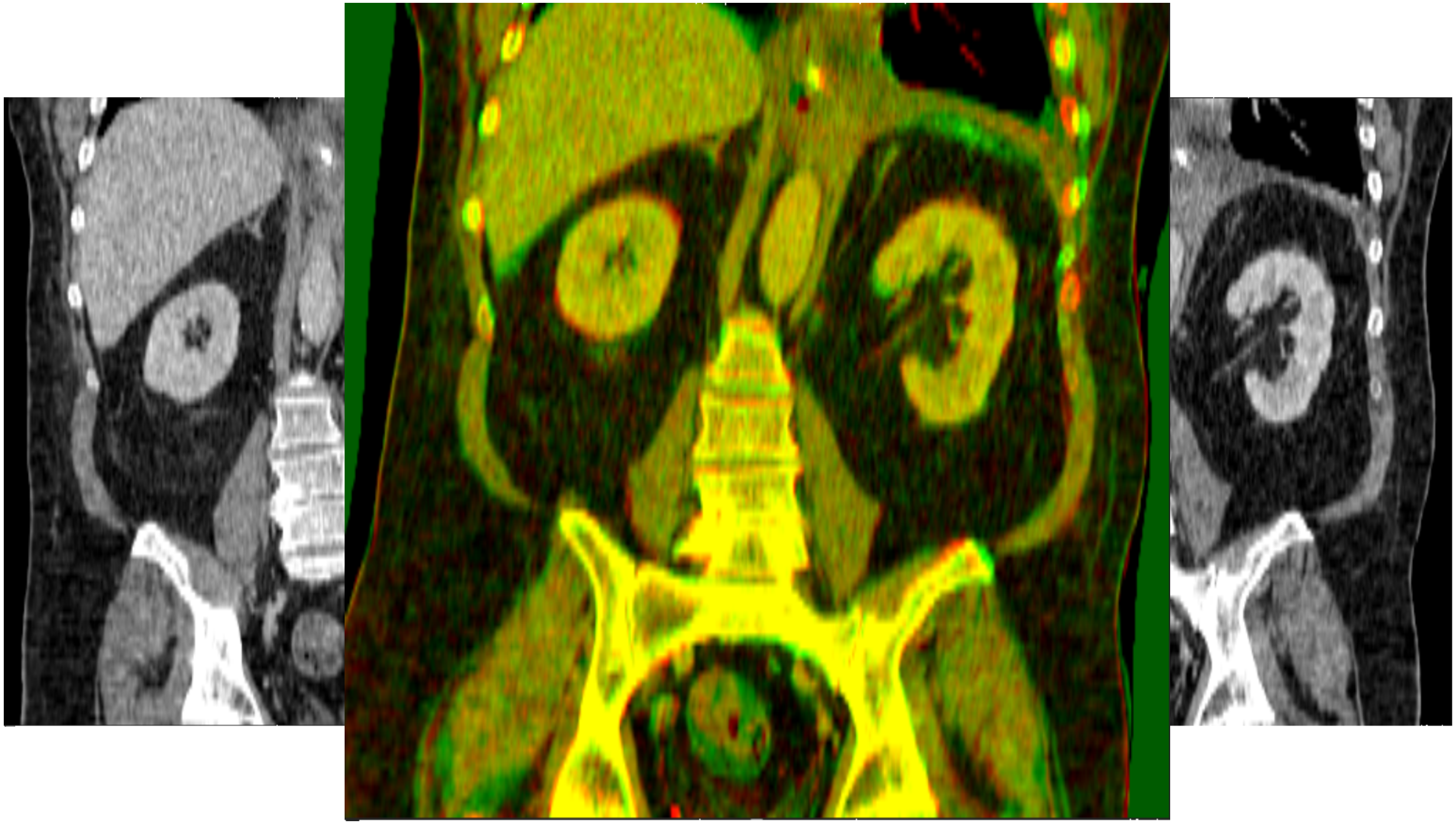

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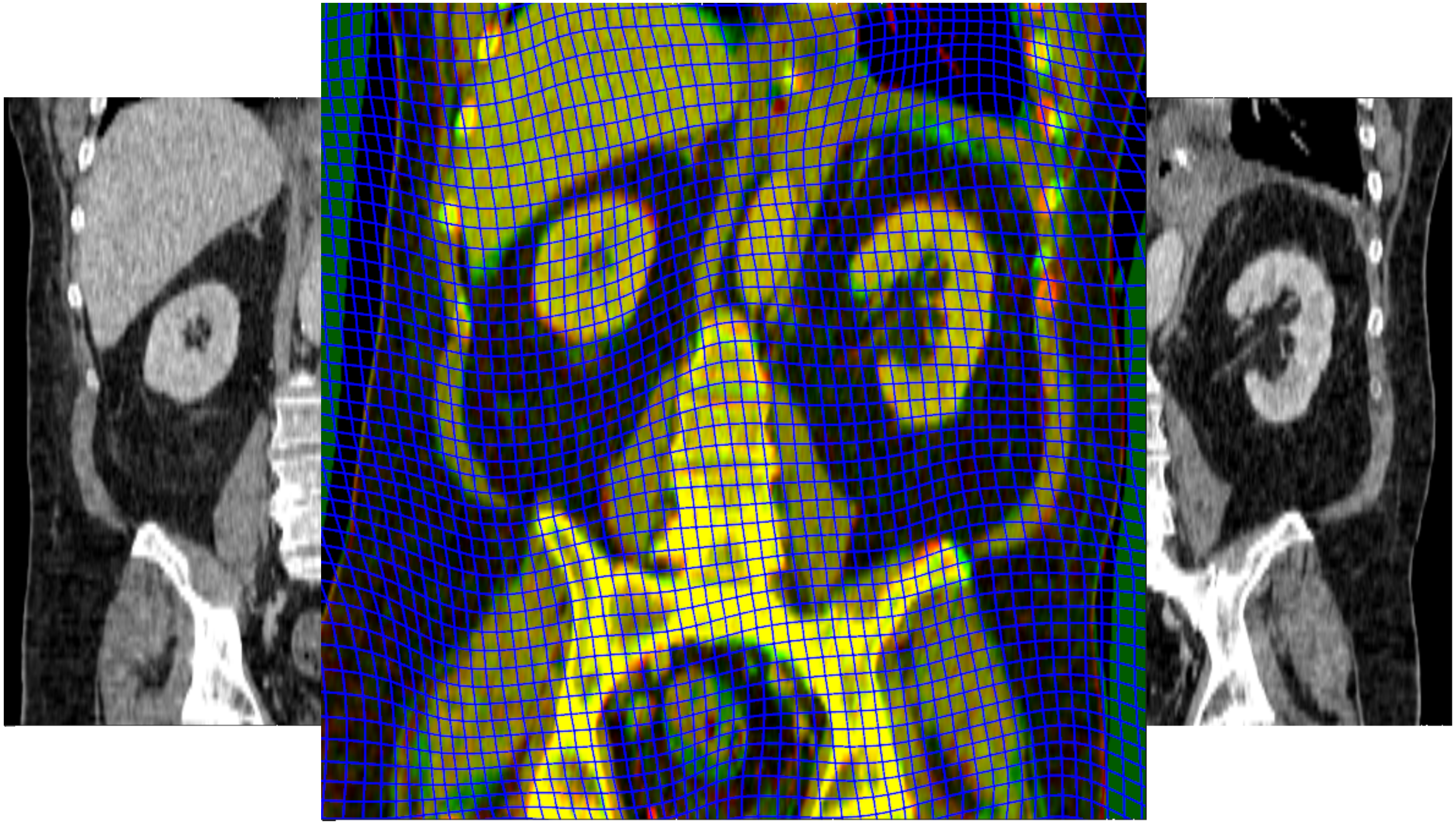

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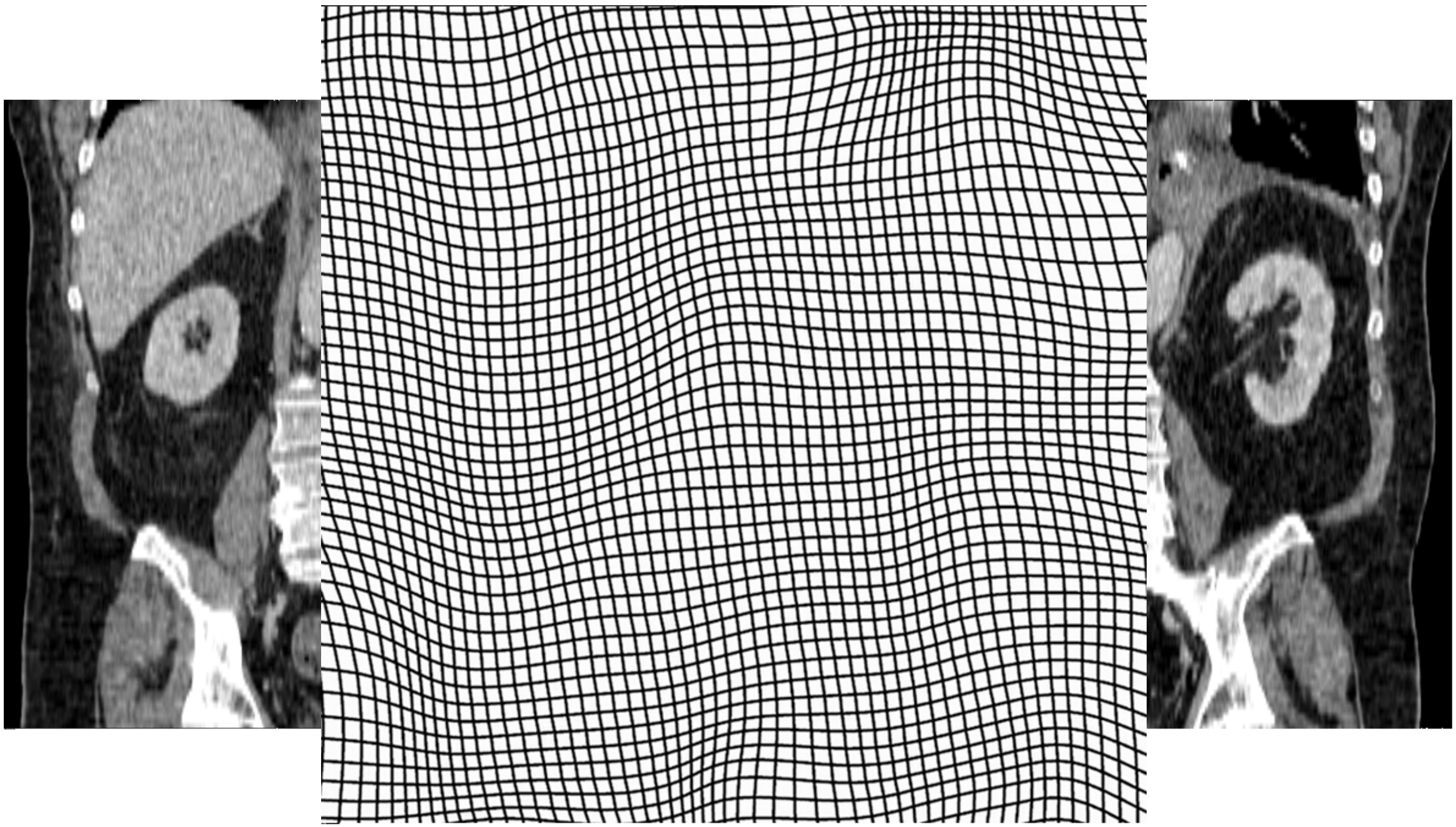

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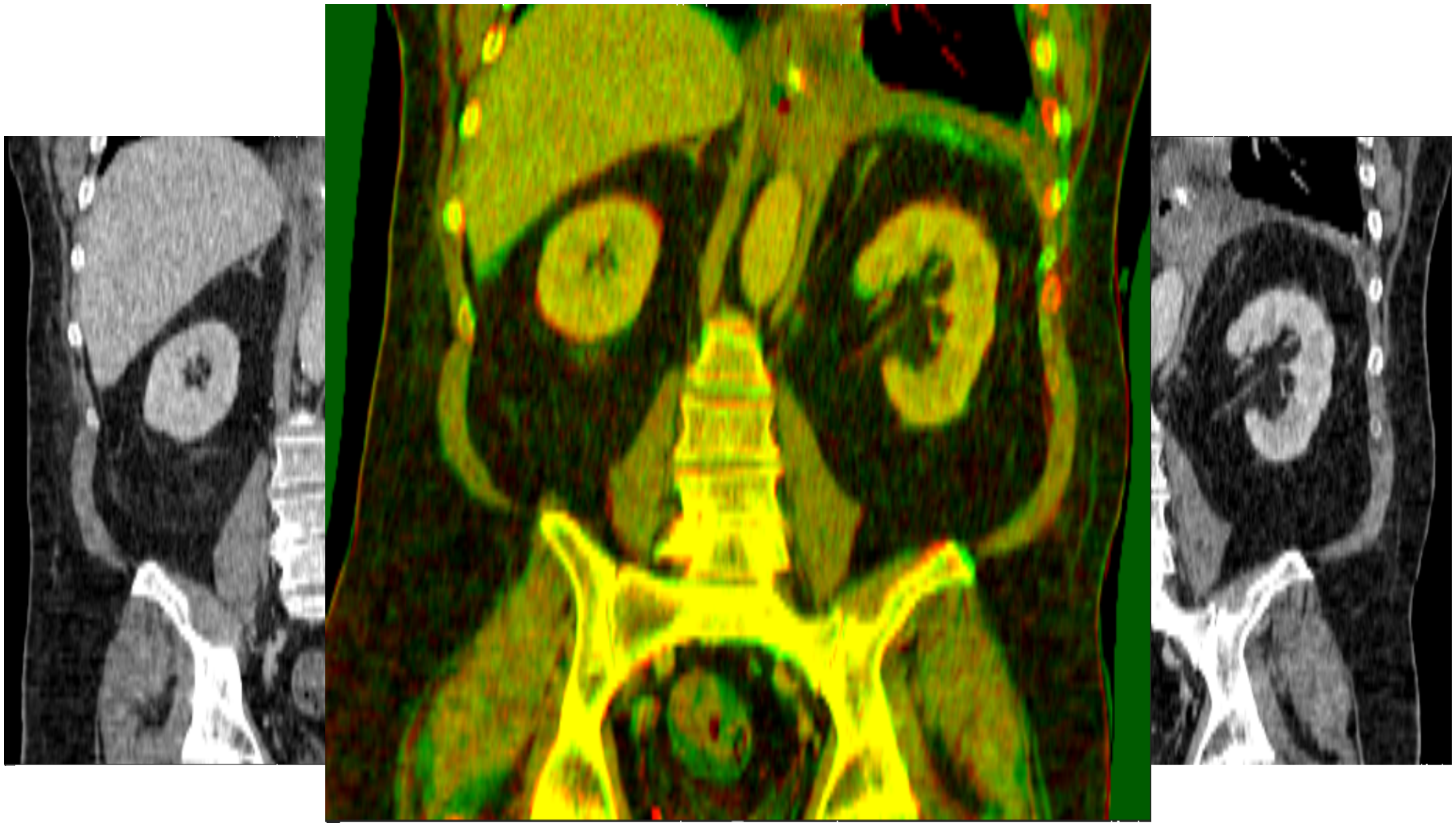

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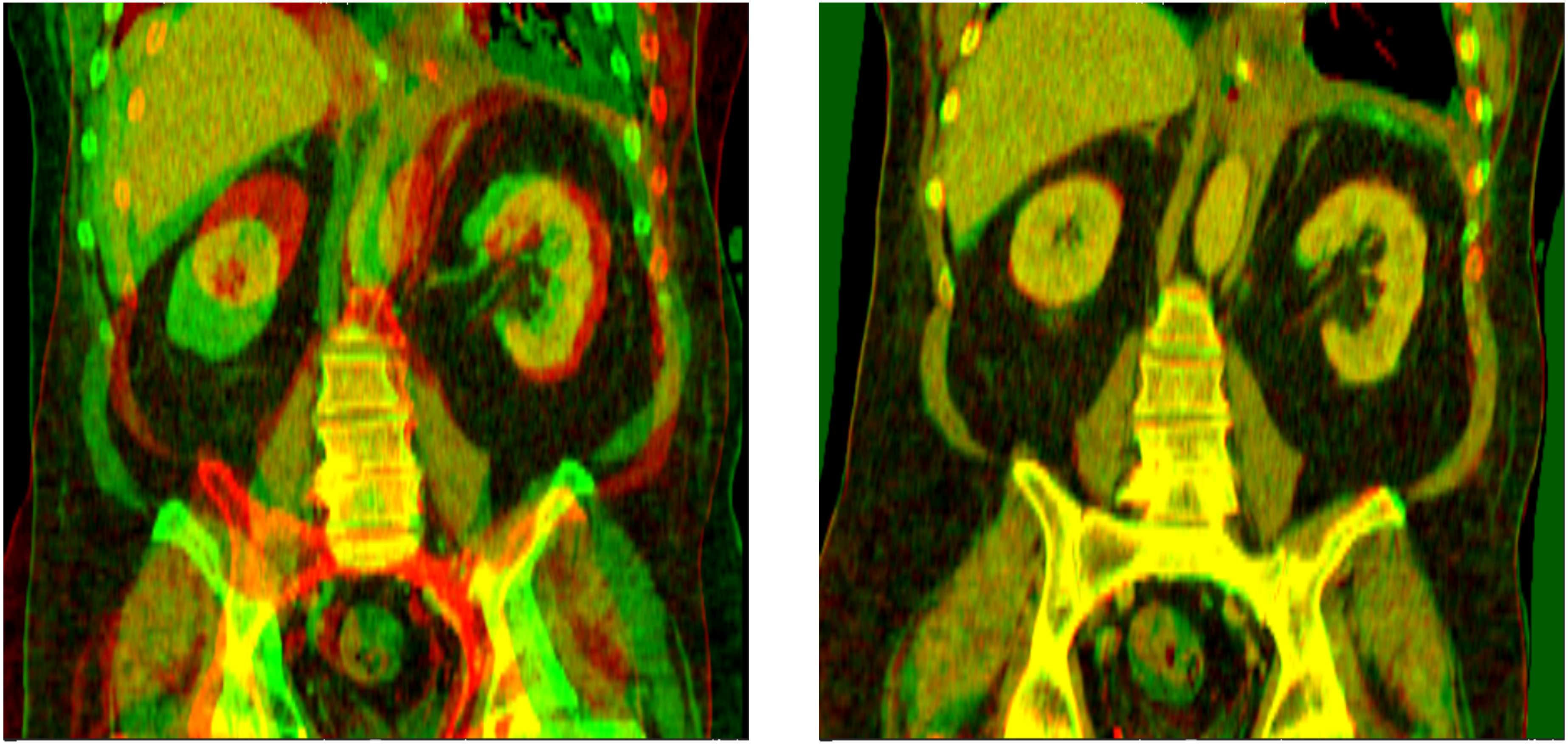

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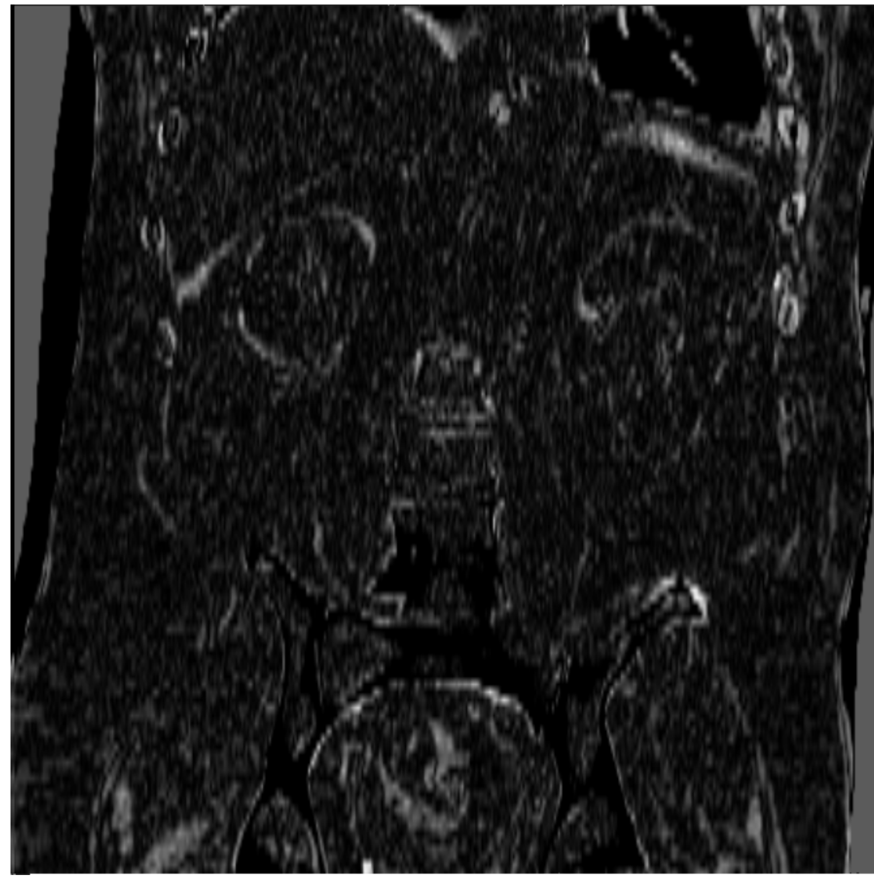


Source: B. Glocker/D. Rueckert – Course on Machine Learning for Imaging – Imperial College London

(Dis)similarity measures

Objective function , cost function, energy function

$$\underbrace{C(\underbrace{T}_{\text{transformation}})}\; = \underbrace{D}_{\text{dissimilarity measure}}(\underbrace{I \circ T}_{\text{moving image}}, \underbrace{J}_{\text{fixed image}})$$

Source: B. Glocker/D. Rueckert – Course on Machine Learning for Imaging – Imperial College London

(Dis)similarity measures

Optimisation problem

$$\hat{T} = \underbrace{\arg}_{\text{return the argument (not the value)}} \min_{T} \underbrace{C(T)}_{\text{cost function}}$$

$\min_T$: search T with minimum cost value

cost function $C : \mathbb{R}^d \to \mathbb{R}$

d: d.o.f./parameters of transform

(Dis)similarity measures

Mono-modal registration

- Image intensities are related by a (simple) function

Multi-modal registration

- Image intensities are related by a complex function or statistical relationship

(Dis)similarity measures

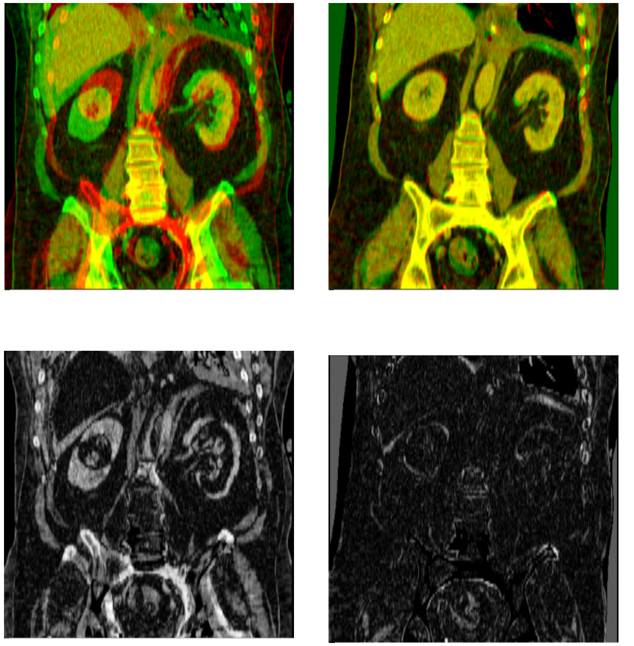
Intensity differences

Sum of squared differences (SSD)

$$D_{SSD}(I \circ T, J) = \frac{1}{N}\sum_{i=1}^{N}(I(T(x_i)) - J(x_i))^2$$

Sum of absolute differences (SAD)

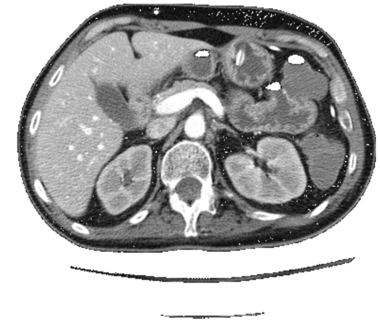
$$D_{SAD}(I \circ T, J) = \frac{1}{N}\sum_{i=1}^{N}|I(T(x\_i\ ))-J(x\_i)|$$

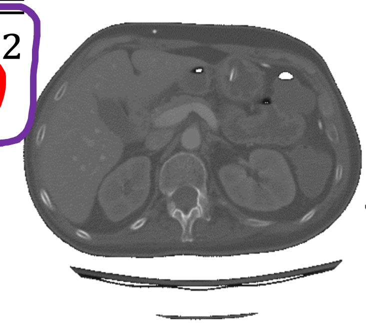


Assumption: identity relationship between intensity distributions

Application: mono-modal registration (e.g. CT-CT)

(Dis)similarity measures





Correlation coefficient (CC)

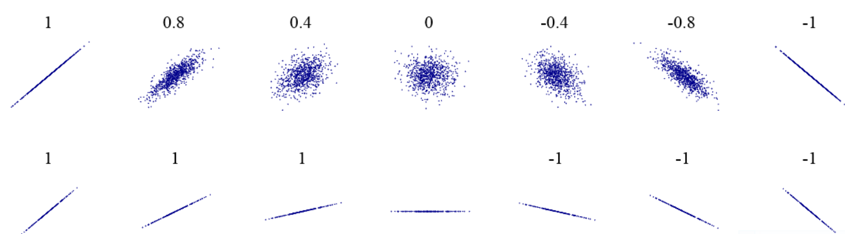
$$D_{CC}(I \circ T, J) = -\frac{\overbrace{\frac{1}{N}\sum_{i=1}^{N}\left(I(T(x_i)) - \mu_I\right)\left(J(x_i) - \mu_J\right)}^{cov(I,J)}}{\underbrace{\sqrt{\frac{1}{N}\sum_{i=1}^{N}\left(I\left(T(x_i)\right) - \mu_I\right)^2}}_{\sigma_I}\underbrace{\sqrt{\frac{1}{N}\sum_{i=1}^{N}\left(J(x_i) - \mu_J\right)^2}}_{\sigma_J}}$$

μ_I: mean intensity of image I

μ_J: mean intensity of image J

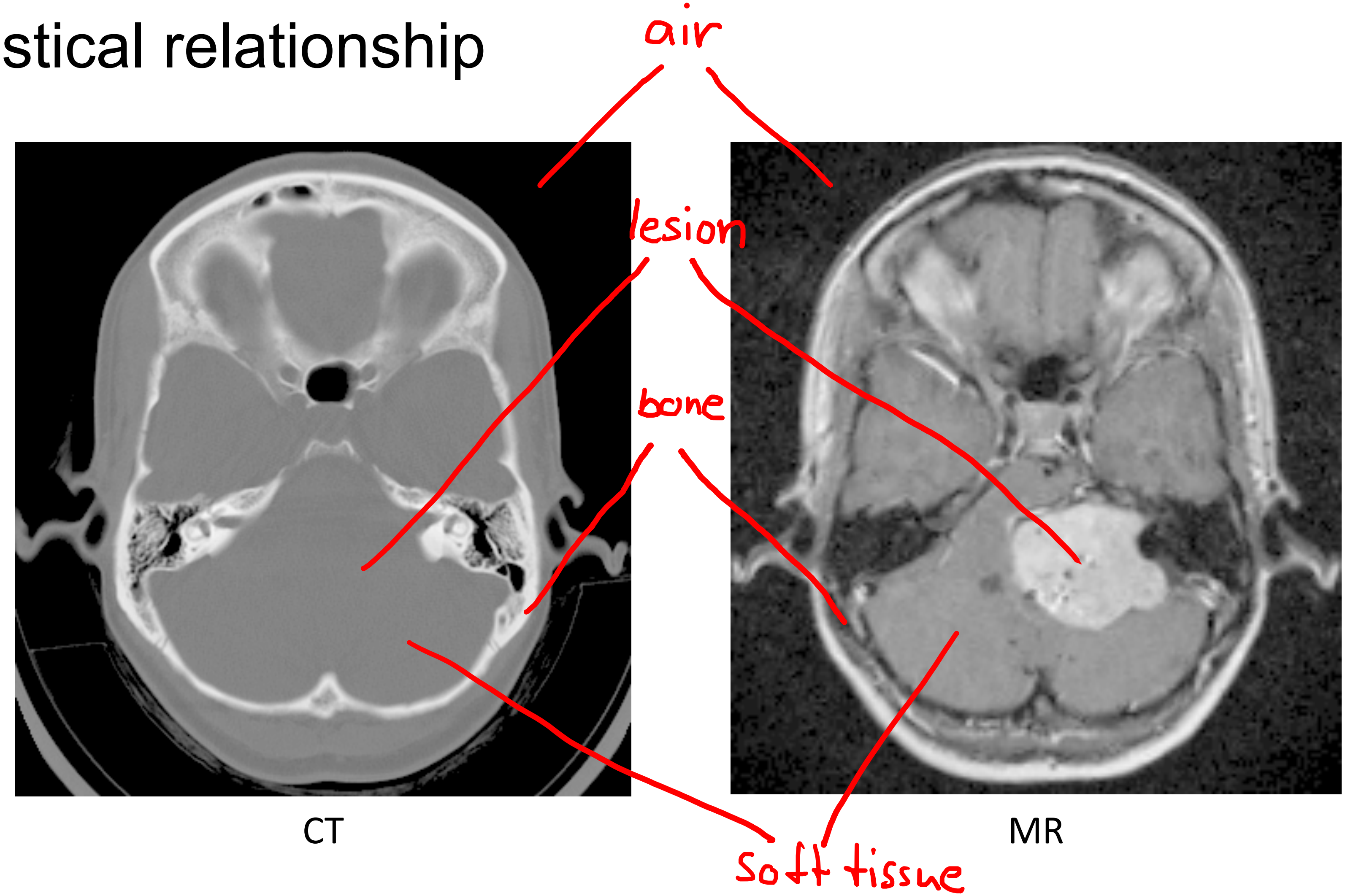
Assumption: linear relationship between intensity distributions

Application: (mainly) mono-modal registration (e.g. MR-MR)



(Dis)similarity measures

Statistical relationship



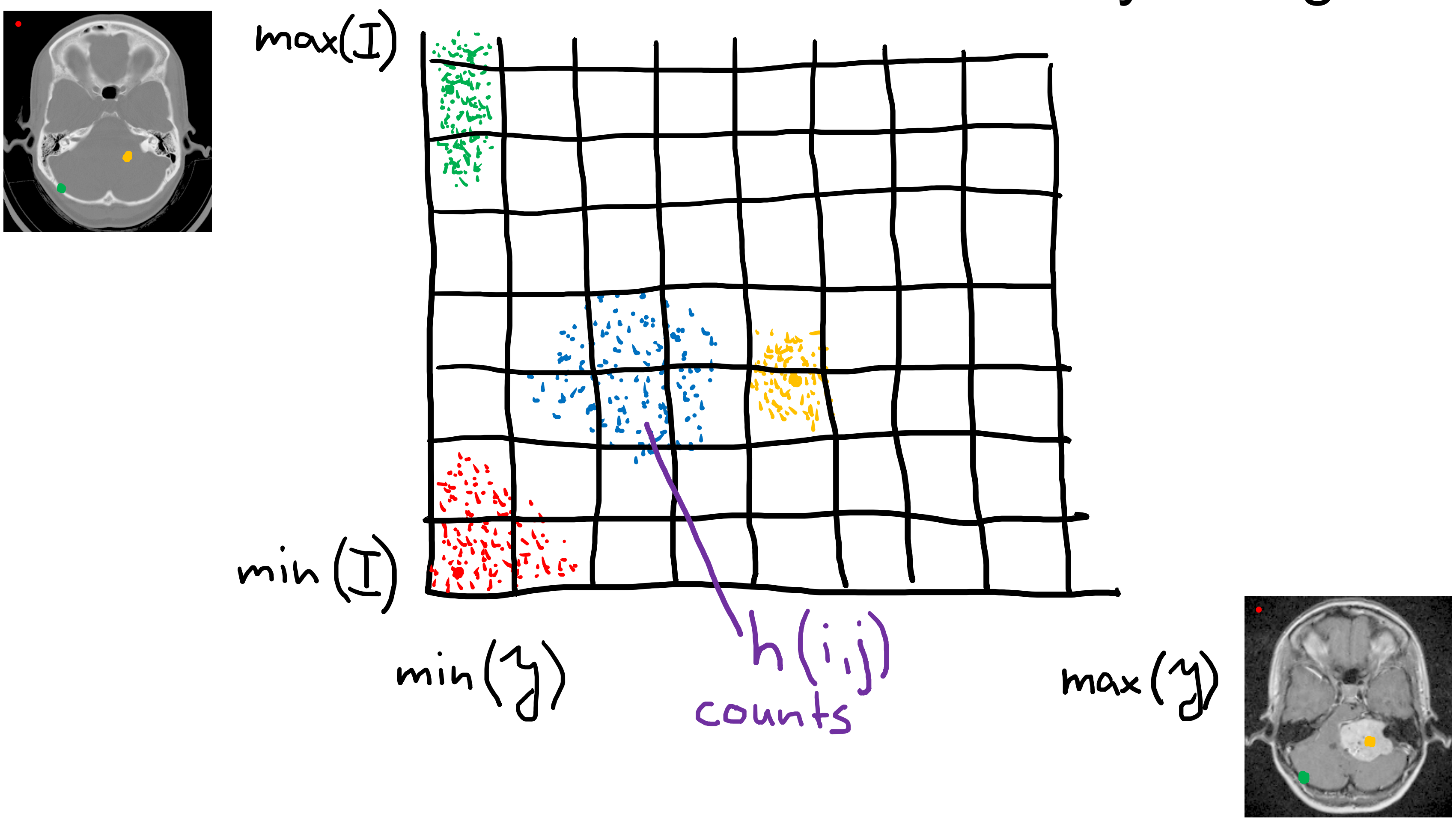
CT

MR

Source: B. Glocker/D. Rueckert – Course on Machine Learning for Imaging – Imperial College London

(Dis)similarity measures

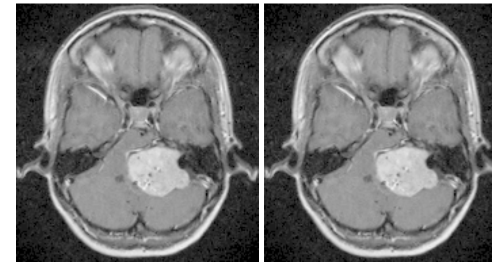
2D intensity histograms

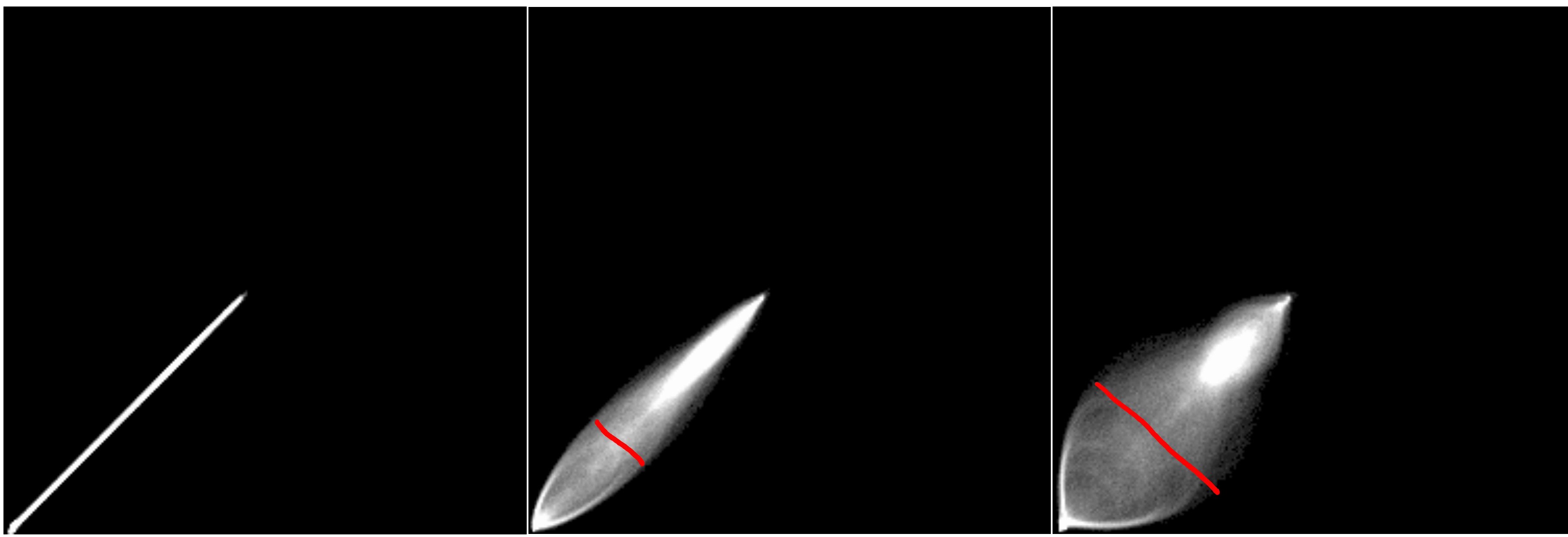


Source: B. Glocker/D. Rueckert – Course on Machine Learning for Imaging – Imperial College London

(Dis)similarity measures

MR/MR





registered

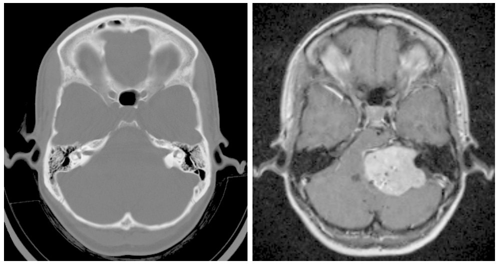
misregistered by 2mm

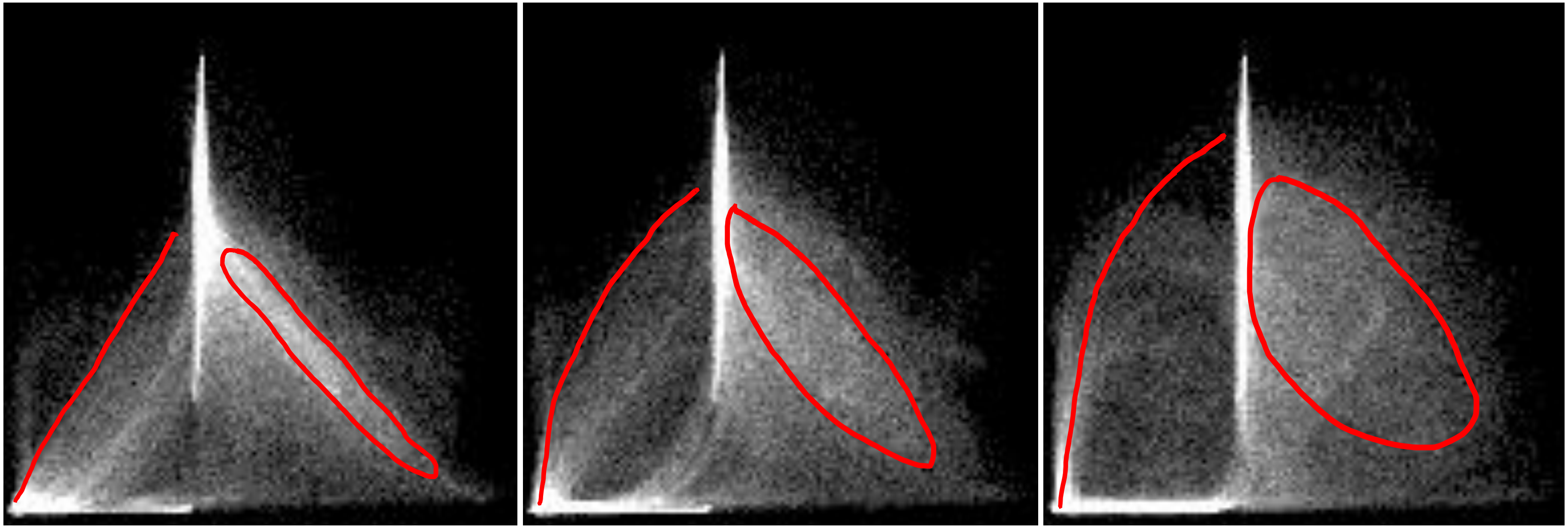
misregistered by 5mm

Source: B. Glocker/D. Rueckert – Course on Machine Learning for Imaging – Imperial College London

(Dis)similarity measures

CT/MR



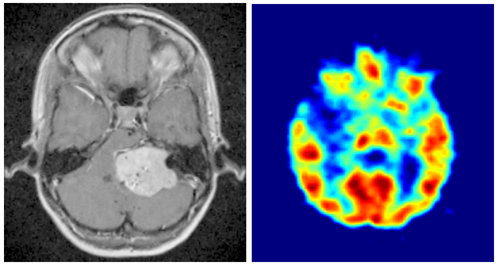


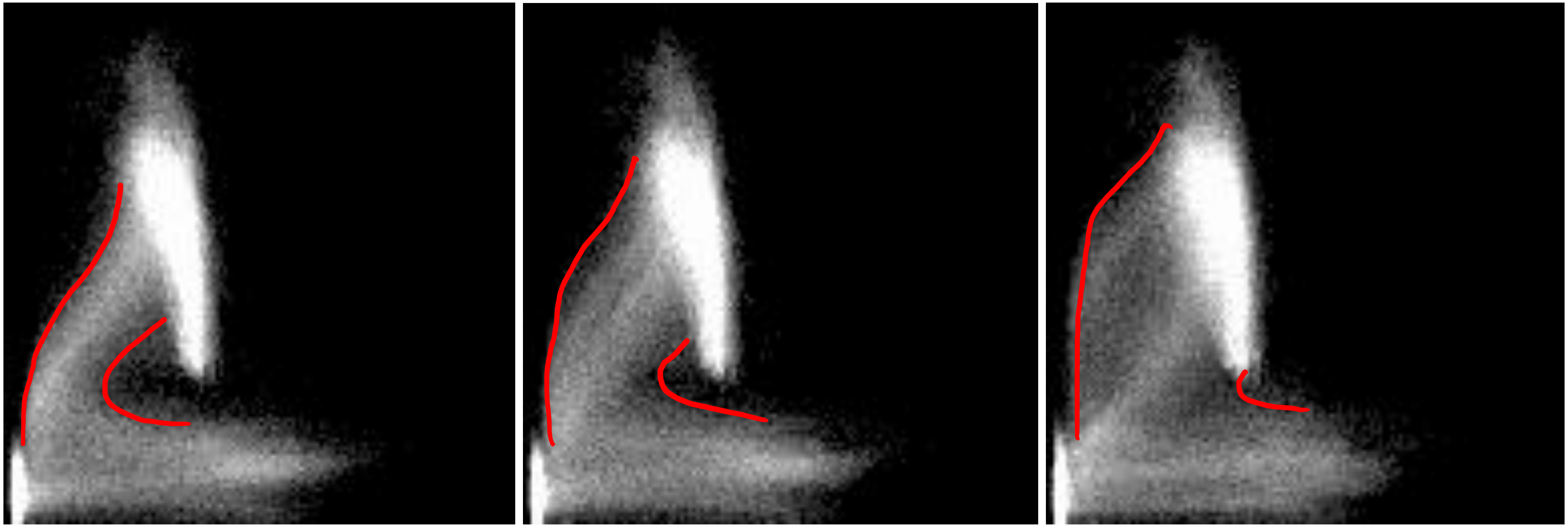
registered | misregistered by 2mm | misregistered by 5mm

Source: B. Glocker/D. Rueckert – Course on Machine Learning for Imaging – Imperial College London

(Dis)similarity measures

MR/PET





registered | misregistered by 2mm | misregistered by 5mm

Source: B. Glocker/D. Rueckert – Course on Machine Learning for Imaging – Imperial College London

(Dis)similarity measures

Intensity distributions

$$p(i,j) = \frac{h(i,j)}{N}$$ — counts in histogram

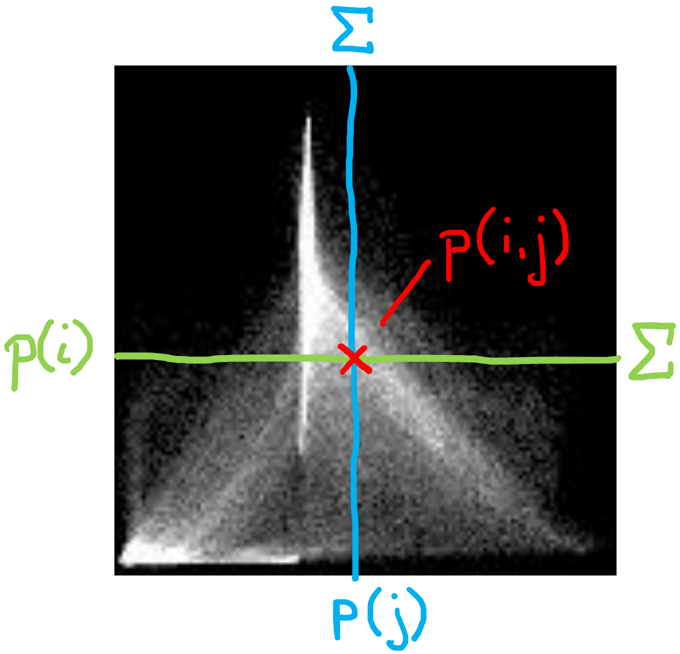
joint probability of an image point
having a value i in image I and value j in image J

$$p(i) = \sum_j p(i,j)$$

marginal probability of an image point
having a value i in image I

$$p(j) = \sum_i p(i,j)$$

marginal probability of an image point
having a value j in image J



Source: B. Glocker/D. Rueckert – Course on Machine Learning for Imaging – Imperial College London

(Dis)similarity measures

Shannon entropy

$$H(I) = -\sum_i p(i) \log p(i)$$

amount of information contained in image I

Joint entropy

$$\boxed{H(I,J) = -\sum_i \sum_j p(i,j) \log p(i,j)}$$

amount of information contained in the combined image I, J

Could be used for registration...

$$D_{JE}(I \circ T, J) = H(I \circ T, J)$$

(Dis)similarity measures

Mutual information [Viola et al. 1995]

$$MI(I,J) = H(I) + H(J) - H(I,J)$$

describes how well one image can be explained by another image

This can be rewritten in terms of marginal and joint probabilities

$$MI(I,J) = -\sum_{i}\sum_{j} p(i,j)\log\frac{p(i,j)}{p(i)\,p(j)}$$

The dissimilarity measure is then defined as

$$D_{MI}(I \circ T, J) = -MI(I \circ T, J)$$

(Dis)similarity measures

Normalised mutual information [Studholme et al. 1999]

$$NMI(I,J) = \frac{H(I) + H(J)}{H(I,J)}$$

is independent of the amount of overlap between images

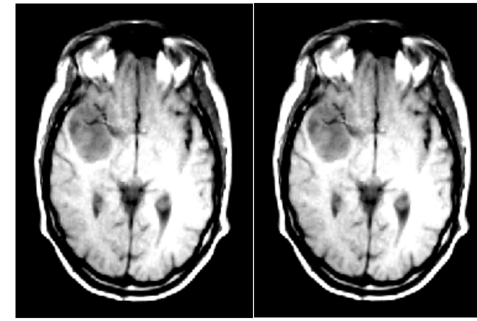
The dissimilarity measure is then defined as

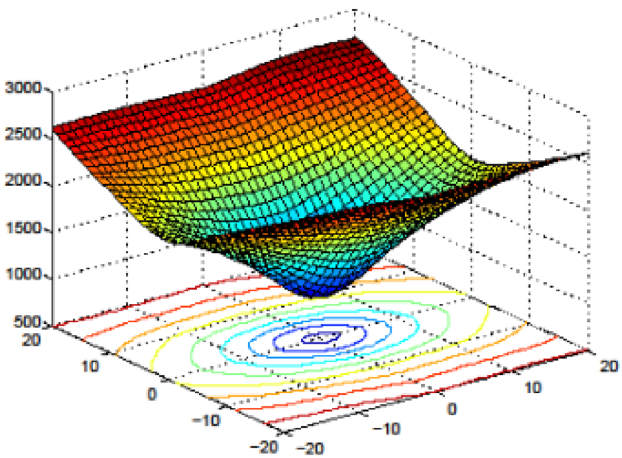
$$D_{NMI}(I \circ T, J) = -NMI(I \circ T, J)$$

Assumption: statistical relationship between intensity distributions
Application: (mainly) multi-modal registration (e.g. CT-MR)

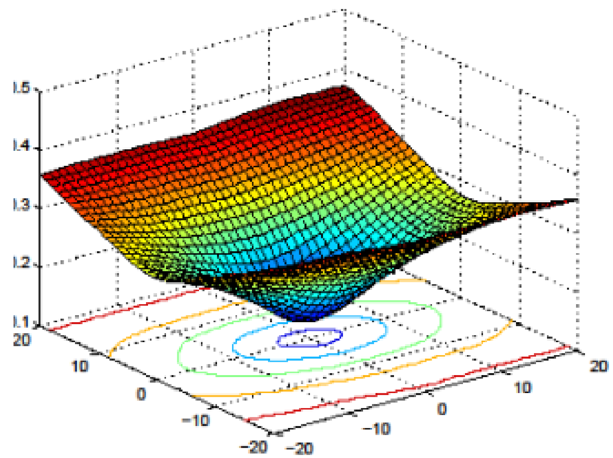
(Dis)similarity measures

Translation experiment: mono-modal

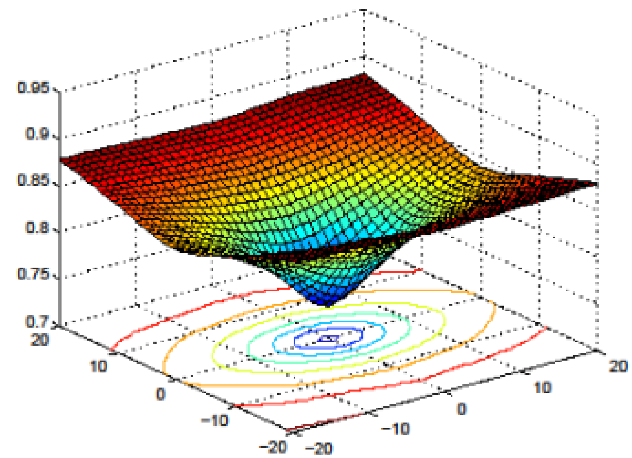




D_{SSD}



D_{CC}

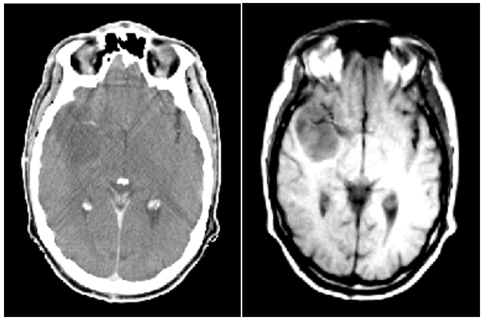


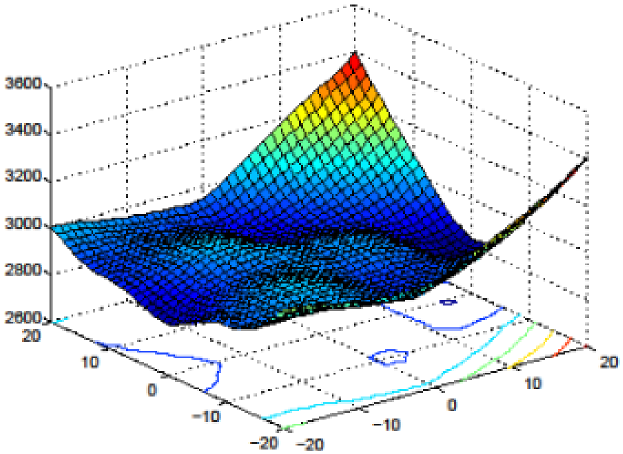
D_{NMI}

Source: B. Glocker/D. Rueckert – Course on Machine Learning for Imaging – Imperial College London

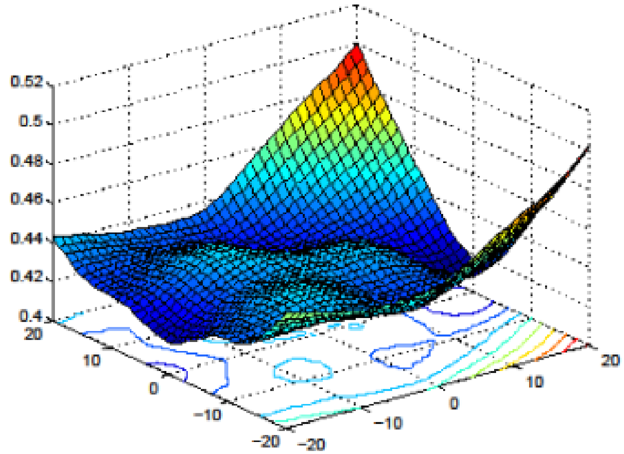
(Dis)similarity measures

Translation experiment: multi-modal

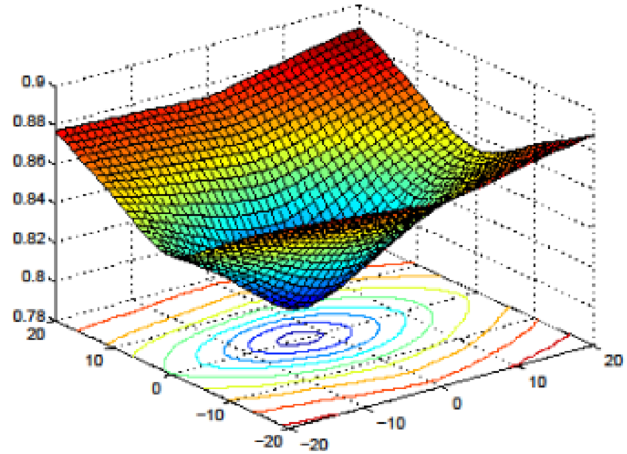




D_{SSD}



D_{CC}

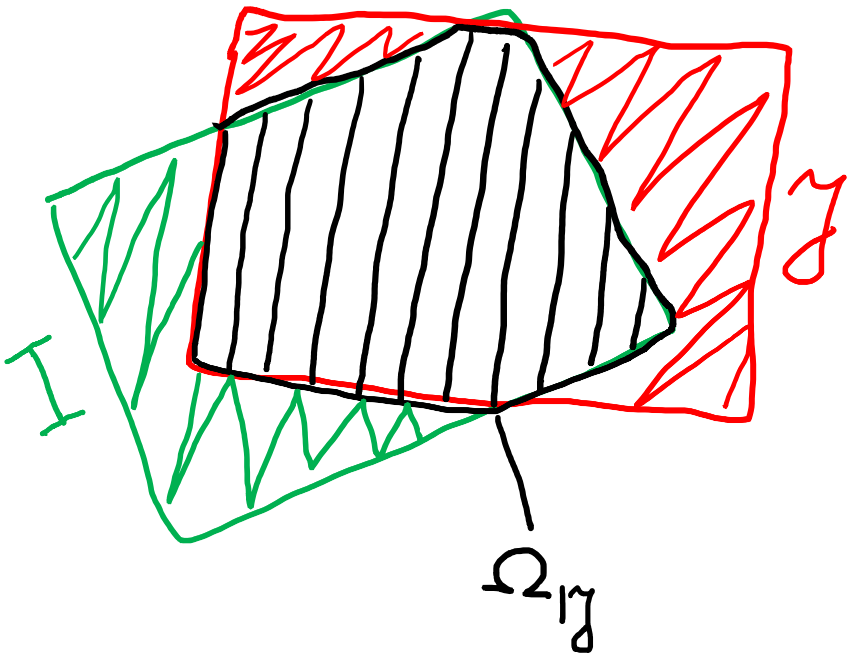


D_{NMI}

Source: B. Glocker/D. Rueckert – Course on Machine Learning for Imaging – Imperial College London

(Dis)similarity measures

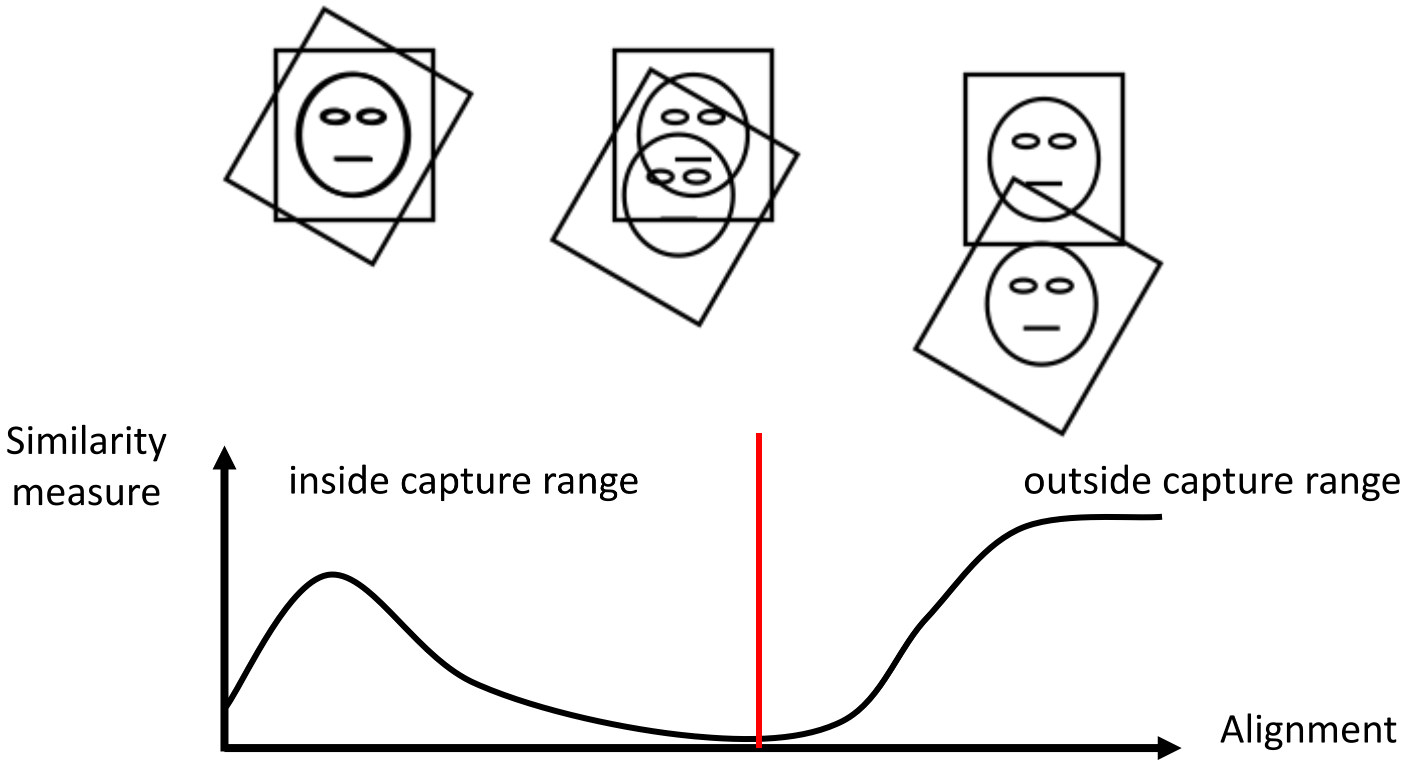
(Dis)similarity measures are evaluated in the overlapping region of the two images



Source: B. Glocker/D. Rueckert – Course on Machine Learning for Imaging – Imperial College London

(Dis)similarity measures

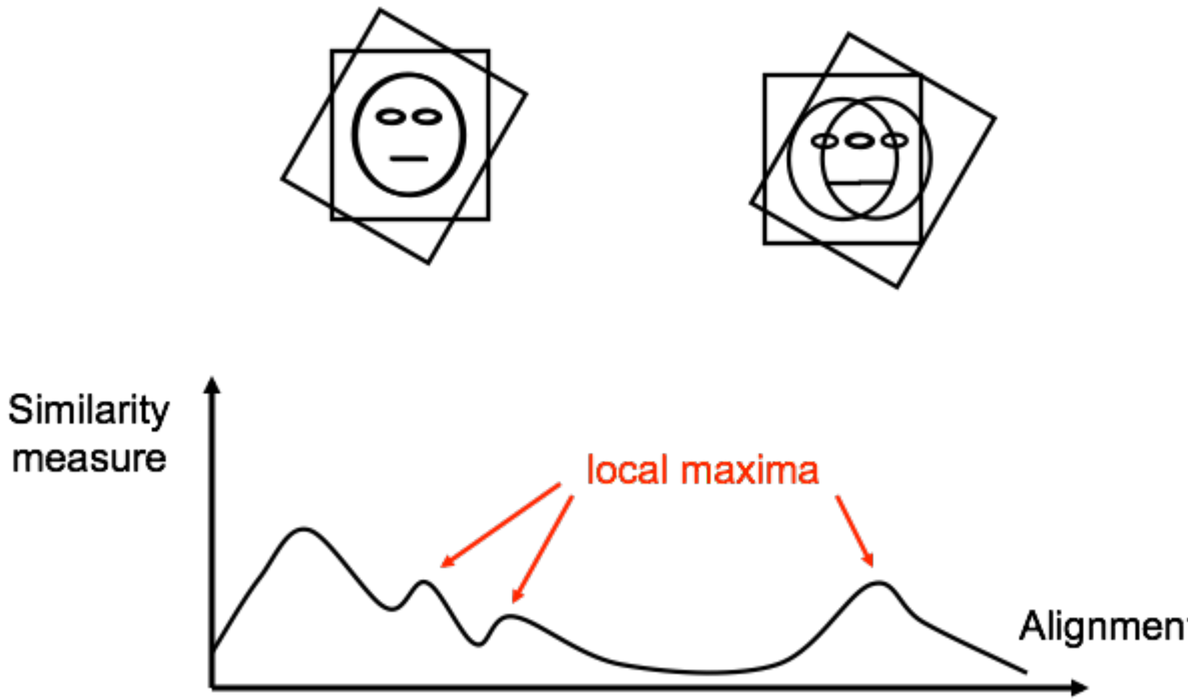
Capture Range



Source: B. Glocker/D. Rueckert – Course on Machine Learning for Imaging – Imperial College London

(Dis)similarity measures

Local Optima

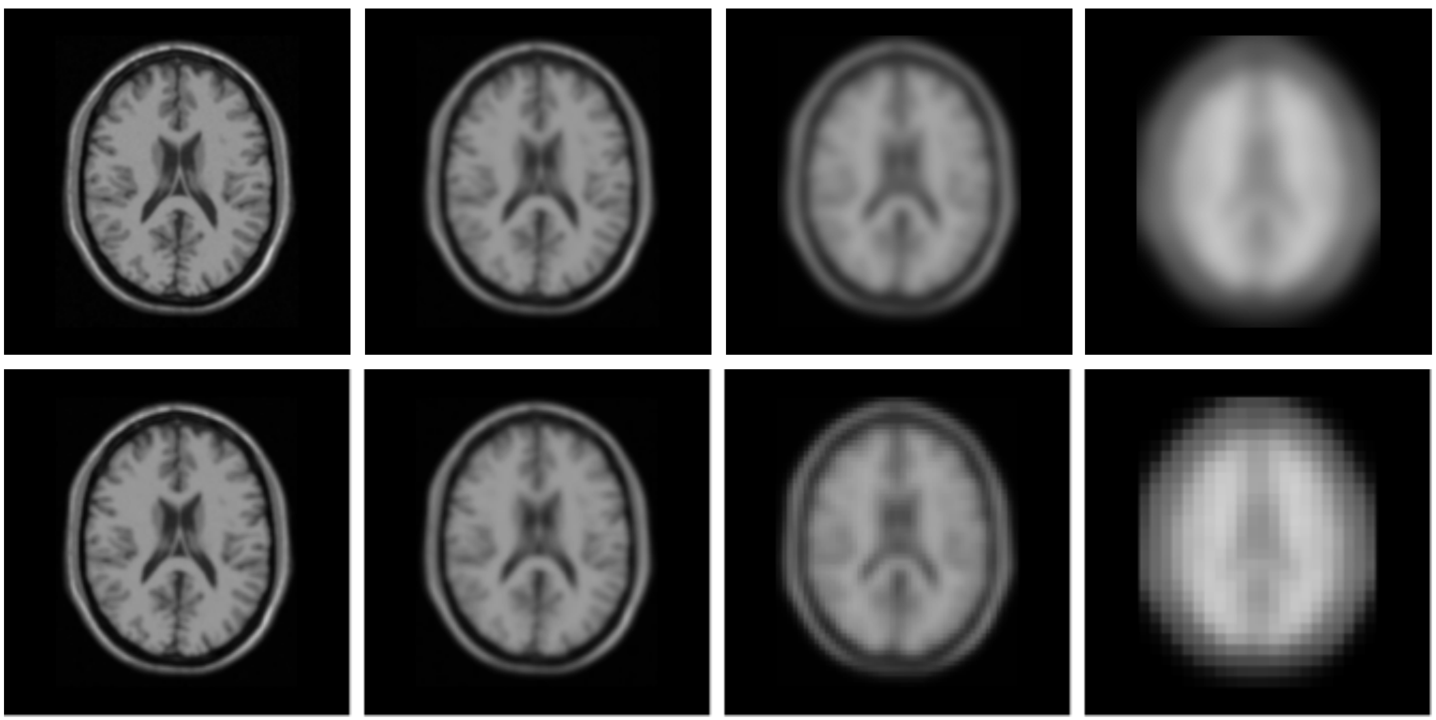


Source: B. Glocker/D. Rueckert – Course on Machine Learning for Imaging – Imperial College London

(Dis)similarity measures

Multi-scale, hierarchical Registration

- Successively increase degrees of freedom
- Gaussian image pyramids

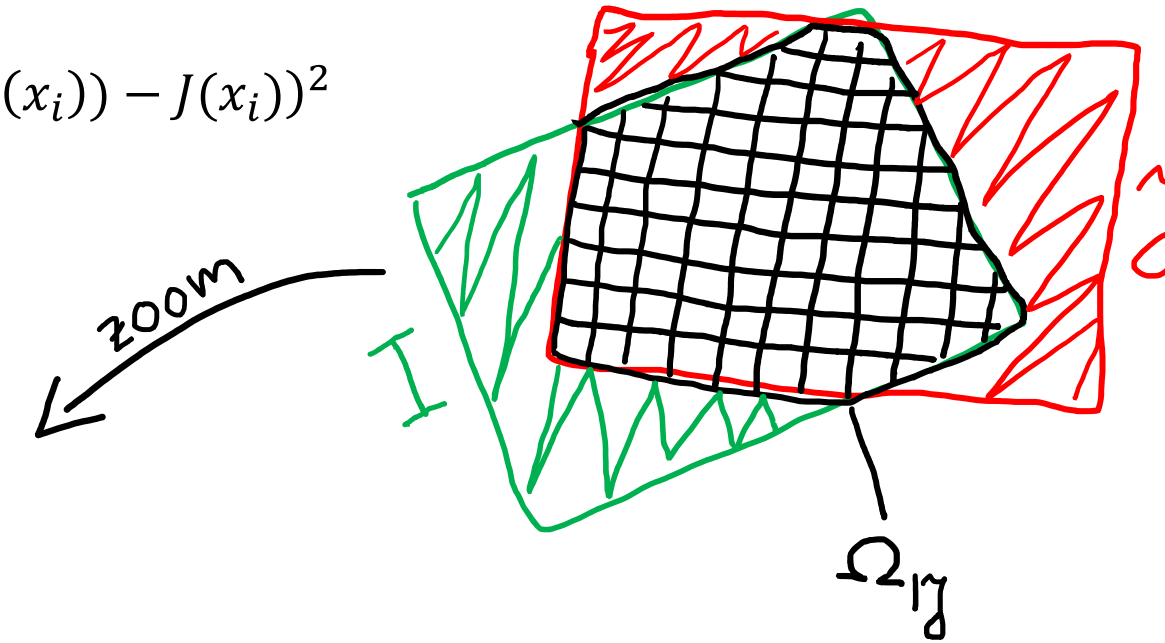


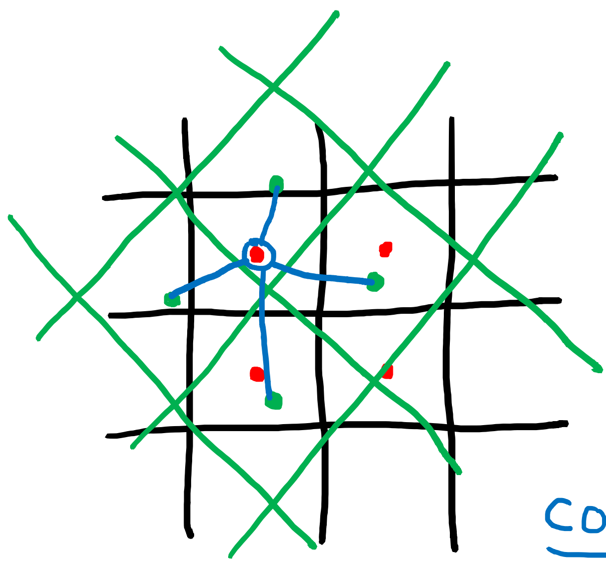
Part 8 – Registration

8.4 Other technical aspects

Interpolation

$$D_{SSD}(I \circ T, J) = \frac{1}{N}\sum_{i=1}^{N}(I(T(x_i)) - J(x_i))^2$$





compute weighted sum for $I(T(x_i))$

interpolation

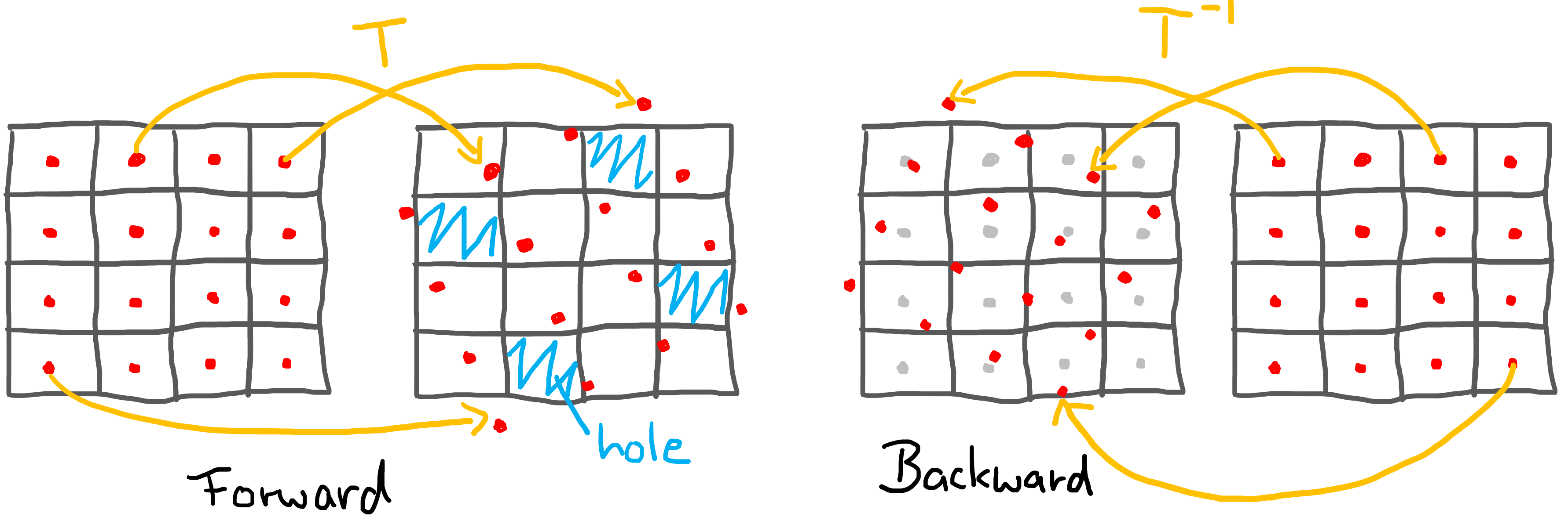
Resampling

Forward warping

- Cycle through original image, and transport intensities forward
- Holes can occur!

Backward warping

- Cycle through the new image grid, and do backward look up in original imag



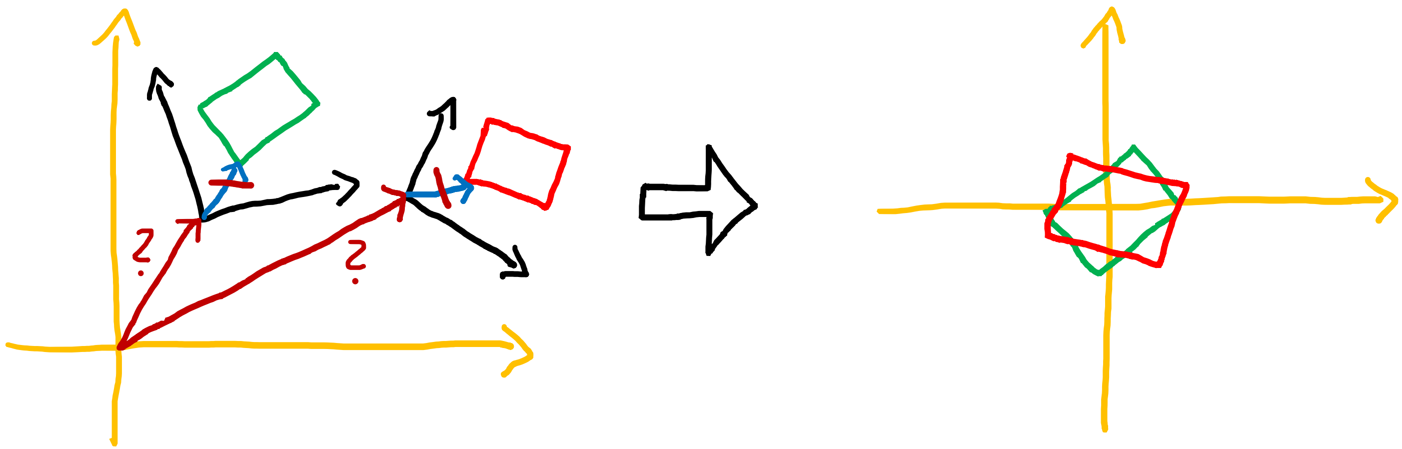
Source: B. Glocker/D. Rueckert – Course on Machine Learning for Imaging – Imperial College London

Initialisation

Initialisation is critical for intensity-based registration

Two common heuristics to deal with initialisation:

1) Ignore image specific origin information, align image centres



Initialisation

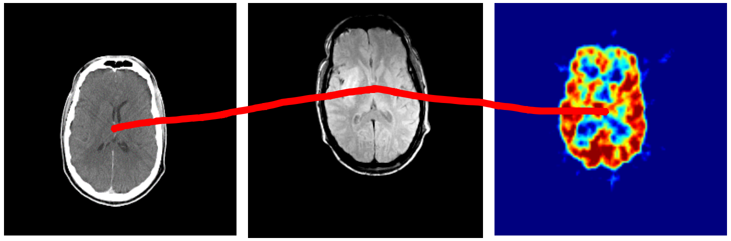
Initialisation is critical for intensity-based registration

Two common heuristics to deal with initialisation:

2) Align the centres of intensity masses

$$c_I = \frac{1}{Z}\sum_{i=1}^{N} (I(x_i) - \min(I)) \cdot T_{ItW} x_i$$

with $Z = \sum_{i=1}^{N} (I(x_i) - \min(I))$

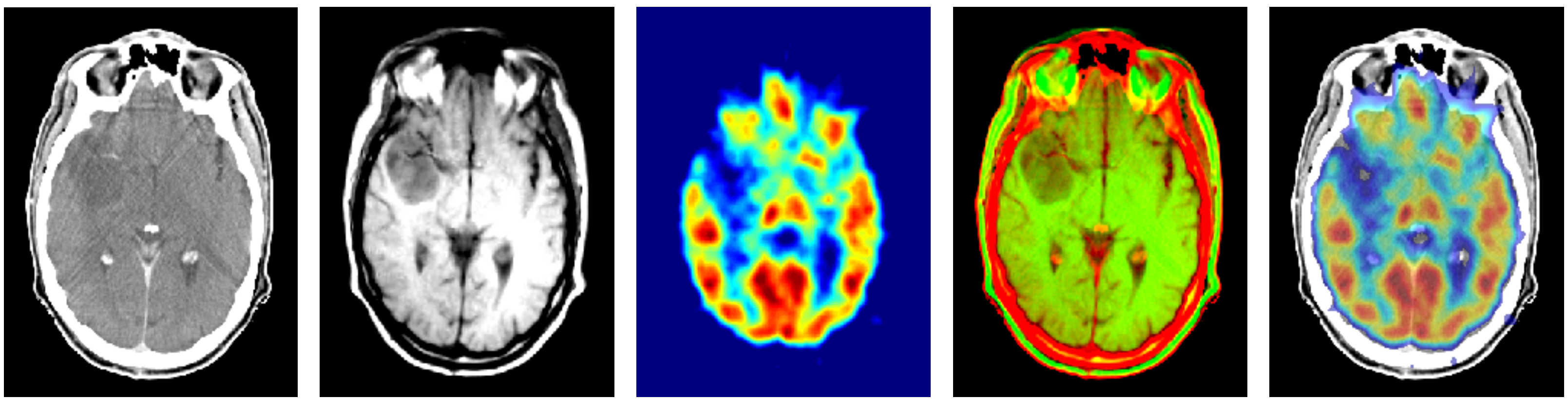


Source: B. Glocker/D. Rueckert – Course on Machine Learning for Imaging – Imperial College London

Part 8 – Registration

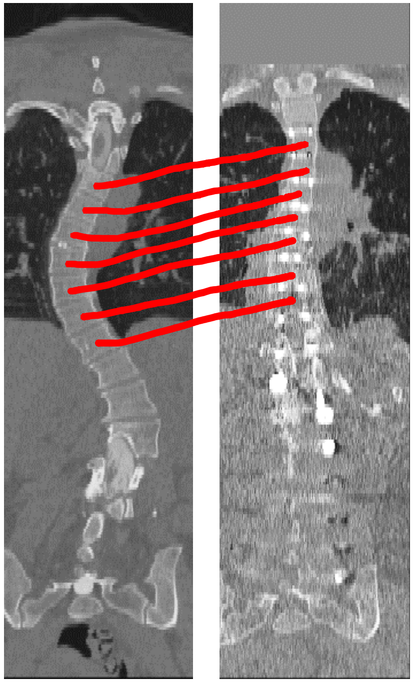
8.5 Applications

Multimodal image fusion



Source: B. Glocker/D. Rueckert – Course on Machine Learning for Imaging – Imperial College London

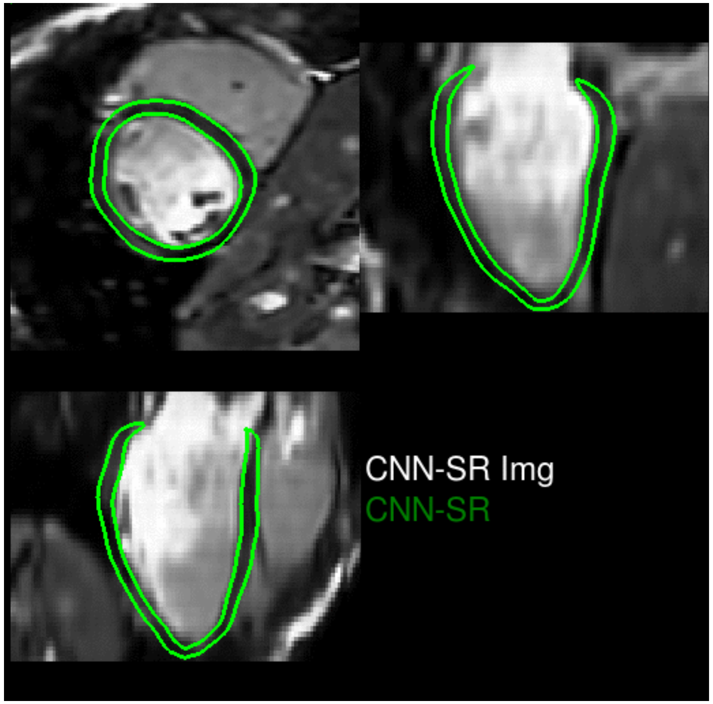
Pre and post-op (surgical operation)



Source: B. Glocker/D. Rueckert – Course on Machine Learning for Imaging – Imperial College London

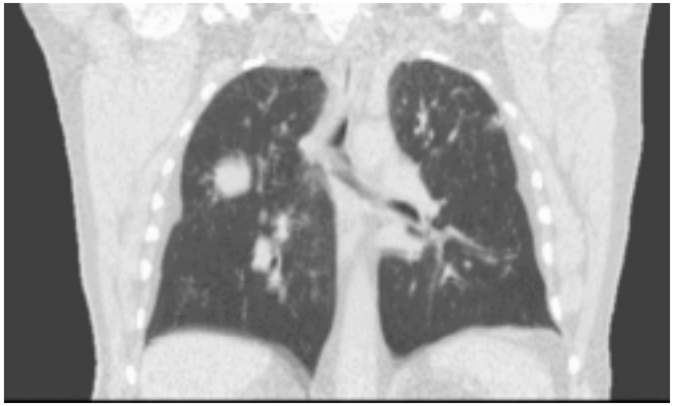
Motion

Cardiac Motion



Source: Oktay et al. MICCAI 2016

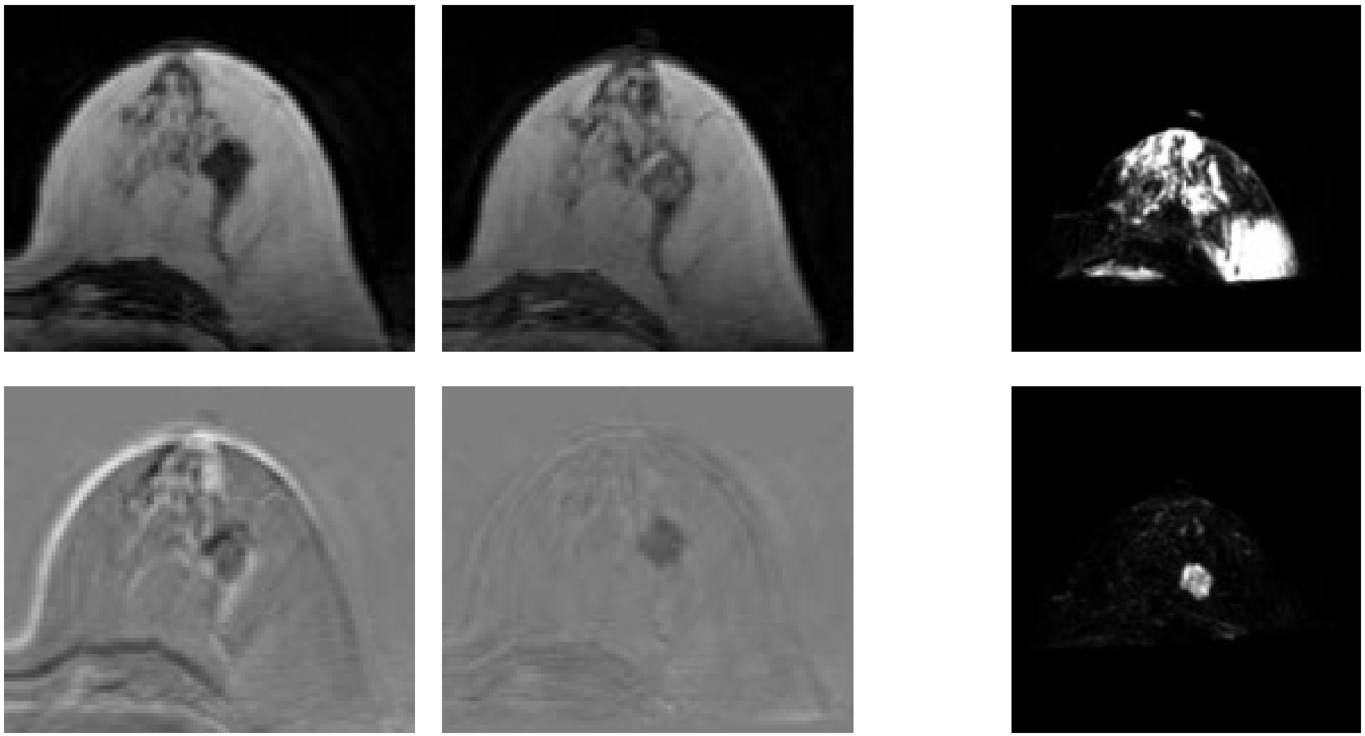
Respiratory Motion



Source: B. Glocker/D. Rueckert – Course on Machine Learning for Imaging – Imperial College London

Contrast and non-contrast images

Contrasted and non-contrasted images [Rueckert et al. 1999]

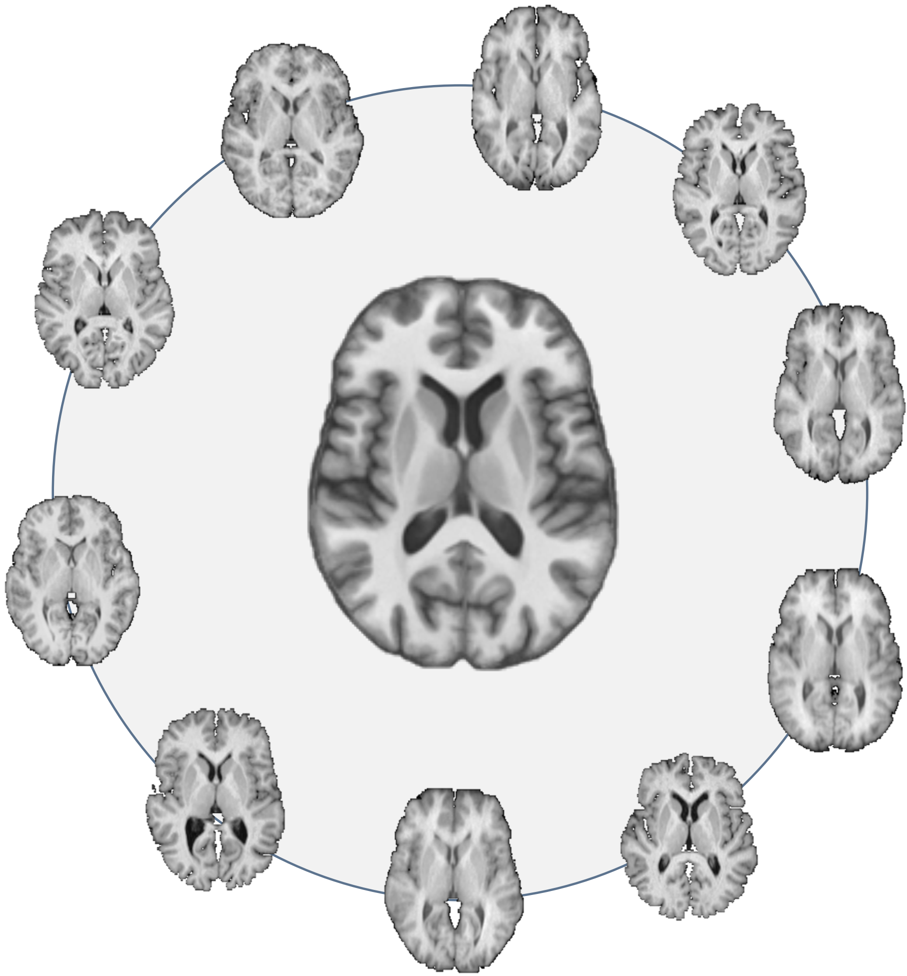


Source: B. Glocker/D. Rueckert – Course on Machine Learning for Imaging – Imperial College London

Atlas construction

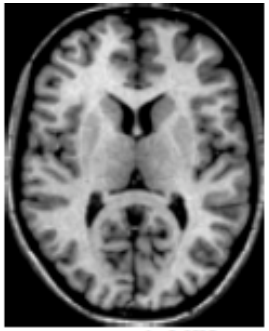
Atlas construction

- Builds an “average” of a group of participants
- This avoids chosing an arbitrary patient as a target when registering N (N>2) patients together
- The “average” is called an atlas or template
- Two options when doing inter-subject registration (with N>2)
    - Build an atlas from the group of patients
    - Use a predefined atlas (built from another population)



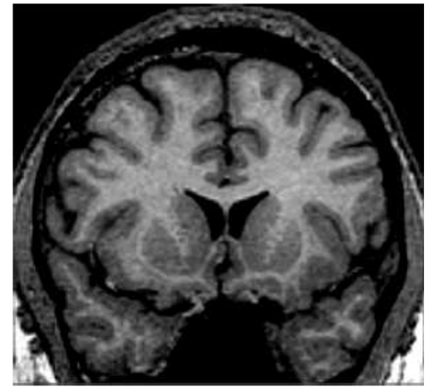
Source: B. Glocker/D. Rueckert – Course on Machine Learning for Imaging – Imperial College London

Segmentation based on registration

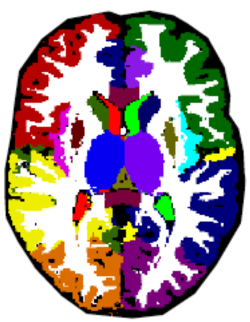


Reference MRI

Registration:
compute
transformation
ϕ

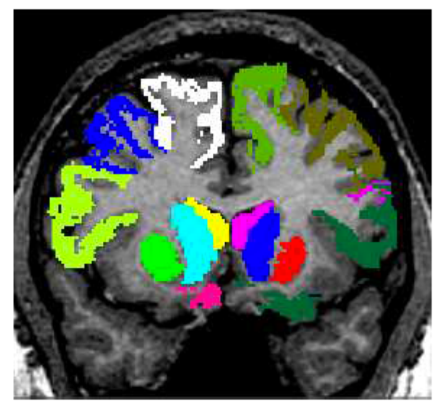


MRI to
segment



Reference
segmentation

Apply
transformation
ϕ

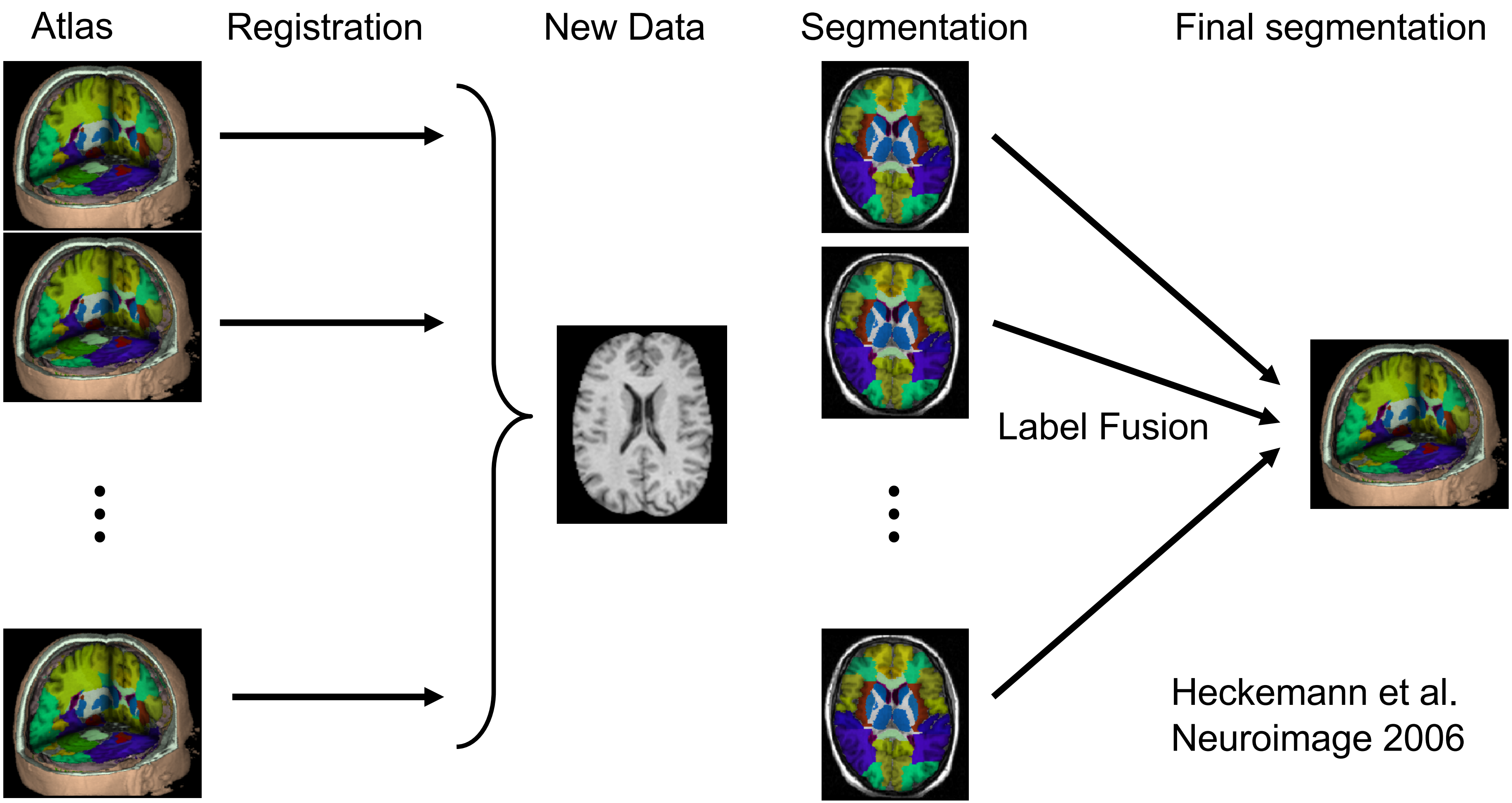


Obtained
segmentation

Collins et al, 1999

With a single reference

Segmentation based on registration



With a multiple references (better handling of anatomical variability)

Source: B. Glocker/D. Rueckert – Course on Machine Learning for Imaging – Imperial College London

Segmentation based on registration

- Multi-atlas registration-based segmentation
  - Was the state of the art before deep learning
  - Is still a competitive method, thanks to its precision and robustness

Source: B. Glocker/D. Rueckert – Course on Machine Learning for Imaging – Imperial College London

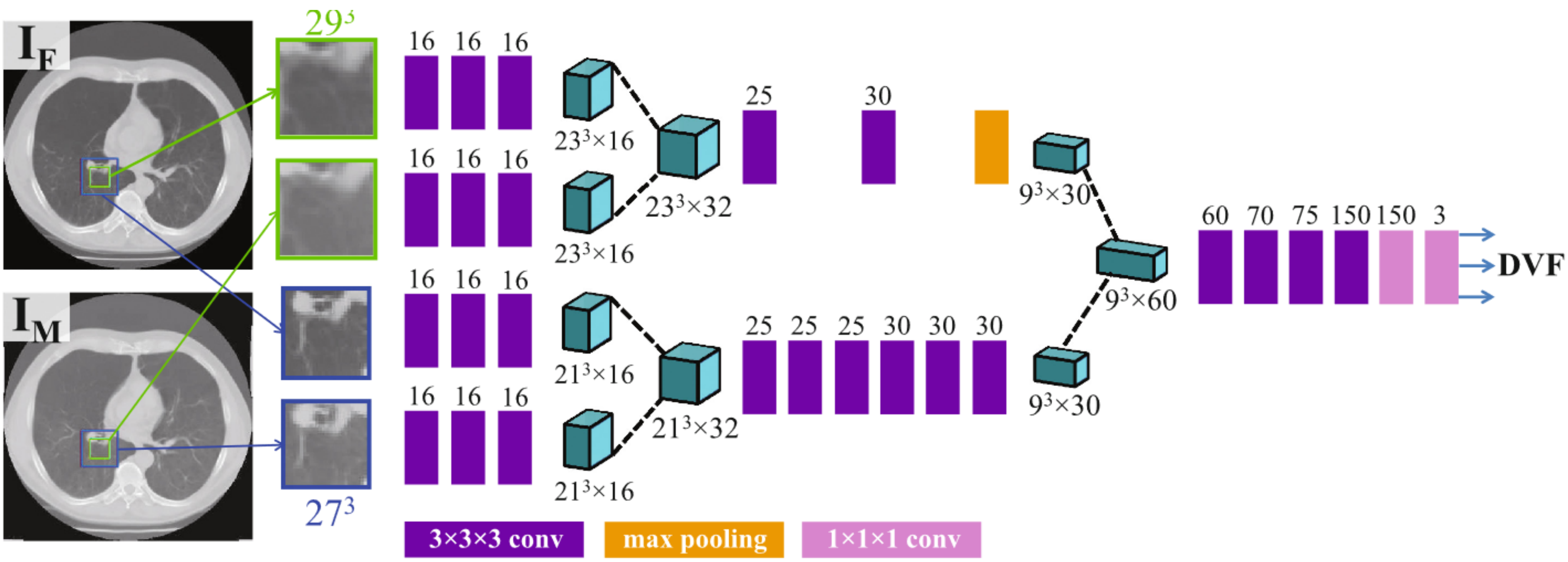
Part 8 – Registration

8.6 Registration using deep learning

Supervised approaches

Nonrigid Image Registration Using Multi-scale 3D CNNs

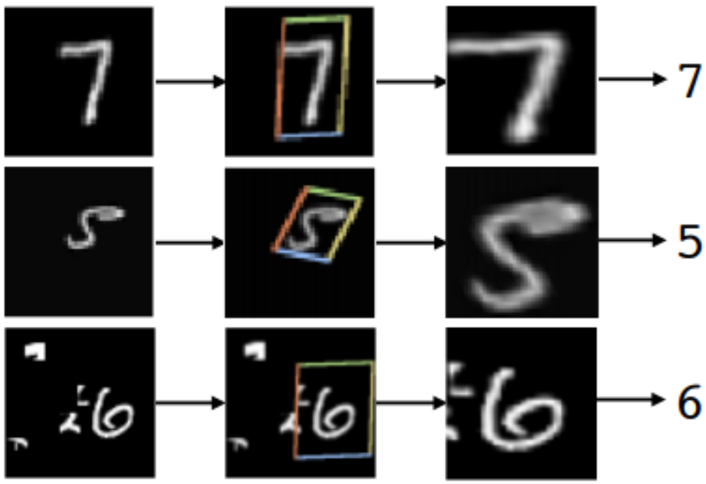
Trained on synthetic deformations

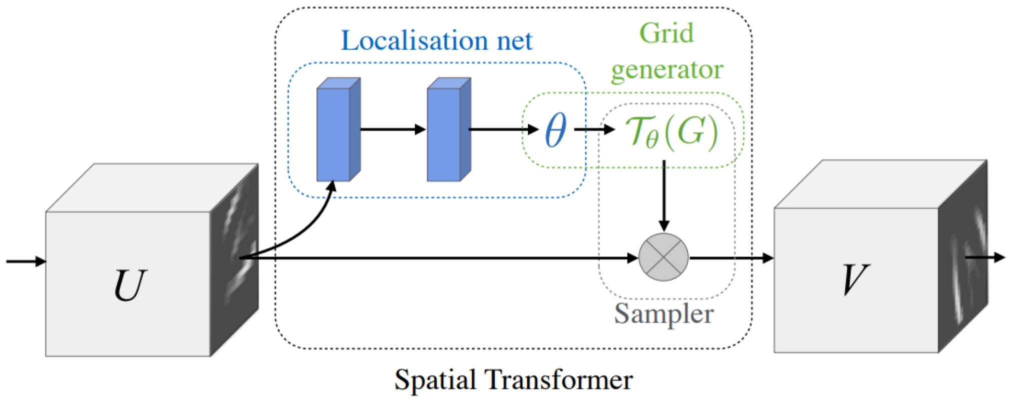


https://doi.org/10.1007/978-3-319-66182-7_27

Unsupervised approaches

Spatial Transformer Networks

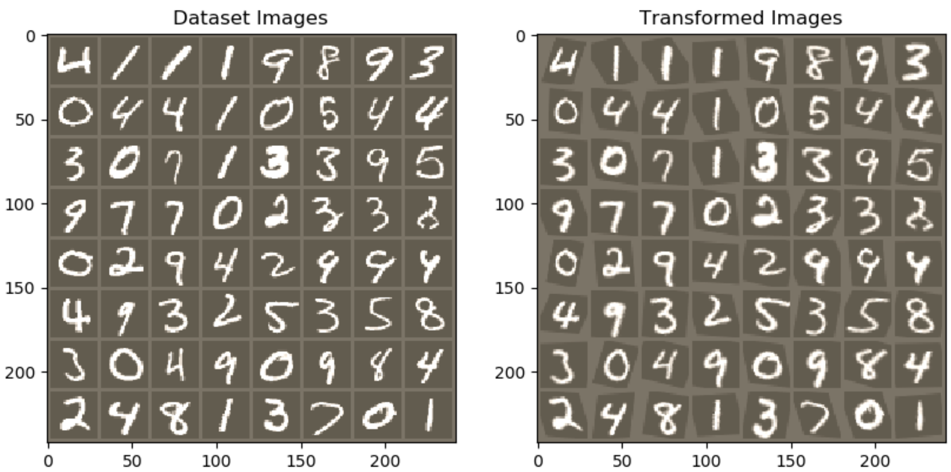


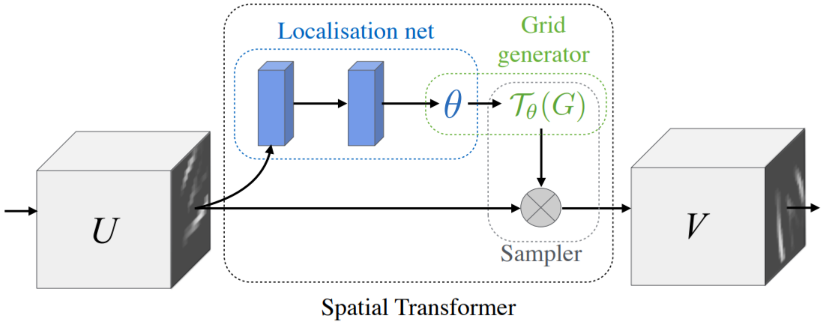


https://arxiv.org/abs/1506.02025

Unsupervised approaches

Spatial Transformer Networks



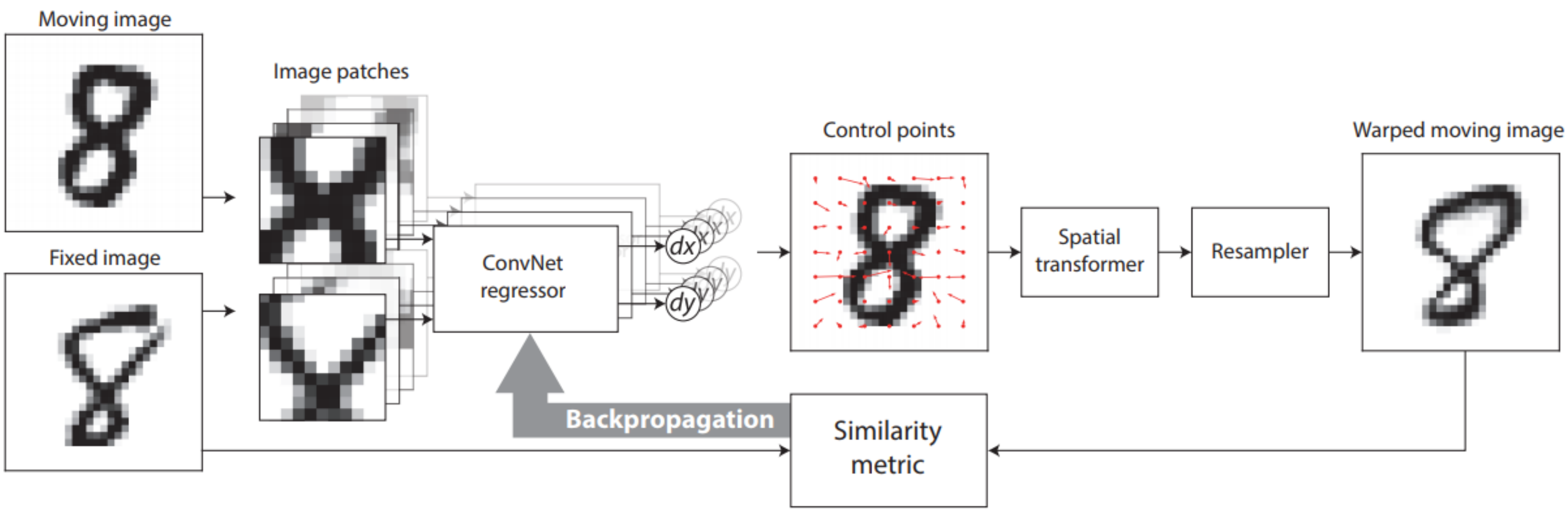


https://pytorch.org/tutorials/intermediate/spatial_transformer_tutorial.html

https://arxiv.org/abs/1506.02025

Unsupervised approaches

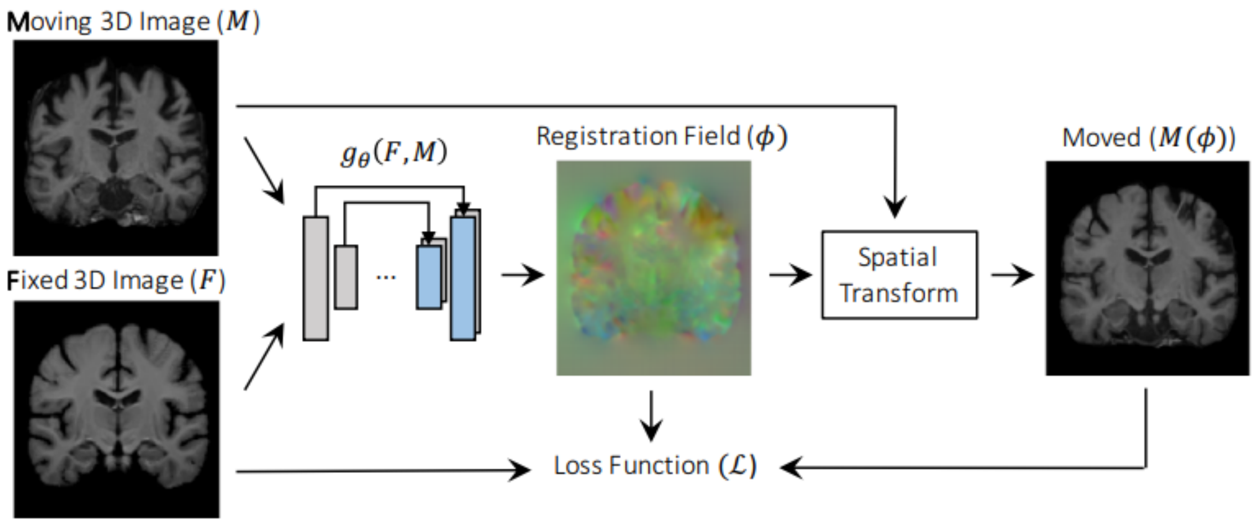
End-to-End Unsupervised Deformable Image Registration with a CNN

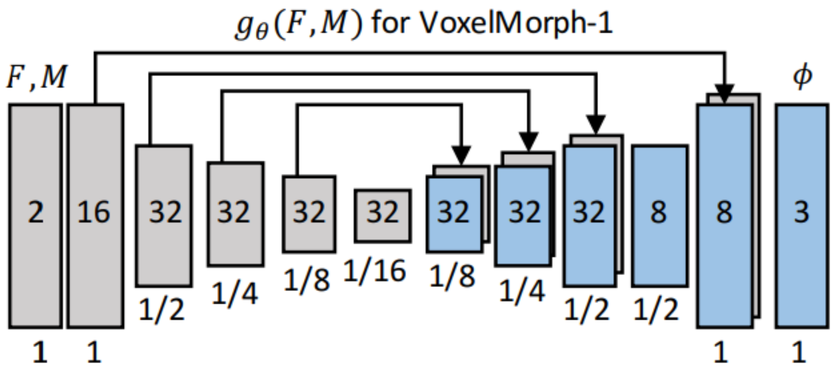


https://arxiv.org/abs/1704.06065

Unsupervised approaches

An Unsupervised Learning Model for Deformable Image Registration

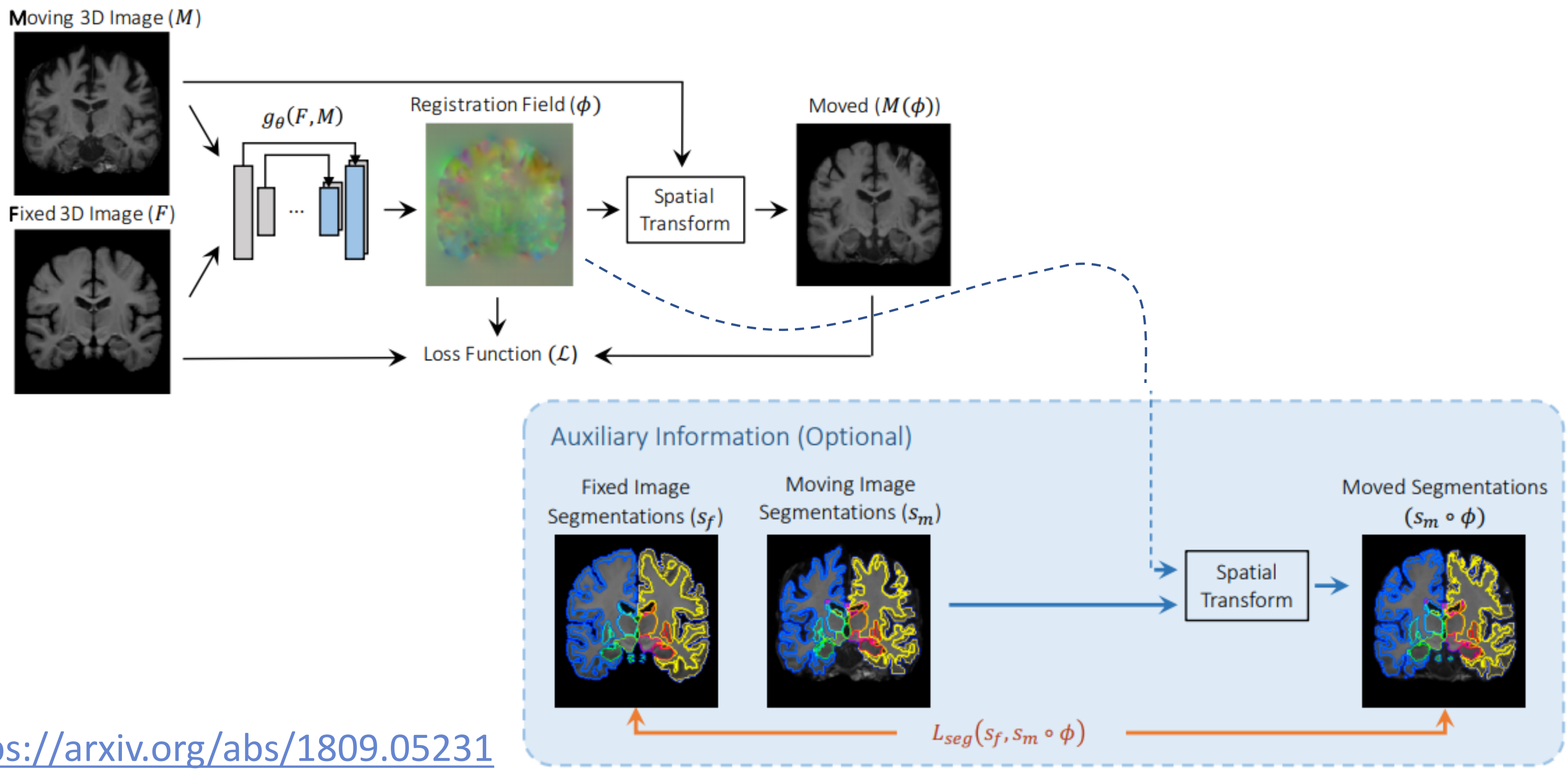




https://arxiv.org/abs/1802.02604

Registration using deep learning

VoxelMorph: A Learning Framework for Deformable Image Registration



https://arxiv.org/abs/1809.05231

Part 8 – Registration

8.7 Some classical registration softwares

Software

- Often, you may need to register your data prior to doing machine learning
- For instance, it is quite common to perform a linear registration before applying deep learning algorithms
  - This often helps the training
- For this, there are some robust and well-validated freely available software developped by the community

Software

- ANTs - http://stnava.github.io/ANTs/
  - Provides different types of deformation models and similarity metrics
    - Linear transformation
    - Non-linear transformation using B-splines
    - Non-linear transformation using diffeomorphisms

- FSL – https://fsl.fmrib.ox.ac.uk/fsl/fslwiki/FSL
  - Very commonly used for linear registration
  - FIRST – linear registration tool
    - https://fsl.fmrib.ox.ac.uk/fsl/fslwiki/FLIRT

- Deformetrica - https://www.deformetrica.org/
  - Diffeomorphic deformations
  - Provides atlas construction and deformation-based analysis
  - Can be used with surface data