Introduction to Medical Image Registration

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Partially adapted from slides by:

1. Prof. Nassir Navab (TUM) and Christian Wachinger (MIT) on Intensity based Image Registration and Feature based Registration.
2. Prof. Dr. Philippe Cattin, University of Basel, Medical Image Registration

Brief Introduction

- **Sailesh Conjeti**

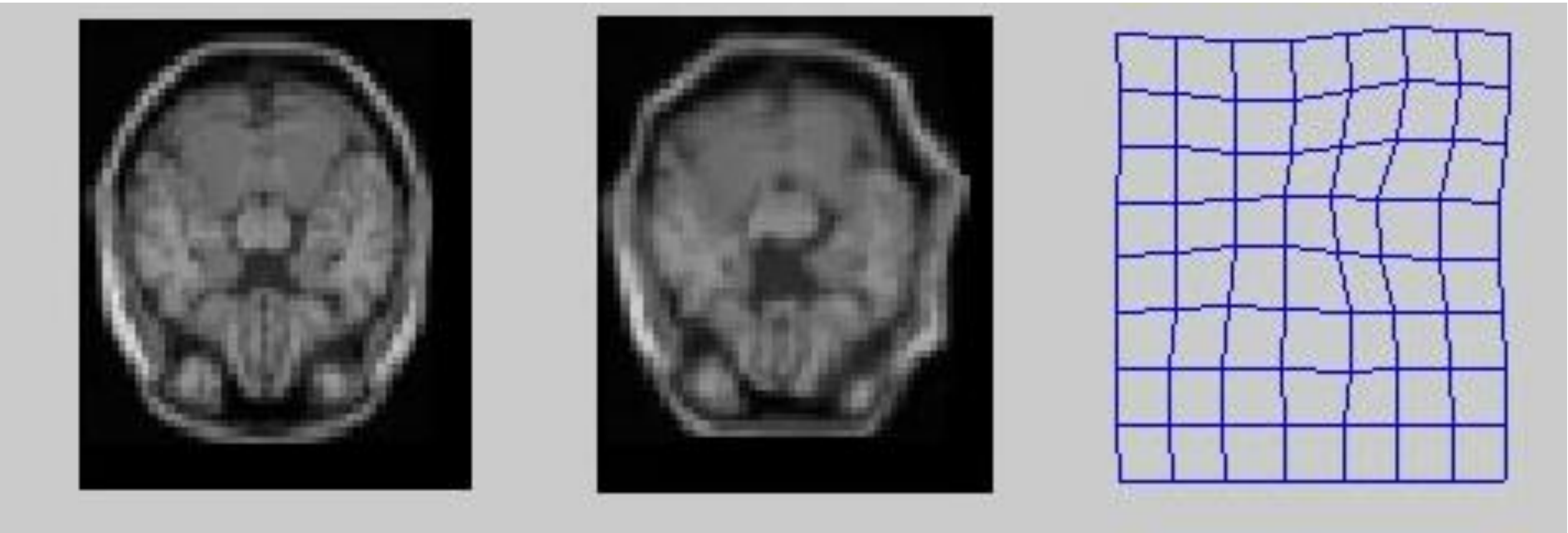
- Currently, Doctoral Student at the Chair for Computer Aided Medical Procedures, Technische Universität München, Germany, under Prof. Nassir Navab and Dr. Amin Katouzian.
- Attended School of Medical Science and Technology, Indian Institute of Technology Kharagpur, India from 2012-14.
- Graduated from Birla Institute of Technology and Science, Pilani – Class of 2012.
- Research Interests: Machine Learning, Medical Image Computing, Image Registration, Biomedical Signal Processing and Wearable Computing.

Please feel free to stop me if you have any questions.

What is the fuss all about?
Lets Consider an imaginary case.

How to align these?

The Solution



The Result

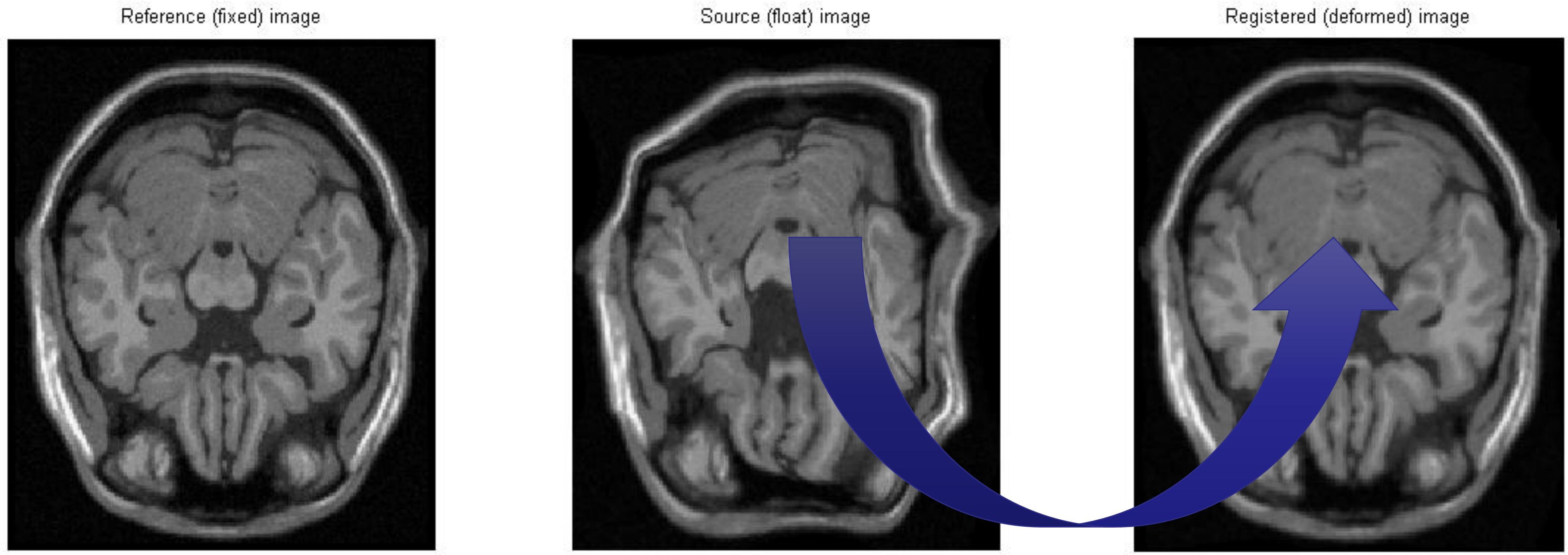


Image Registration

So, lets define Image Registration:

Aligning one image to another,
so that they share the same coordinate system.

Some Terminology:

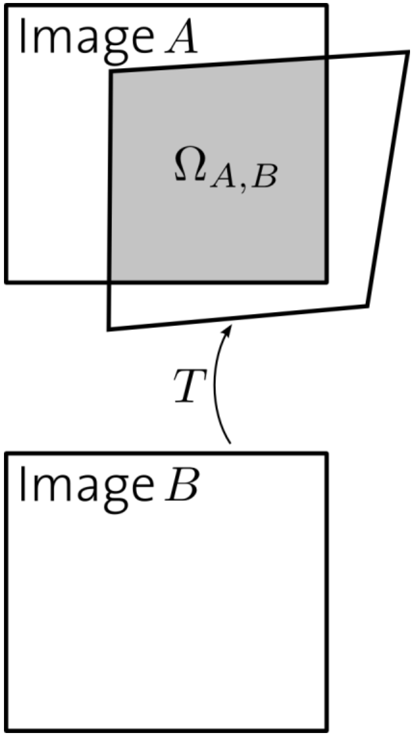
Given:

- **Reference or Target Image**: Fixed during registration.
- **Floating or Sensed Image:** It is spatially warped to align with reference image.

Task:

Find a reasonable transformation T, such that the transformed image is similar to the reference image.

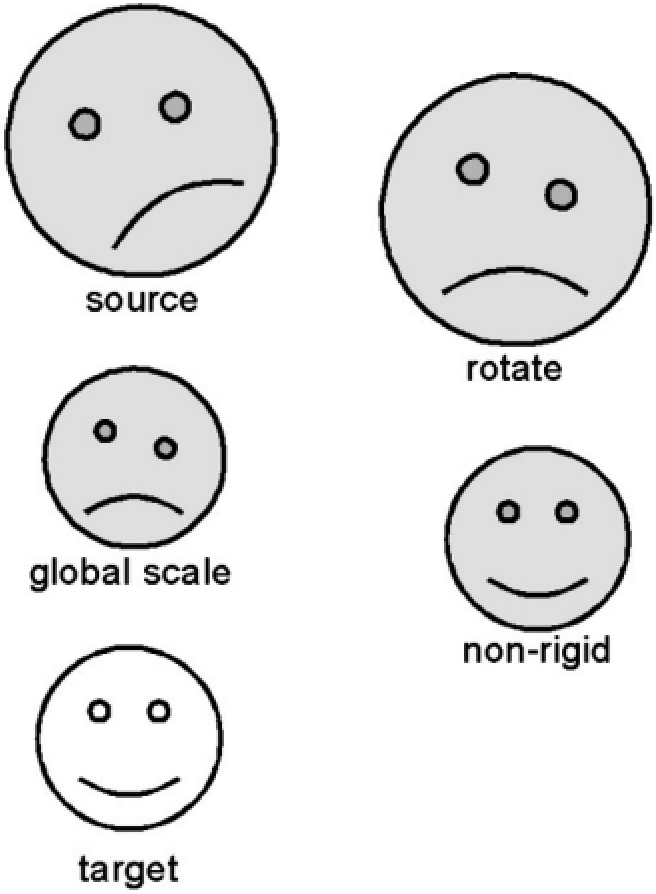
Overlap Domain: Pixels / Voxels overlapping between the two images.



Courtesy: Philippe Cattin

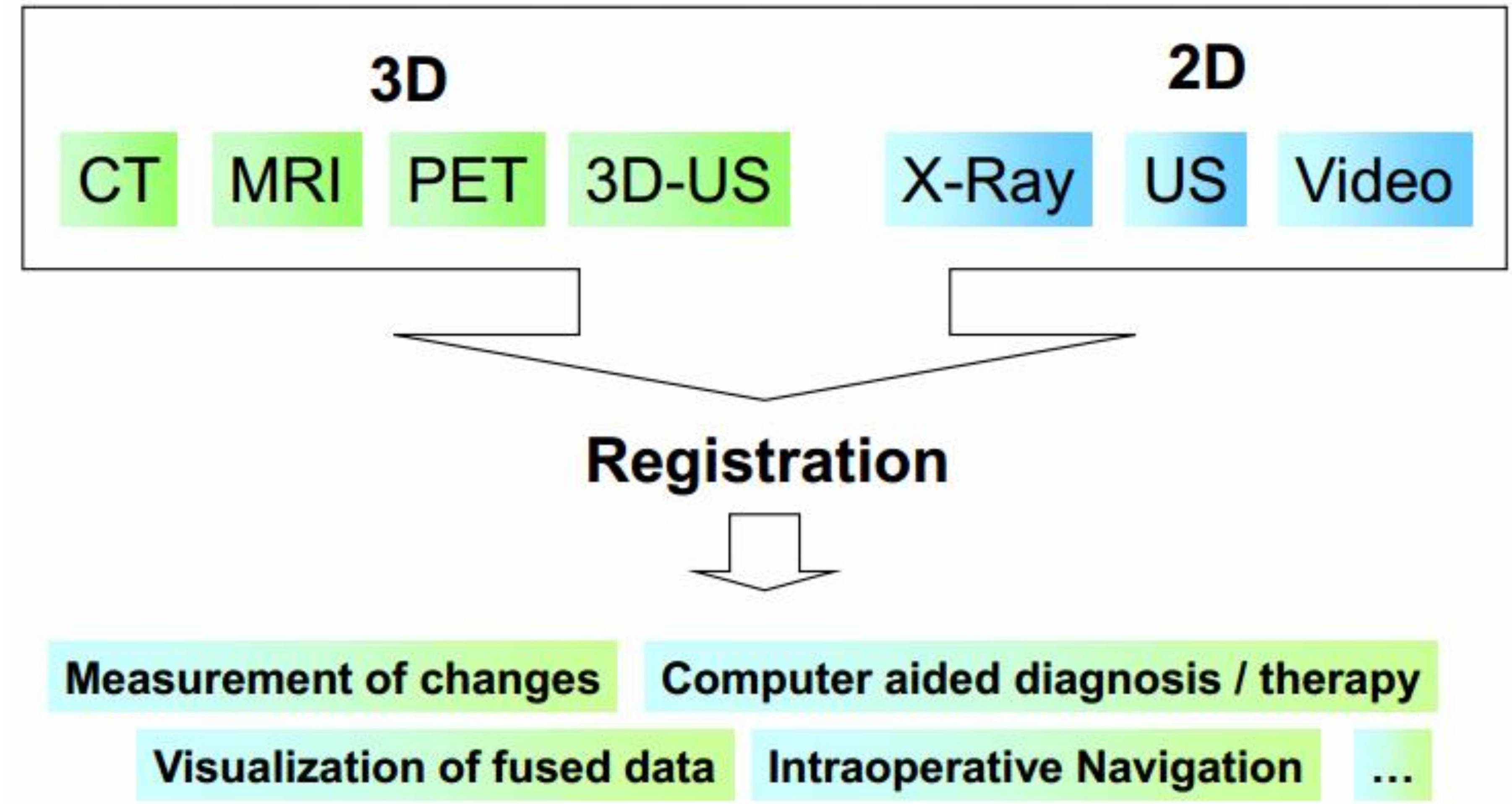
What can you expect from Today's lecture?

- Clinical Need for Image Registration.
- Monomodal Image Registration
- Multimodal Image Registration
- Transformations (Linear)
- Intensity based registration
  - Monomodal (SSD and NCC)
  - Multimodal (Mutual Information)
- Feature based Registration
- Group wise Image Registration
- Non-rigid Registration

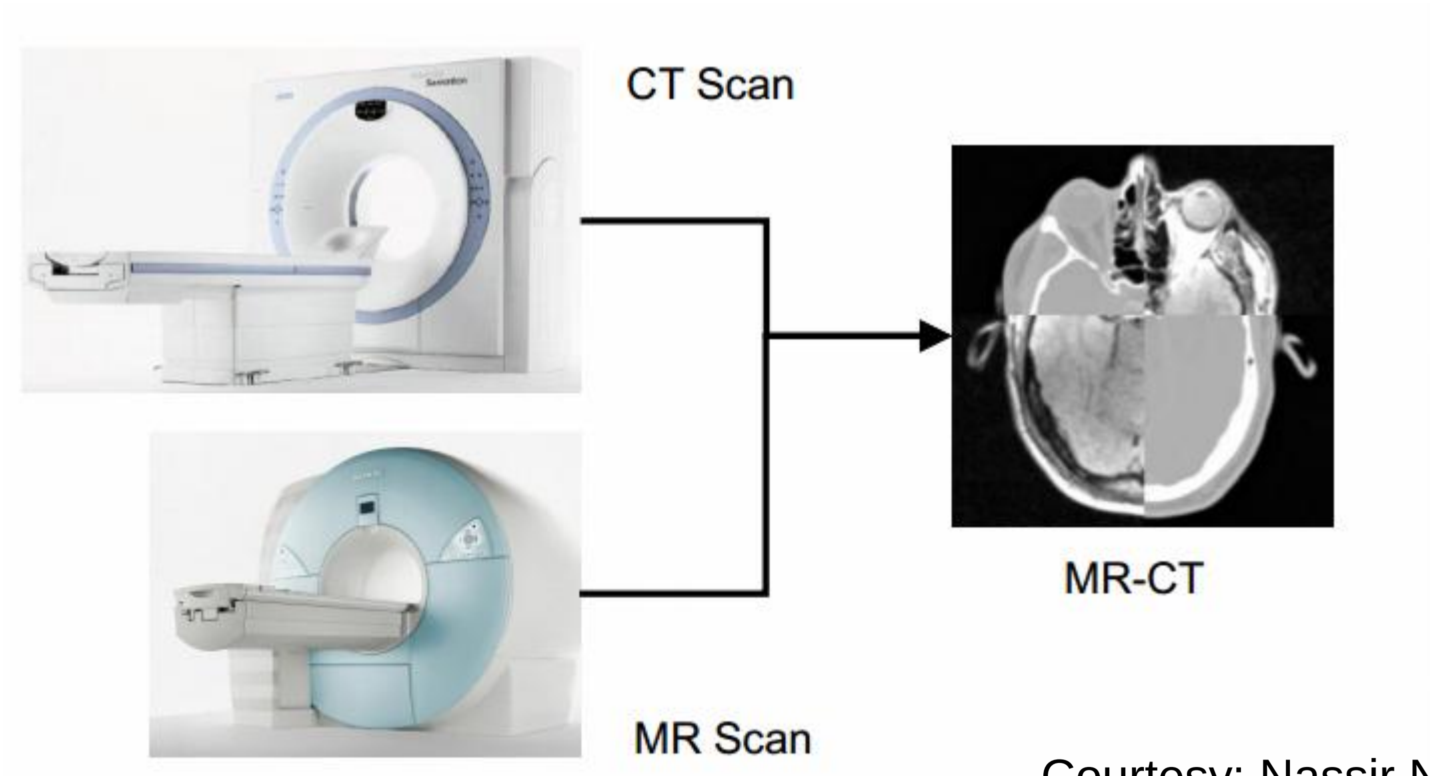


Crum, W. R., Hartkens, T., & Hill, D. L. G. (2014). Non-rigid image registration: theory and practice.

Need for Image Registration



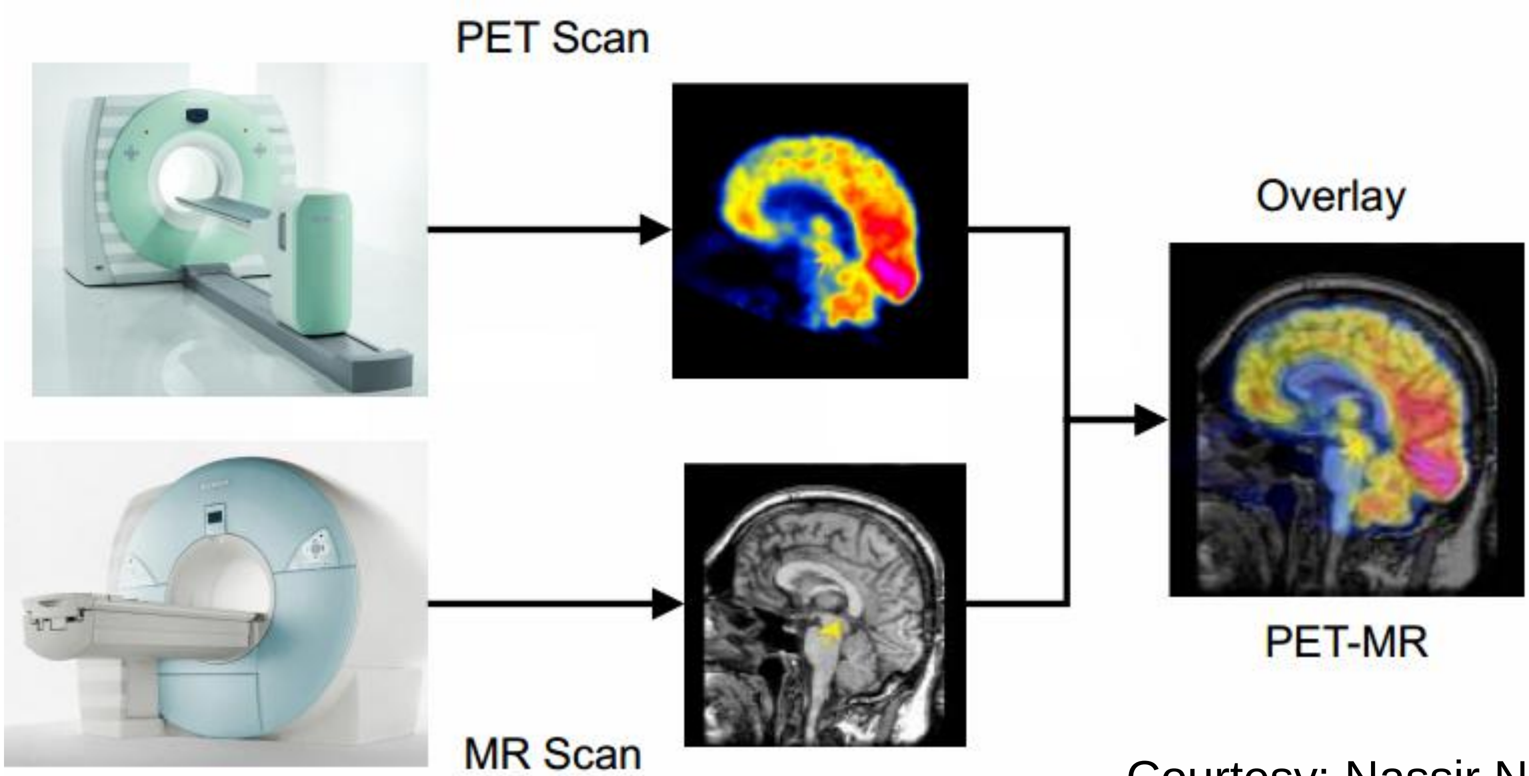
Possible Scenarios – CT to MR Registration



Courtesy: Nassir Navab

3D to 3D Anatomical Registration

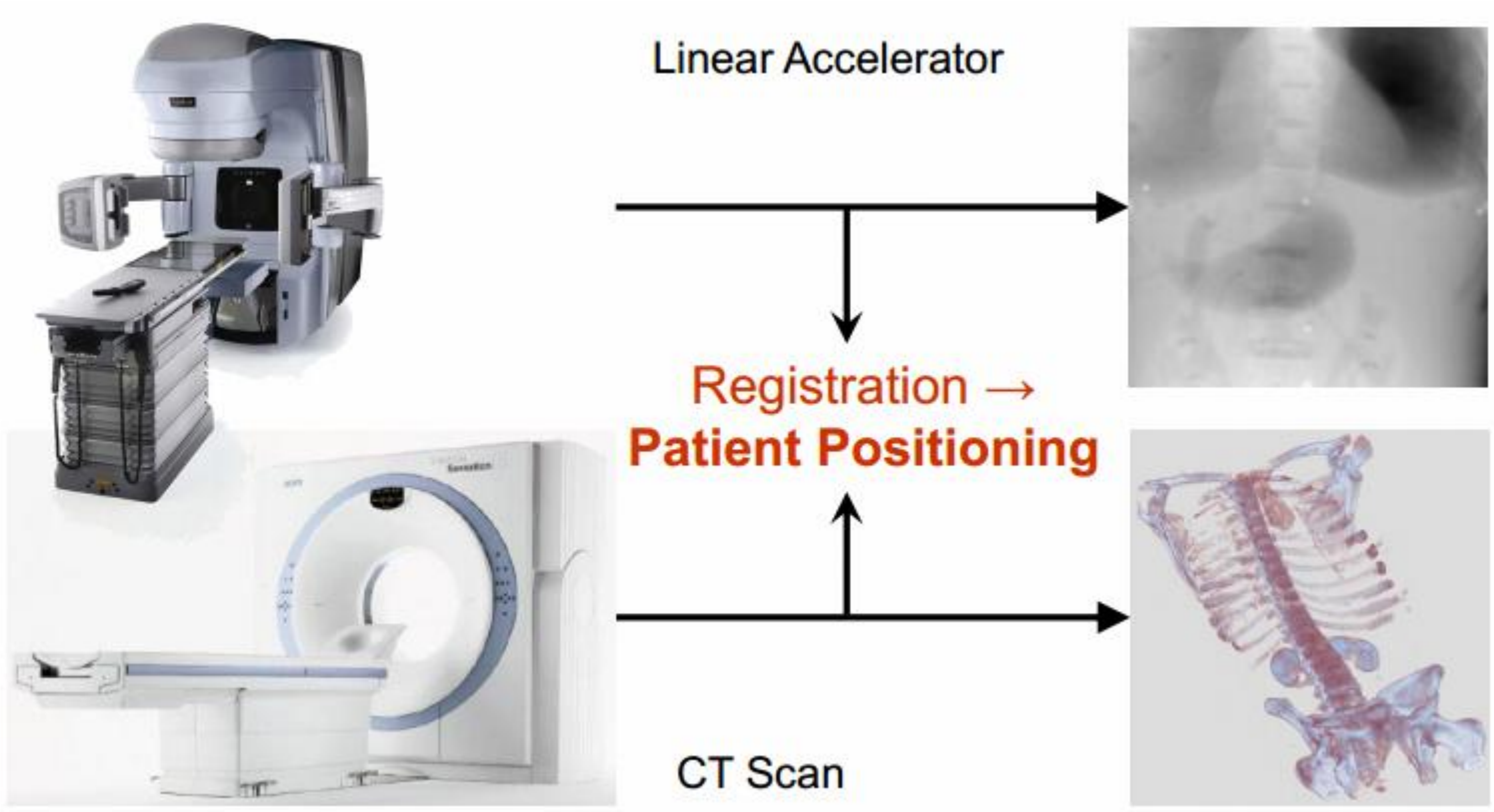
Possible Scenarios – PET to MR Registration



Courtesy: Nassir Navab

Anatomical to Functional Image Registration

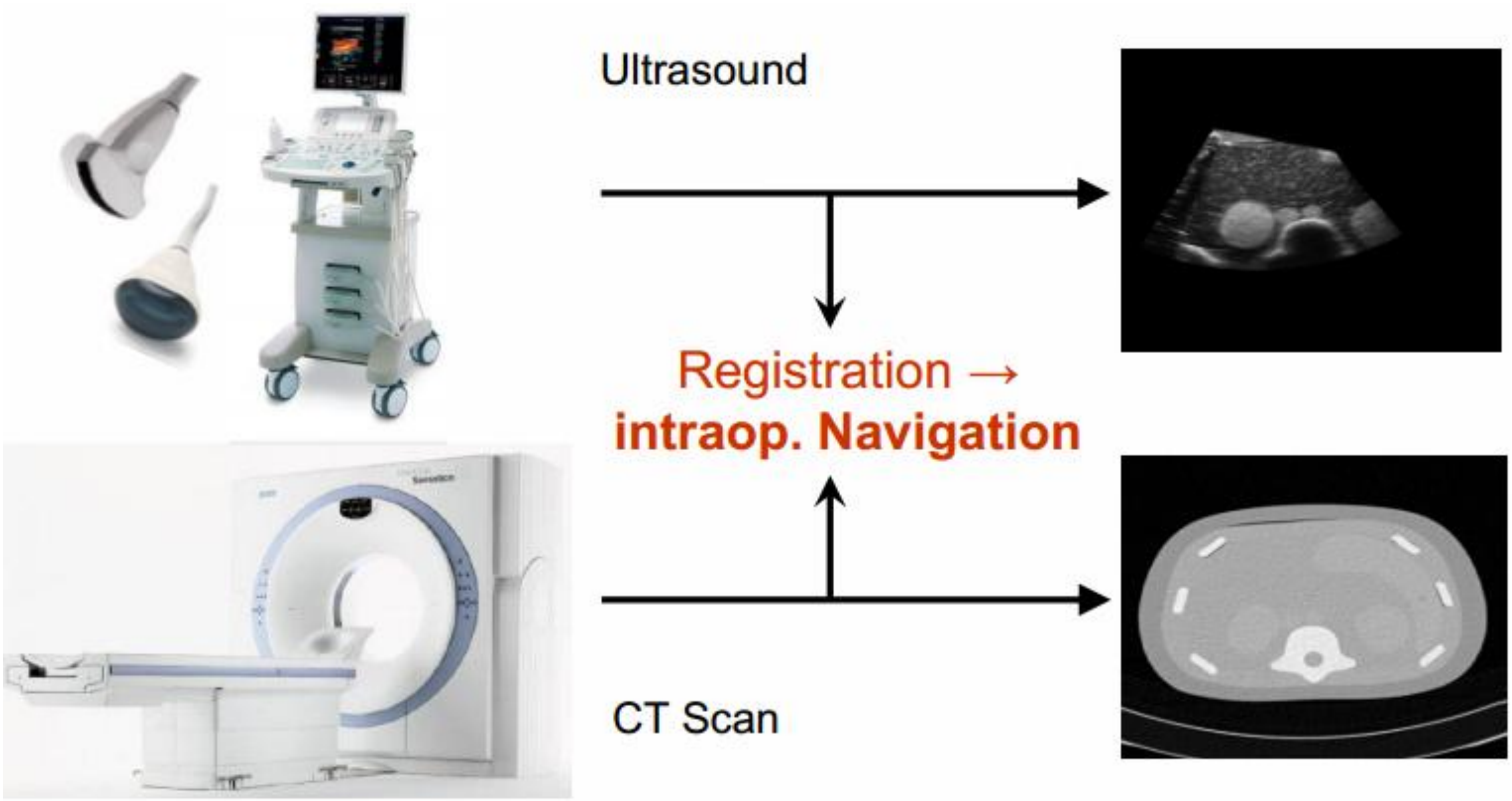
Possible Scenarios – C-arm to CT Registration



Courtesy: Nassir Navab

2D to 3D Image Registration

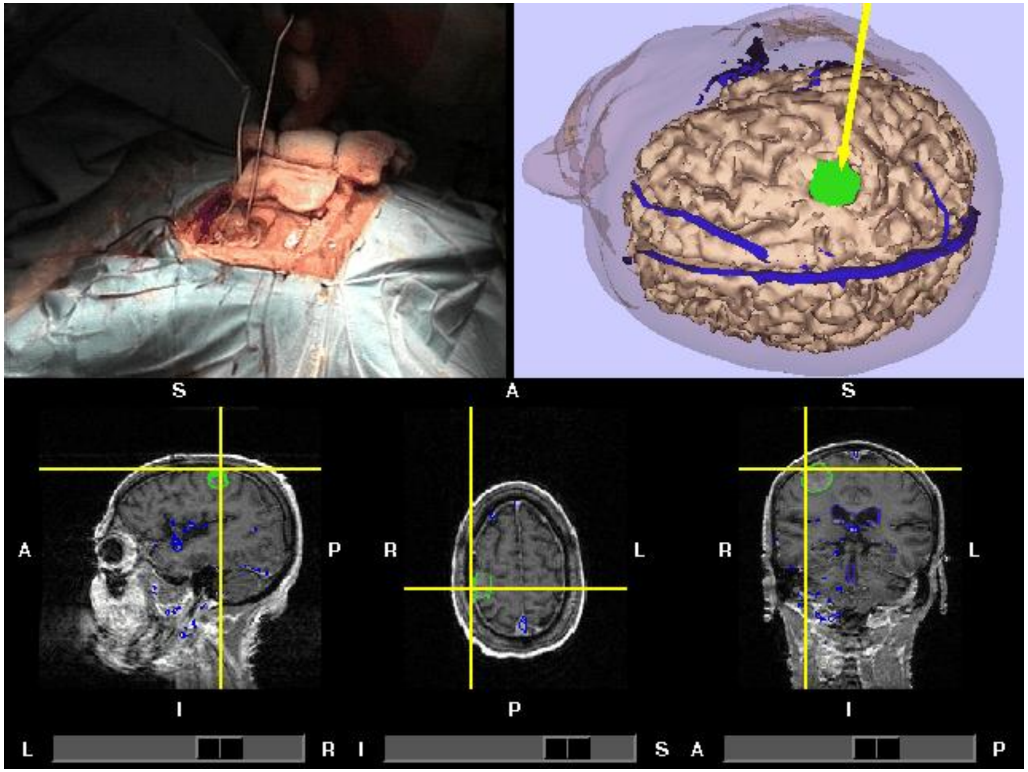
Possible Scenarios – Intra-operative Navigation



Courtesy: Nassir Navab

2D to 3D Multimodal Image Registration

Possible Scenarios – Surgical Planning and Intra-op Navigation



Courtesy: CSAIL, MIT

3D to 3D Multimodal Image Registration

Types of Registration

Dimensionality

- 2D – 2D, 2D – 3D, 3D – 3D, 2D – 4D and so on.

Modalities

- Monomodal, Multimodal

Subject / Object

- Intra-subject
- Inter-subject – Atlas Registration

Transformations

- Rigid, Affine, Projective, Non-Linear (Deformable)

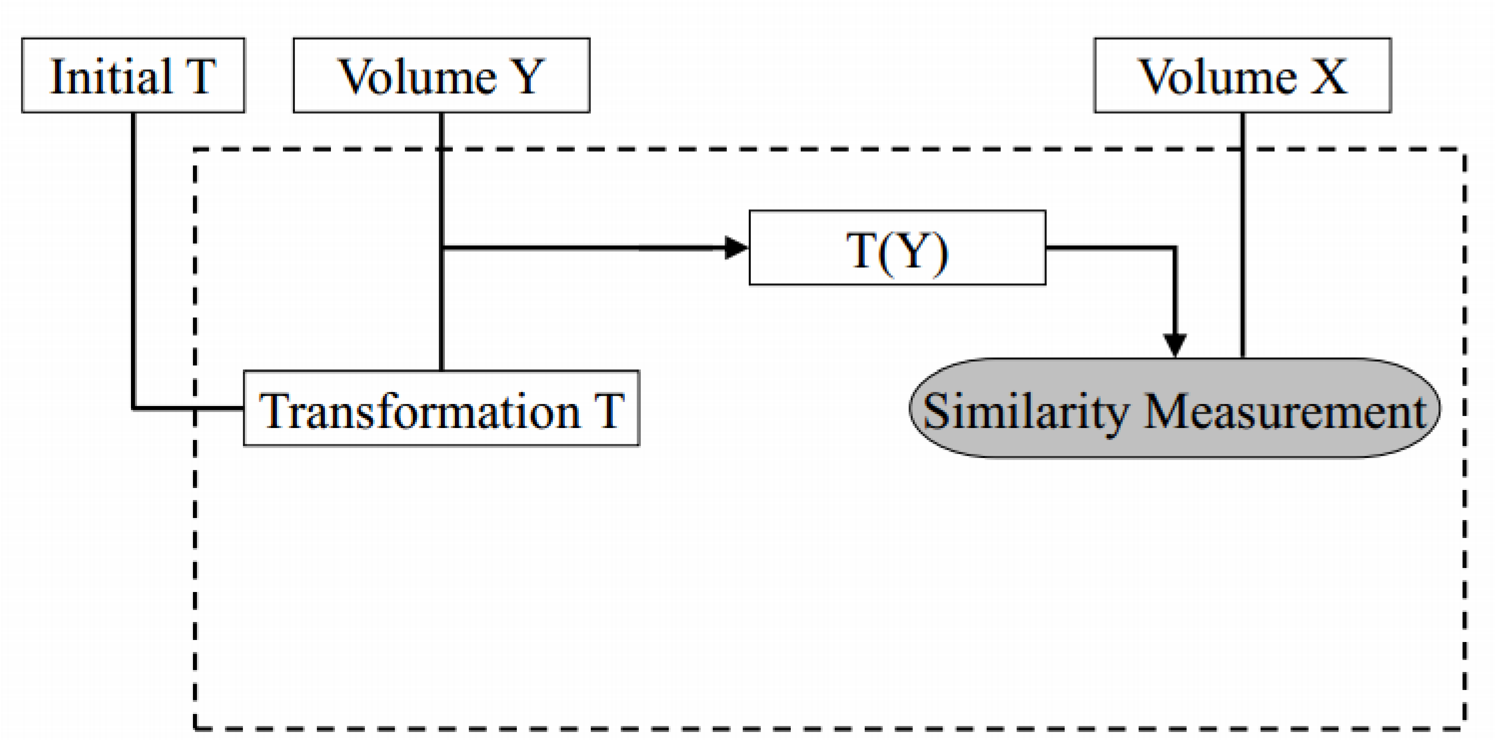
Registration Basis

- Extrinsic (Marker based), Intrinsic

Number of Images

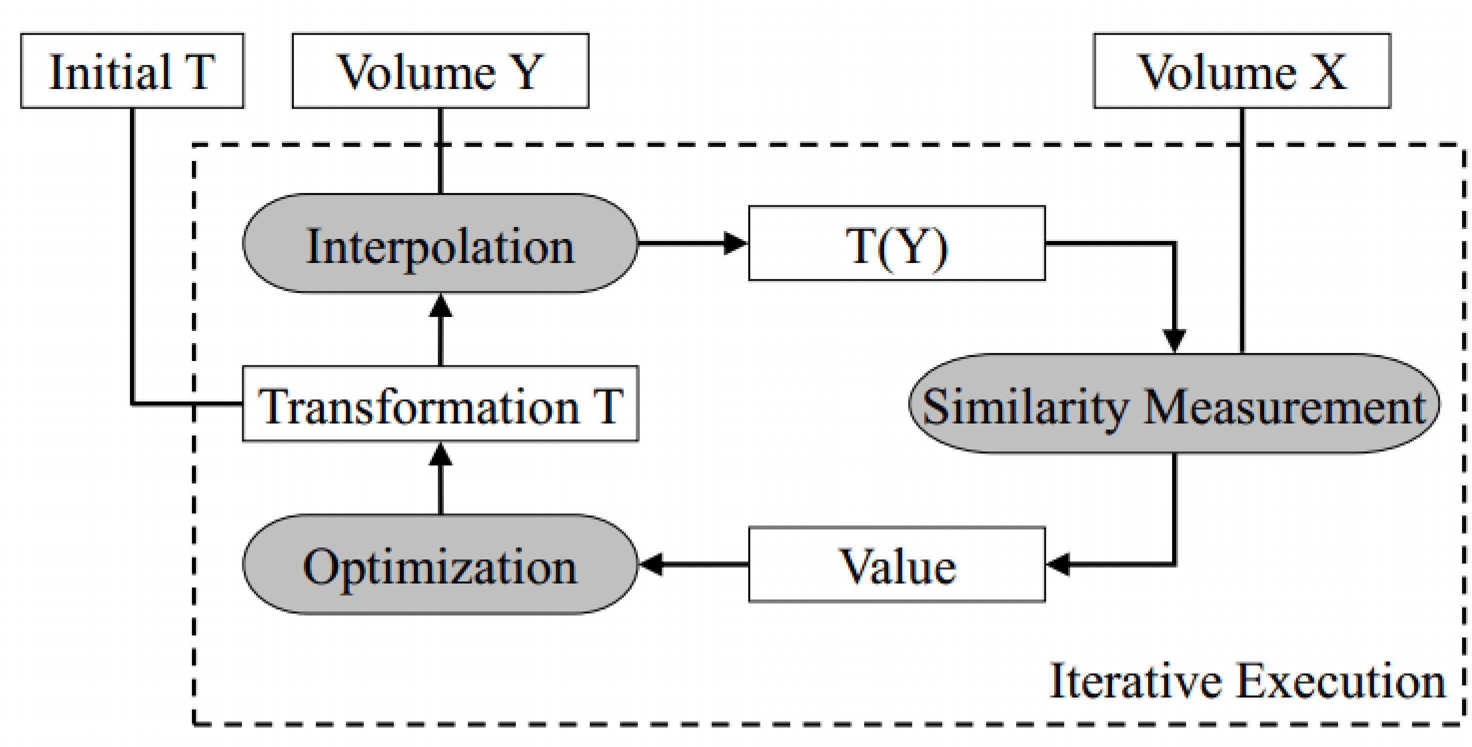
- Pairwise, Group-wise

Image Registration



Courtesy: Nassir Navab, Christian Wachinger

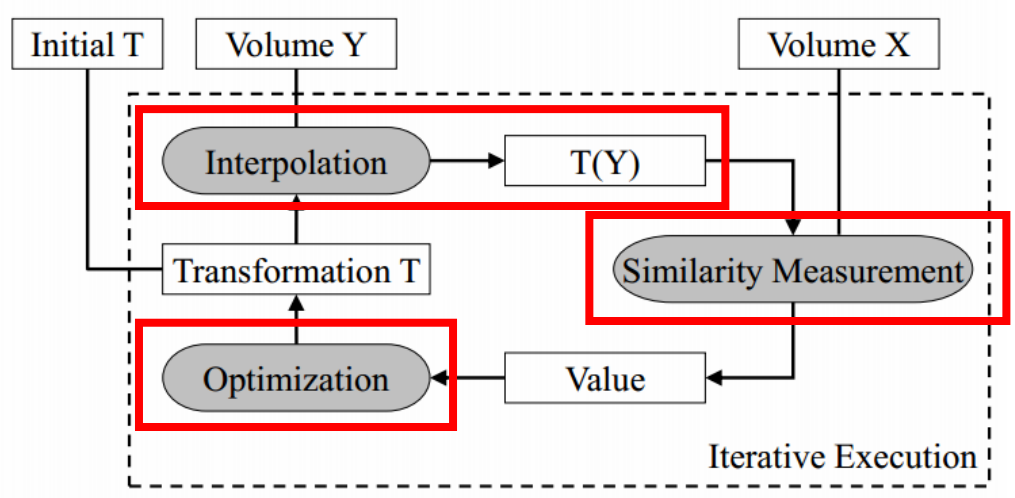
Image Registration – Close the loop



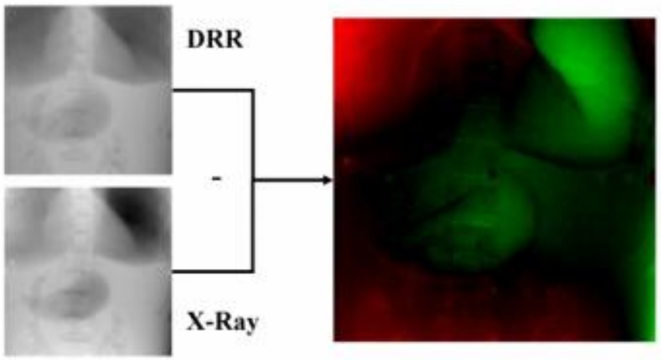
Courtesy: Nassir Navab, Christian Wachinger

Registration – Close the loop

- For each iteration, compute similarity function $Sim(X, T(Y))$, using full image content.
- $T(Y)$ requires interpolation to match resolution and scale of X.
- Maximize $Sim(X, T(Y))$, by performing optimization on transformation parameters.

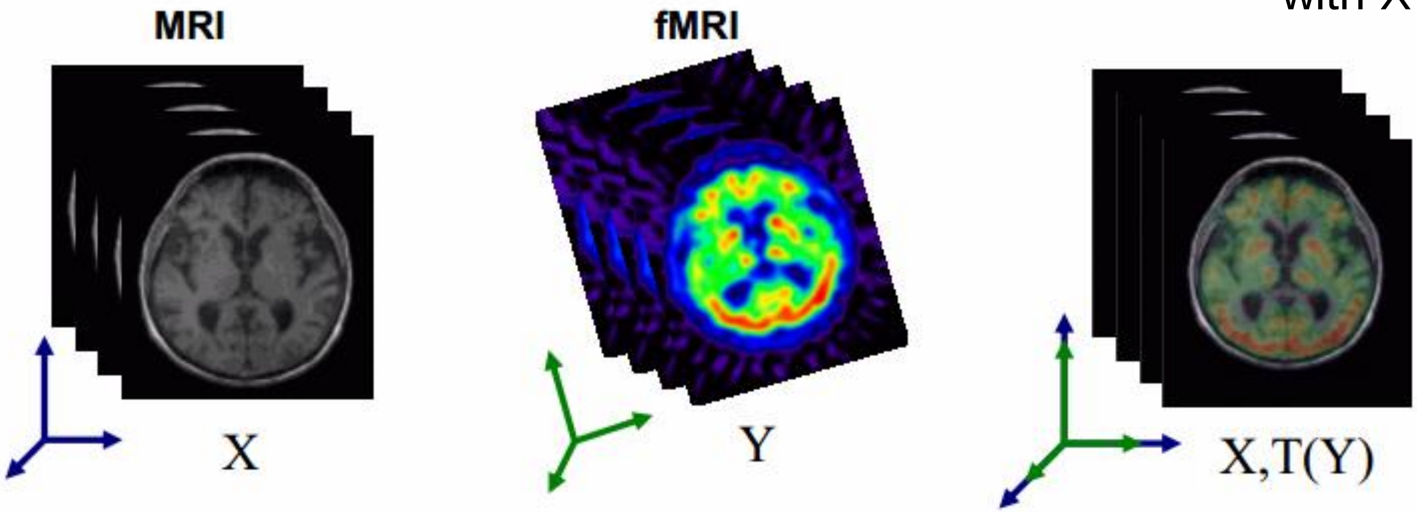


Finding the transformation – Registration Basis

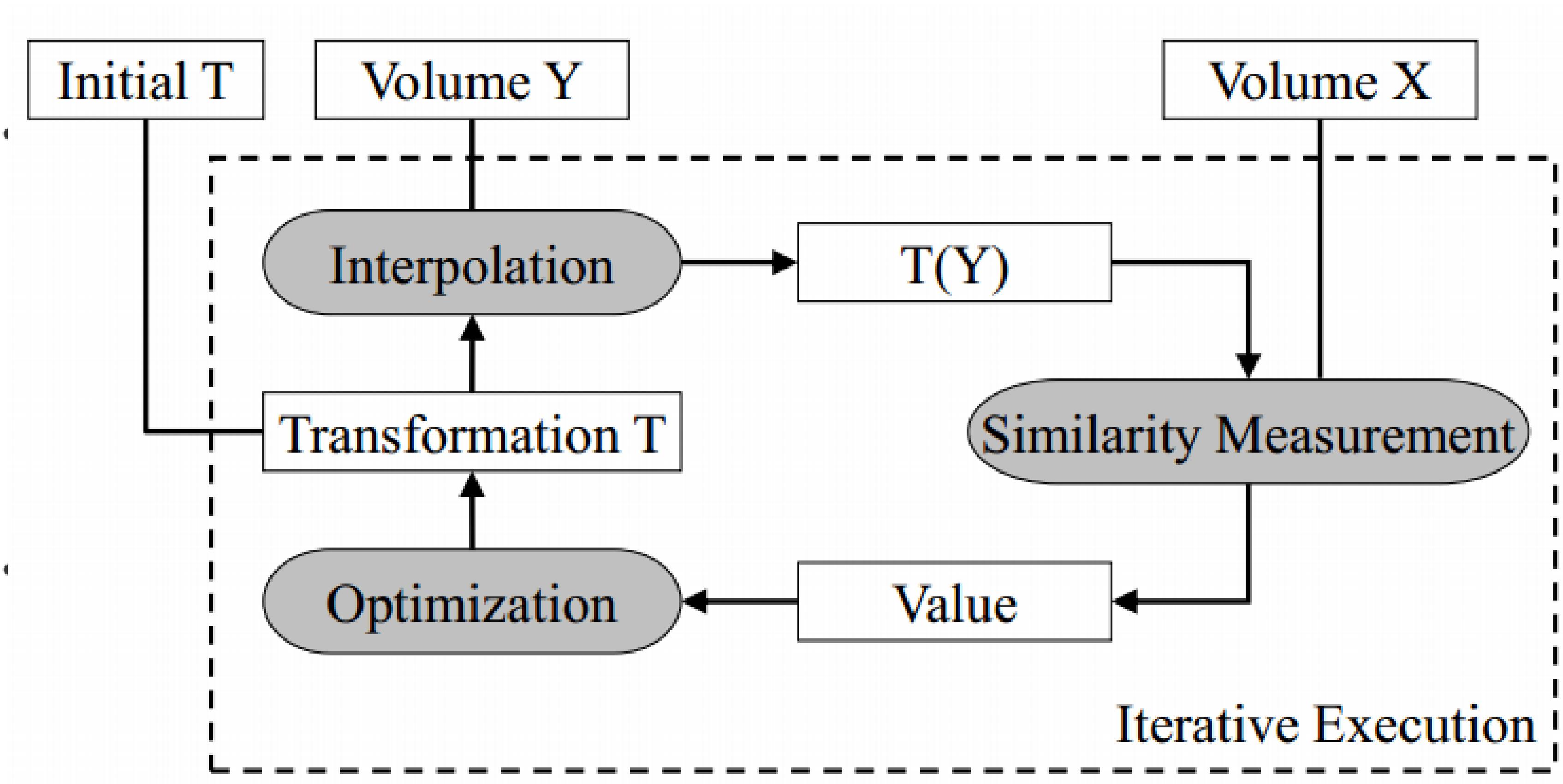


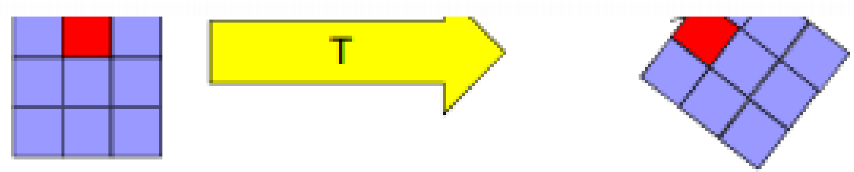
Registering digitally reconstructed radiograph with X-Ray image.

- Intensity based Registration
  – utilizing full image content.
- Define transformation T on one of the image volumes.
- Compare X and T(Y) using full image content.
- Reiterate estimate of T, till convergence.



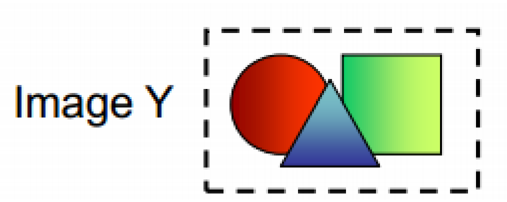
Spatial Transformations

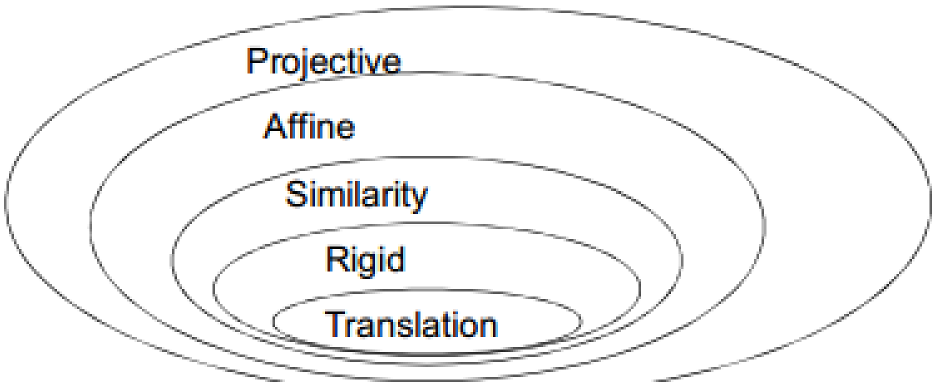


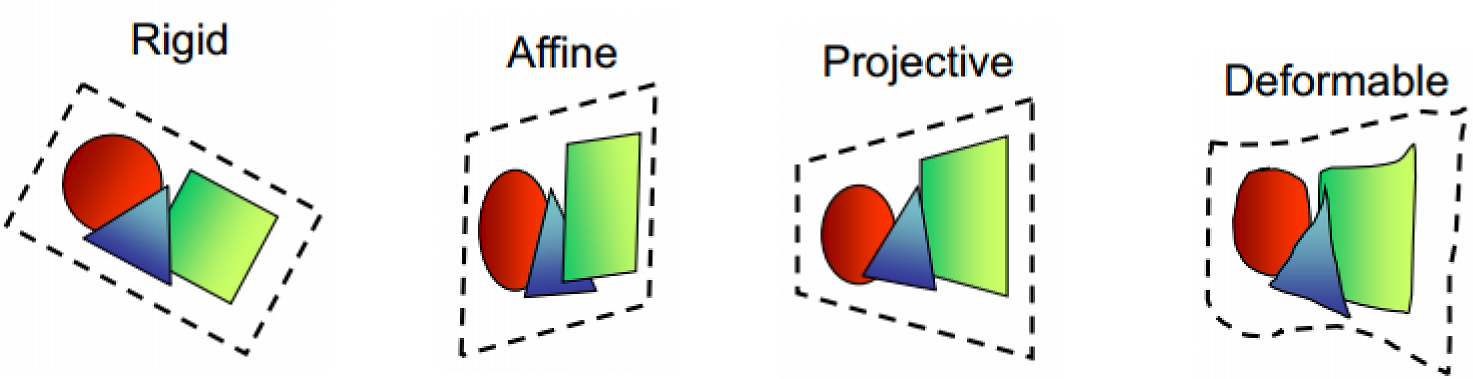


T. Wittmann, Lecture on Image Registration, 2012.

Spatial Transformations







Mathematical Formulation

- Consider image $I_s(i,j)$ to be aligned to target image $I_T(x,y)$. We formulate image registration as:

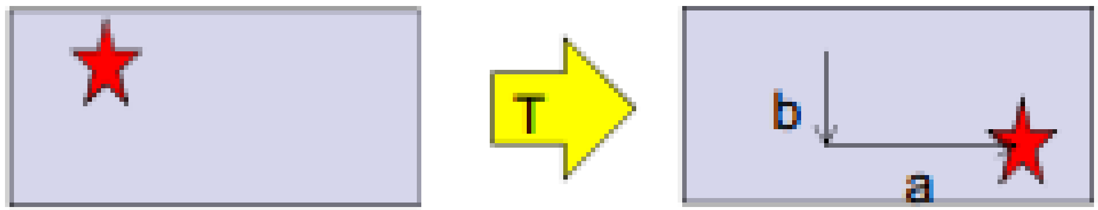
$$I_s(i,j) \sim I_t\left(x = f_x(i,j), y = f_y(i,j)\right)$$

- We can express this coordinate transformation as:

$$\binom{x}{y} = \boxed{f}(i,j,\Theta) = \begin{pmatrix} f_x(i,j;\Theta) \\ f_y(i,j;\Theta) \end{pmatrix}$$

Transformation Function evaluated at each coordinate (i,j)

Translation



- Image is translated in the coordinate space. This transformation can be formulated as:

$$x = i + a$$
$$y = j + b$$

- In form of a linear equation:

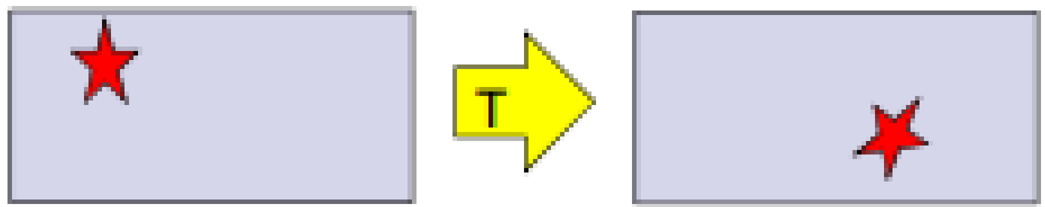
Transformation Function

Homogenous Coordinates

$$\boxed{\begin{bmatrix} x \\ y \\ 1 \end{bmatrix}} = \boxed{\begin{bmatrix} 1 & 0 & a \\ 0 & 1 & b \\ 0 & 0 & 1 \end{bmatrix}} \begin{bmatrix} i \\ j \\ 1 \end{bmatrix}$$

http://graphics.stanford.edu/courses/cs348a-12-winter/Handouts/handout15.pdf

Rigid Transformation



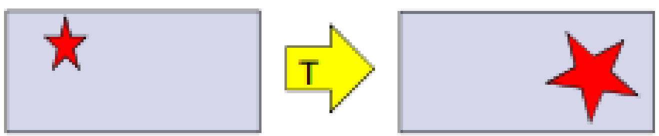
- Involves translation and rotation.
- This can be formulated as: translation of (a, b) and rotation of θ counter-clockwise about origin.

Transformation Function

$$\begin{bmatrix} x \\ y \\ 1 \end{bmatrix} = \boxed{\begin{bmatrix} \cos\theta & \sin\theta & a \\ \sin\theta & -\cos\theta & b \\ 0 & 0 & 1 \end{bmatrix}} \begin{bmatrix} i \\ j \\ 1 \end{bmatrix}$$

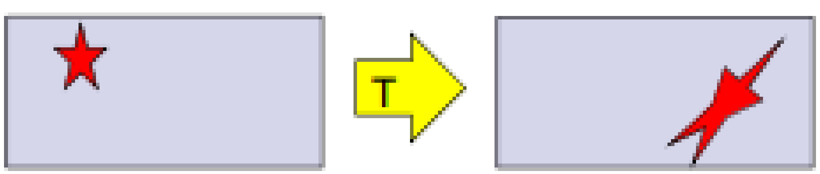
Similarity and Affine Transformation

- Lets introduce further isotropic scaling with a factor of S (called Similarity Transformation)



$$\begin{bmatrix} x \\ y \\ 1 \end{bmatrix} = \begin{bmatrix} S\cos\theta & S\sin\theta & a \\ S\sin\theta & -S\cos\theta & b \\ 0 & 0 & 1 \end{bmatrix} \begin{bmatrix} i \\ j \\ 1 \end{bmatrix}$$

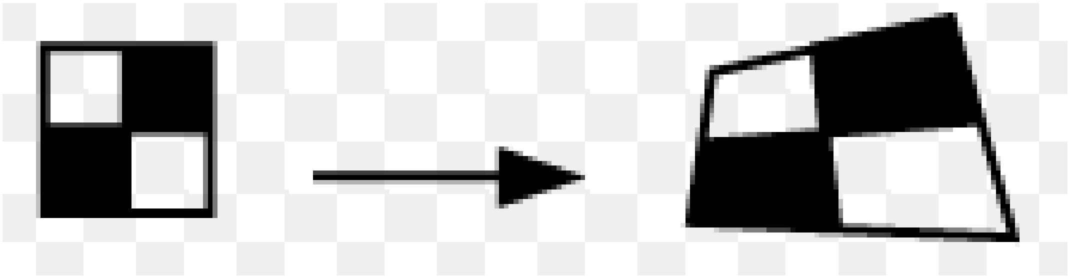
- If we make the scaling anisotropic, we introduce shear effect. Such a transformation is called Affine Transformation.



$$\begin{bmatrix} x \\ y \\ 1 \end{bmatrix} = \begin{bmatrix} A\cos\theta & B\sin\theta & a \\ C\sin\theta & -D\cos\theta & b \\ 0 & 0 & 1 \end{bmatrix} \begin{bmatrix} i \\ j \\ 1 \end{bmatrix}$$

Projective Transformation

- General Linear Transformation (Planar Homography)
- Parallel lines may not remain parallel.
- Models rigid motion in and out of the plane.



- Formulated as

$$\begin{bmatrix} x \\ y \\ 1 \end{bmatrix} = \begin{bmatrix} A & B & C \\ D & E & F \\ G & H & 1 \end{bmatrix} \begin{bmatrix} i \\ j \\ 1 \end{bmatrix}$$

3D Rigid-body Transformations

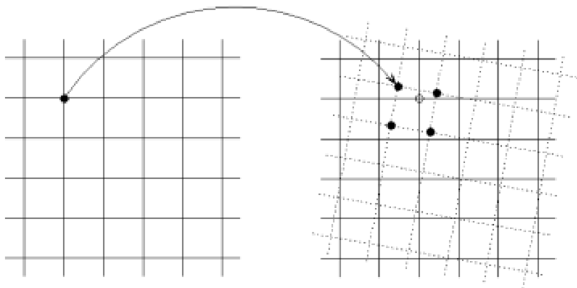
- A 3D rigid body transform is defined by:
  - 3 translations - in X, Y & Z directions
  - 3 rotations - about X, Y & Z axes
- The order of the operations matters

$$\begin{pmatrix} 1 & 0 & 0 & X_{trans} \\ 0 & 1 & 0 & Y_{trans} \\ 0 & 0 & 1 & Z_{trans} \\ 0 & 0 & 0 & 1 \end{pmatrix} \times \begin{pmatrix} 1 & 0 & 0 & 0 \\ 0 & \cos\Phi & \sin\Phi & 0 \\ 0 & -\sin\Phi & \cos\Phi & 0 \\ 0 & 0 & 0 & 1 \end{pmatrix} \times \begin{pmatrix} \cos\Theta & 0 & \sin\Theta & 0 \\ 0 & 1 & 0 & 0 \\ -\sin\Theta & 0 & \cos\Theta & 0 \\ 0 & 0 & 0 & 1 \end{pmatrix} \times \begin{pmatrix} \cos\Omega & \sin\Omega & 0 & 0 \\ -\sin\Omega & \cos\Omega & 0 & 0 \\ 0 & 0 & 1 & 0 \\ 0 & 0 & 0 & 1 \end{pmatrix}$$

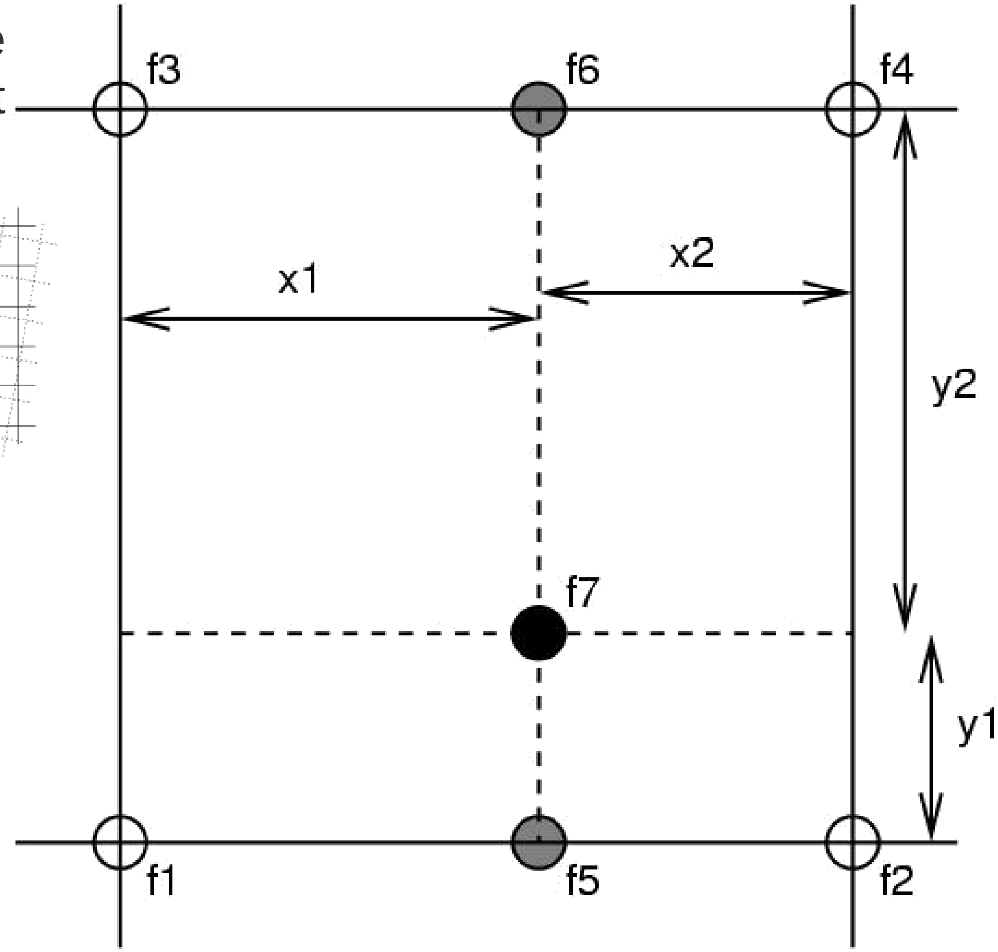
Translations	Pitch about x axis	Roll about y axis	Yaw about z axis

Simple Interpolation

- What if after transformation the image coordinates are not integers?



- Nearest neighbour
  - Take the value of the closest voxel
- Tri-linear
  - Just a weighted average of the neighbouring voxels
  - $f_5 = f_1\, x_2 + f_2\, x_1$
  - $f_6 = f_3\, x_2 + f_4\, x_1$
  - $f_7 = f_5\, y_2 + f_6\, y_1$



Problem: Transformation

- Given an image:

0	1	4
2	5	1
0	1	0

- **Task:** Apply 45 degree counter clockwise rotation and translate by (1,1). Scale by a factor of 1.5. Consider Nearest Neighbour interpolation. Zero Pad if necessary.
- Find the value of coordinate (4,2) in the transformed image.

- **Step 1**: Construct the transformation matrix.
- $\begin{bmatrix} x \\ y \\ 1 \end{bmatrix} = \begin{bmatrix} S\cos\theta & S\sin\theta & a \\ S\sin\theta & -S\cos\theta & b \\ 0 & 0 & 1 \end{bmatrix} \begin{bmatrix} i \\ j \\ 1 \end{bmatrix}$ $\quad \begin{bmatrix} x \\ y \\ 1 \end{bmatrix} = \begin{bmatrix} 1.5\cos\pi/4 & 1.5\sin\pi/4 & 1 \\ 1.5\sin\pi/4 & -1.5\cos\pi/4 & 1 \\ 0 & 0 & 1 \end{bmatrix} \begin{bmatrix} i \\ j \\ 1 \end{bmatrix}$

Problem: Transformation

$$\begin{bmatrix} x \\ y \\ 1 \end{bmatrix} = \begin{bmatrix} 1.06 & 1.06 & 1 \\ 1.06 & -1.06 & 1 \\ 0 & 0 & 1 \end{bmatrix} \begin{bmatrix} i \\ j \\ 1 \end{bmatrix}$$

- **Step 2:** Calculate inverse transformation.

$$\begin{bmatrix} i \\ j \\ 1 \end{bmatrix} = \begin{bmatrix} 0.4717 & 0.4717 & -0.9434 \\ 0.4717 & -0.4717 & 1 \\ 0 & 0 & 1 \end{bmatrix} \begin{bmatrix} x \\ y \\ 1 \end{bmatrix}$$

- **Step 3:** For $(x, y) = (4,2)$, find (i, j).

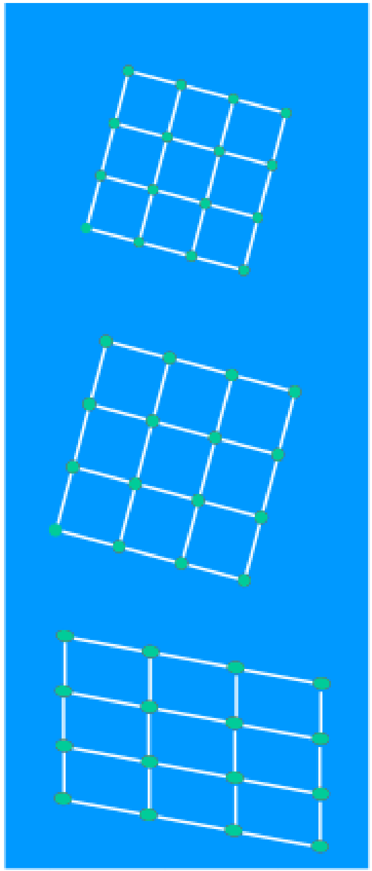
$$(i, j) = (1.88, 0.94)$$

- **Step 4:** Perform nearest neighbour interpolation.

$$I(i, j) \sim I(2,1) = 2.$$

Take Home: Try Tri-linear Interpolation for the same point.

Finding the transformation



Rigid transform:
- global patient repositioning (intra-subject)

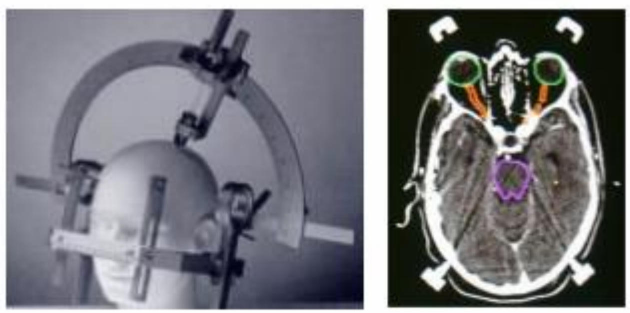
Similarity transform:
- shape analysis

Affine transform:
- first step in non-linear registration

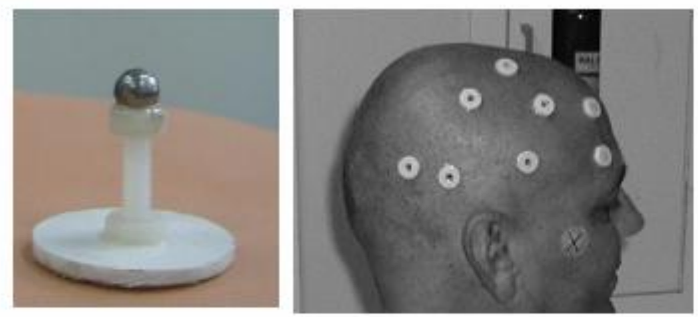
Courtesy: Niels Chr. Overgaard

Finding the transformation – Registration Basis

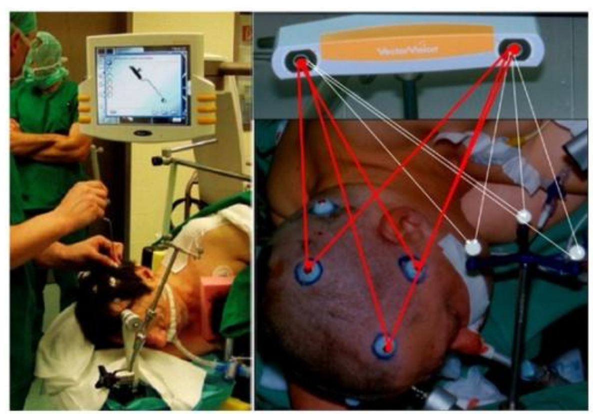
Marker Based – Extrinsic – Results in 3D point sets available for registration.



Invasive Stereotaxy

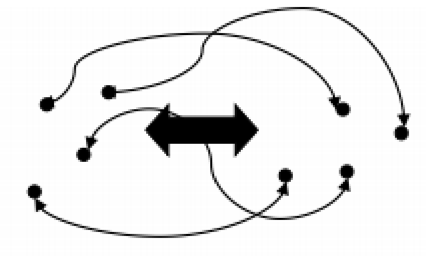


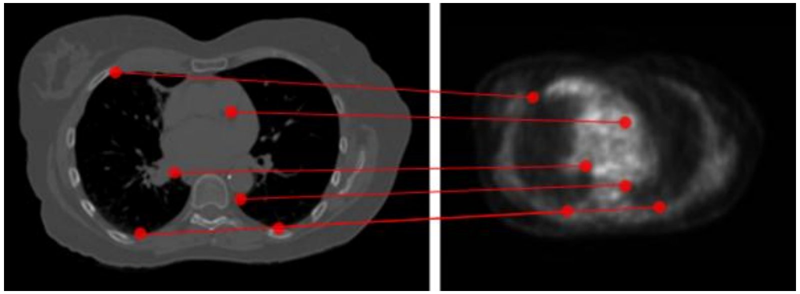
Non-invasive Fiducial Markers

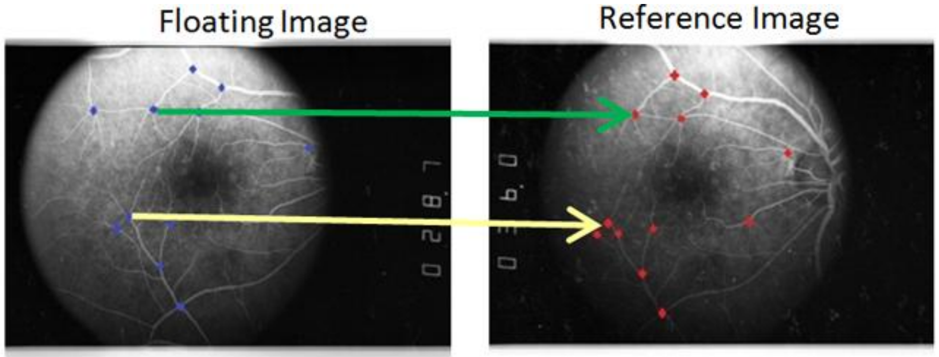


Finding the transformation – Registration Basis

- Intrinsic Registration basis – uses information available within the images to estimate the transformation.
- Landmark Based – establish point-wise correspondences.

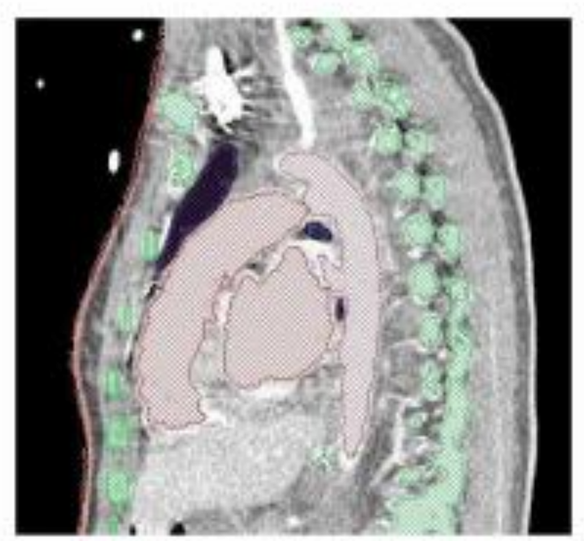


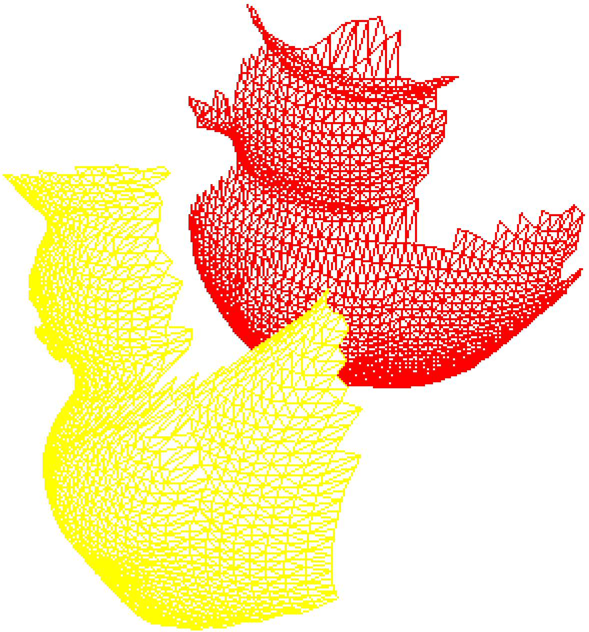




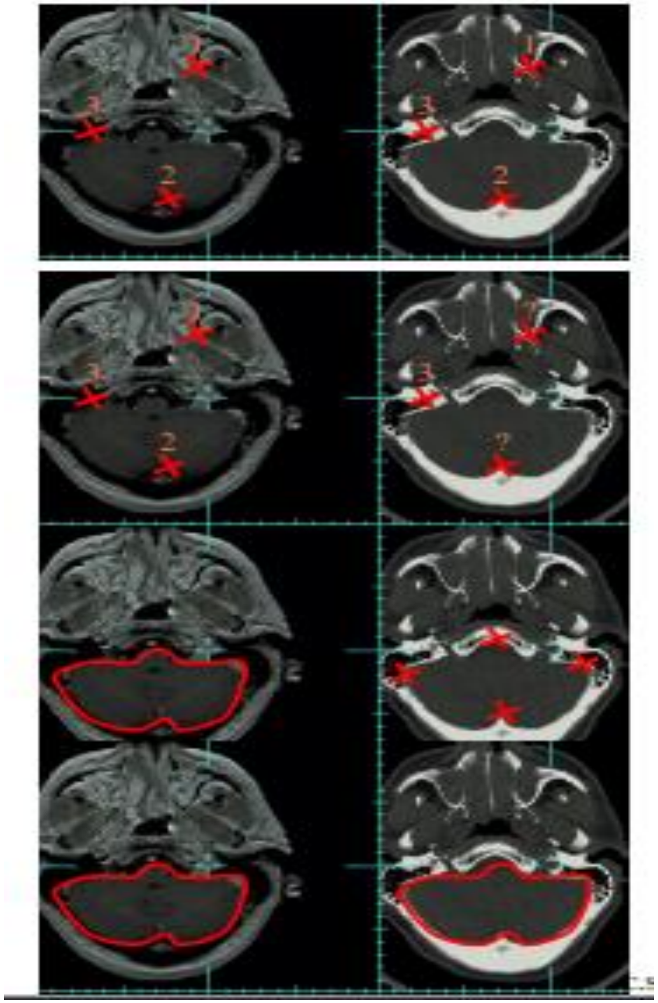
Finding the transformation – Registration Basis

- Segmented Surfaces / Objects can be used for registration.
- Surface – to – surface registration





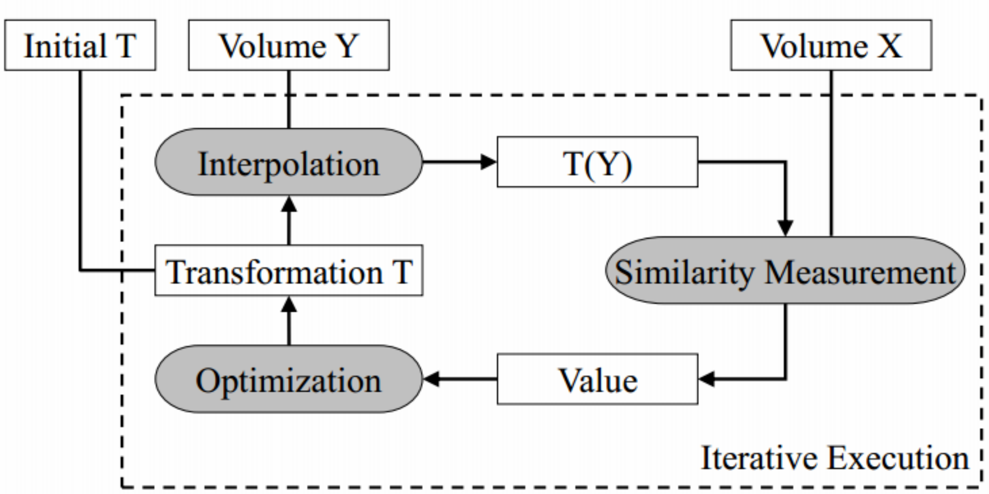
Feature Based Registration

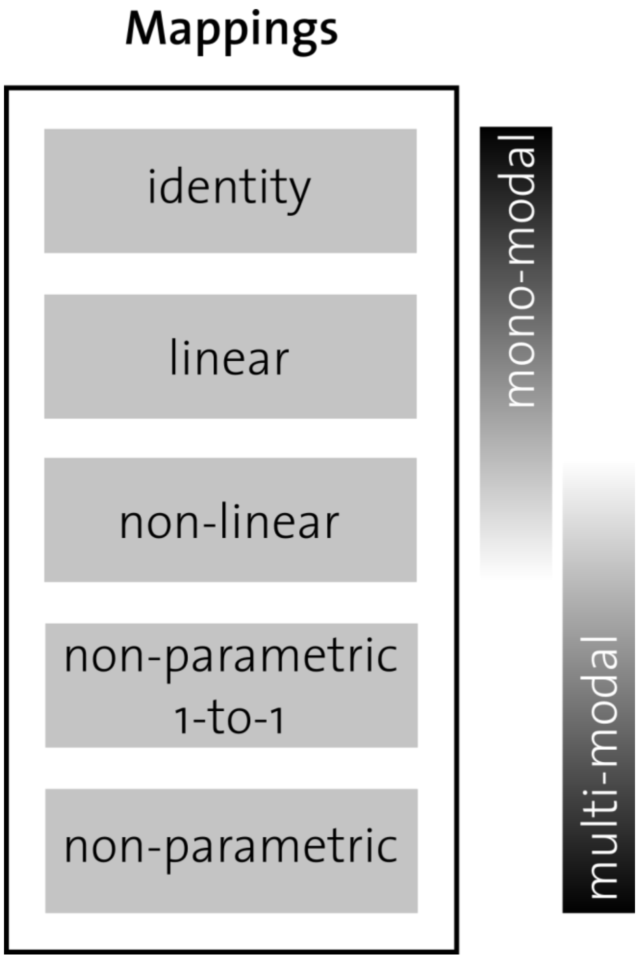


- Point Set to Point Set Registration - with correspondences
- Point Set to Point Set Registration - without correspondences
- Surface to Point Set Registration
- Surface to Surface Registration

Intensity based Registration

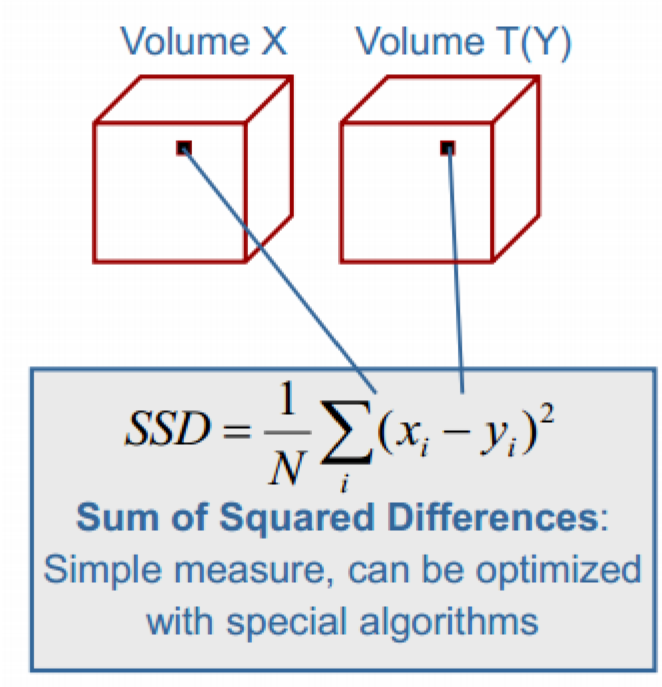
- Depending on the intensity relationship between the two modalities, similarity measures can be
  - Monomodal (for registering same modalities)
  - Multimodal (for registering different modalities)

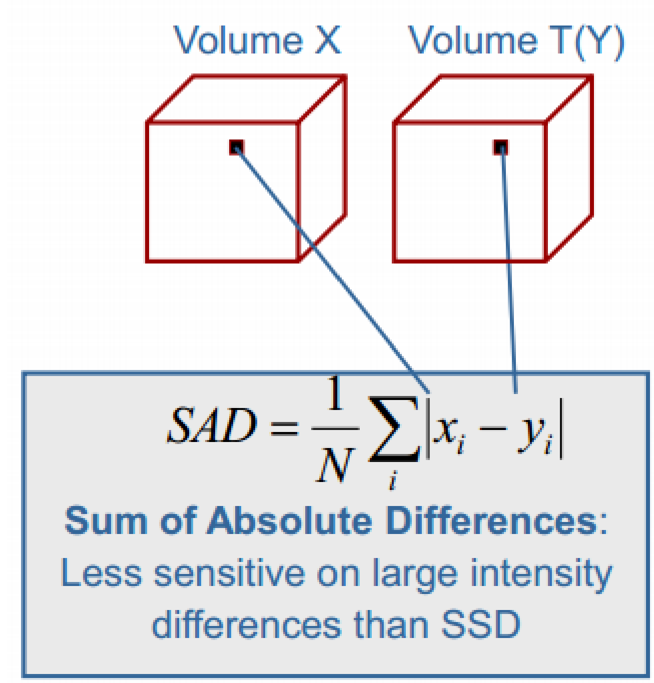




Lets take a closer look: Intensity based Similarity Measures

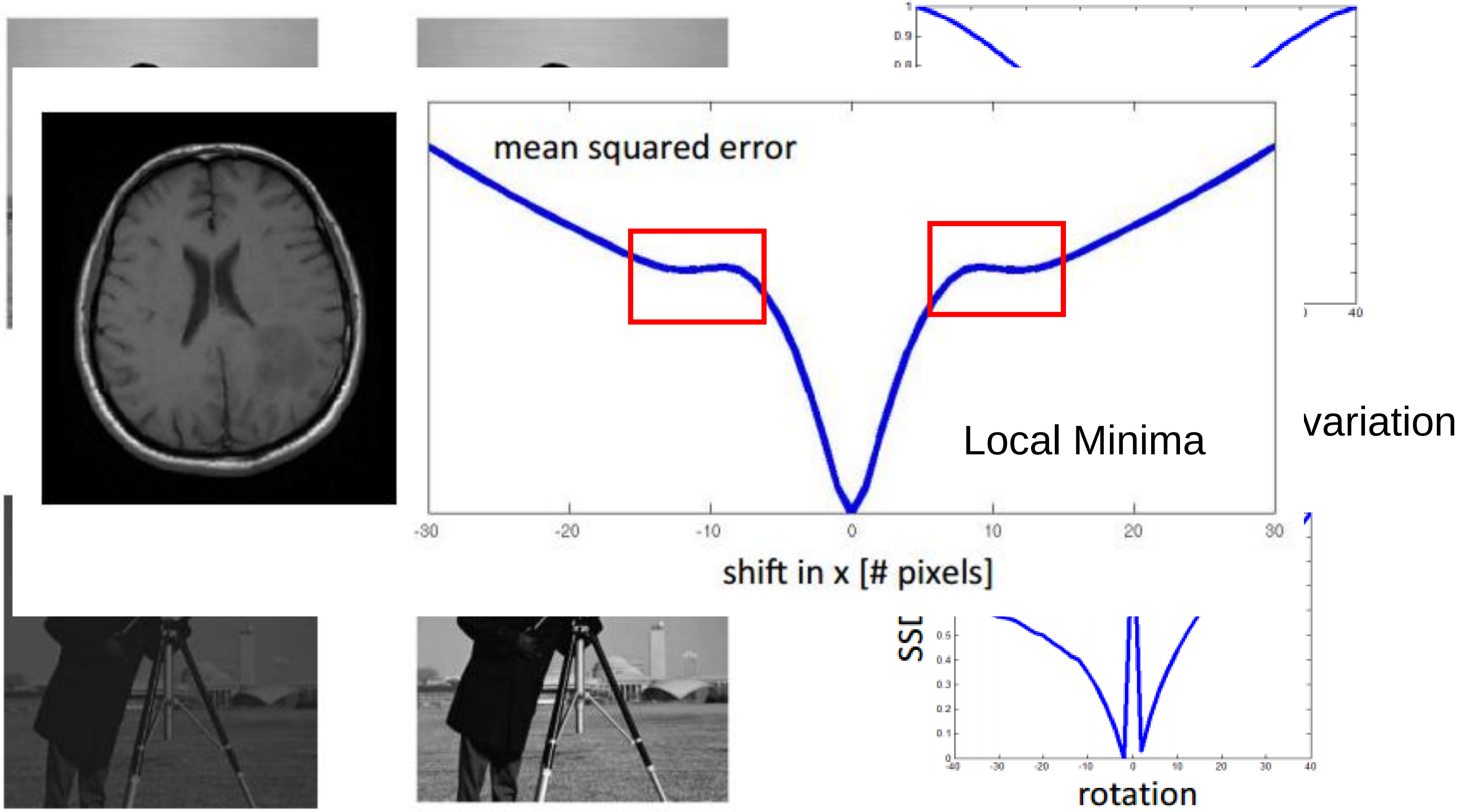
Monomodal Similarity Measures – SSD , SAD





- Can be used for registering CT to CT or MR to MR.

Understanding behaviour of SSD



Problem: Understanding SAD Similarity Function Behaviour

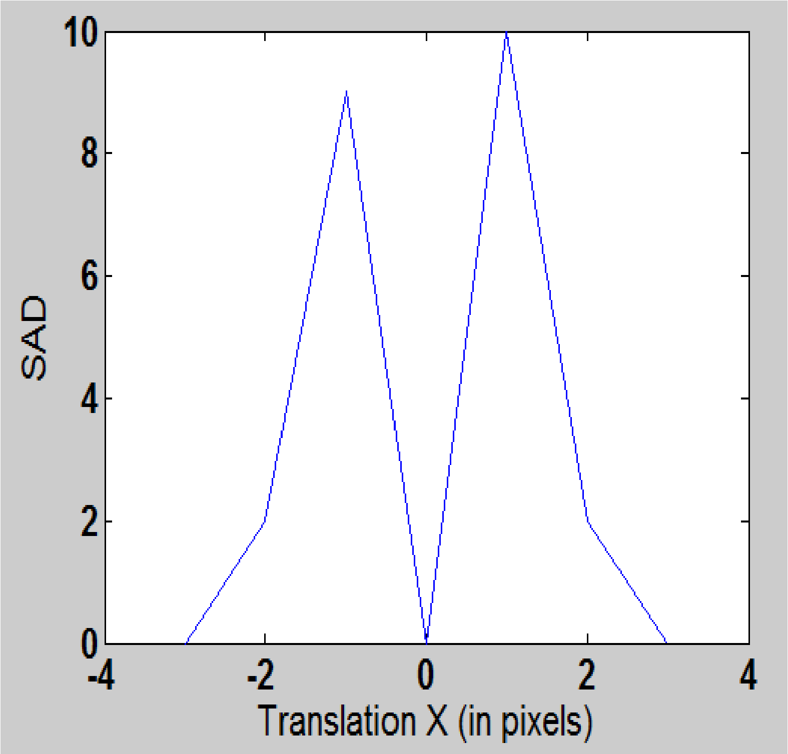
- Given an Target image I =

0	1	0
2	4	0
0	1	0

- **Task 1:** Plot the SAD similarity function plot for X-translation of -2 to + 2 pixels. Zero Pad if necessary. Perform Nearest Neighbour Interpolation if necessary.

- **Task 2:** Under a different scanner, the image illumination is halved. Perform similar SSD similarity function plot and investigate whether SAD is suitable for such scenarios? What should be the steps to overcome this?

Problem: Understanding SAD Similarity Function Behaviour



Task 1

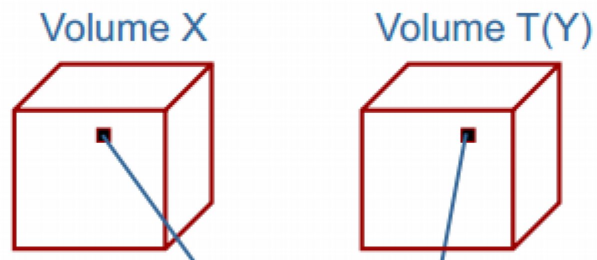
0	1	0
2	4	0
0	1	0

0	0.5	0
1	2	0
0	0.5	0

Task 2 is take home.

Monomodal Similarity Measures

- SSD, SAD are prone to errors when illumination changes, we need a measure which takes this into account.
- Normalized Cross Correlation – looser dependence on intensities.



σ_x : Standard deviation

$\bar{x}$: Mean

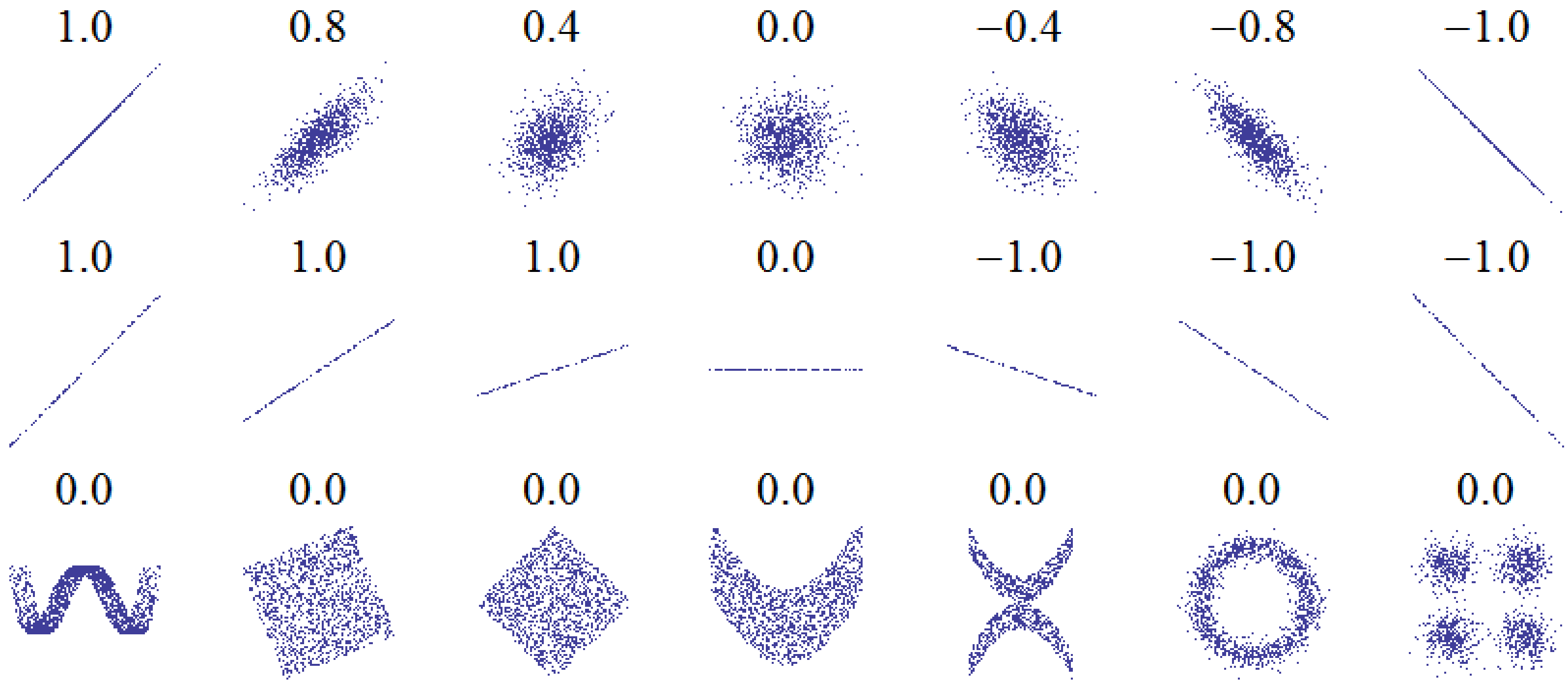
N : Number of pixels

$$NCC = \frac{1}{N}\sum_i \frac{(x_i - \bar{x})(y_i - \bar{y})}{\sigma_x \sigma_y}$$

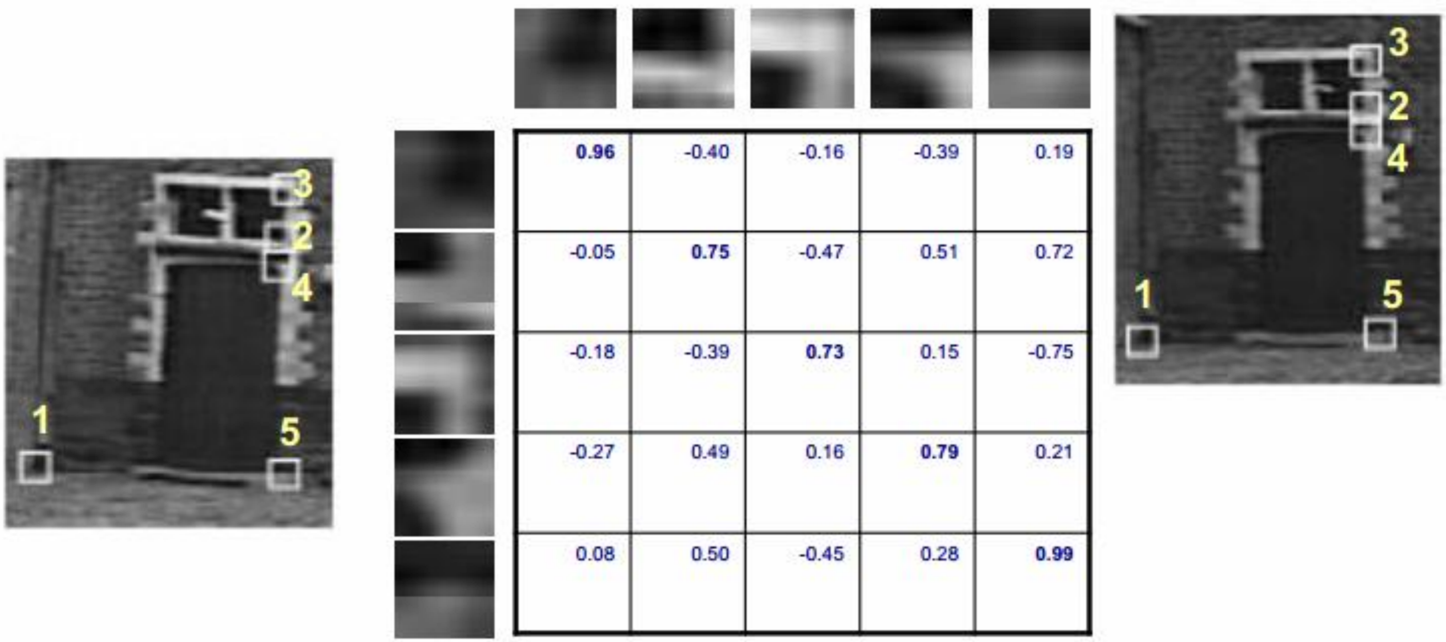
Normalized Cross Correlation:
Expresses the linear relationship between voxel intensities in the two volumes

NCC can be used
for multimodal registration too.

Behaviour of NCC Similarity Function



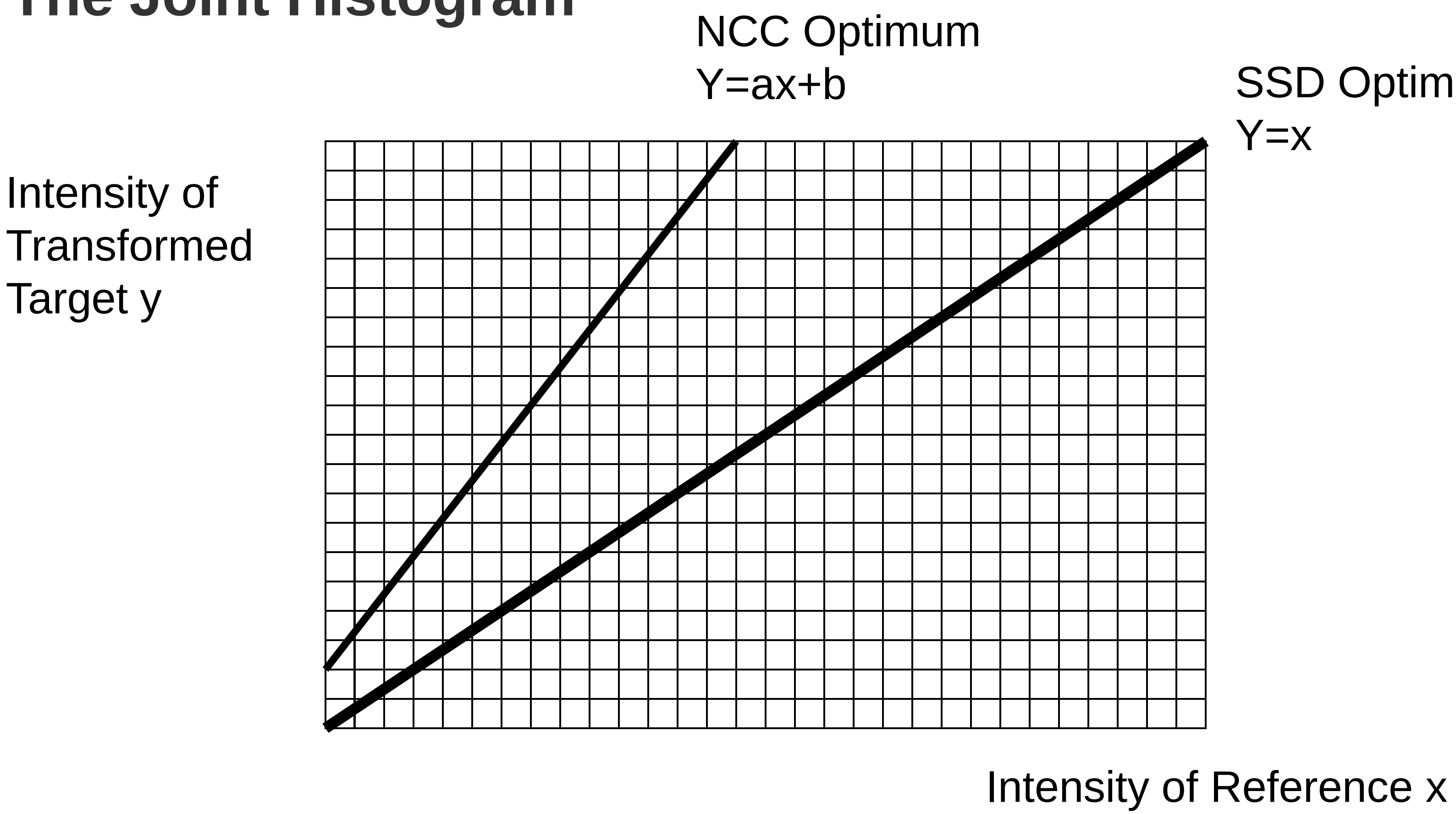
Behaviour of NCC:



0.96	-0.40	-0.16	-0.39	0.19
-0.05	**0.75**	-0.47	0.51	0.72
-0.18	-0.39	**0.73**	0.15	-0.75
-0.27	0.49	0.16	**0.79**	0.21
0.08	0.50	-0.45	0.28	**0.99**

Gives satisfying results
(for small image motions)

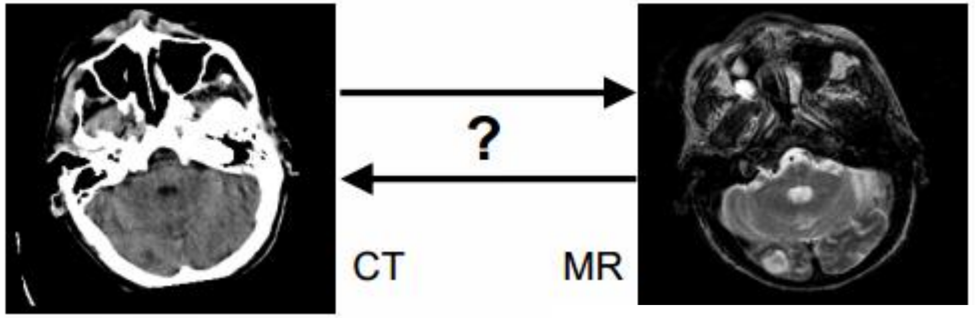
The Joint Histogram



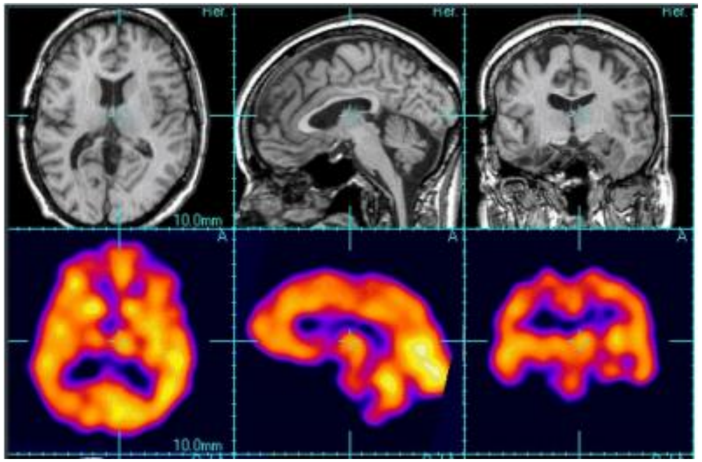
Multi-modal Image Registration

- More complex intensity relationships, so direct application of SSD or SAD would not work.

Computed tomography (CT), shows bony structures – very accurate



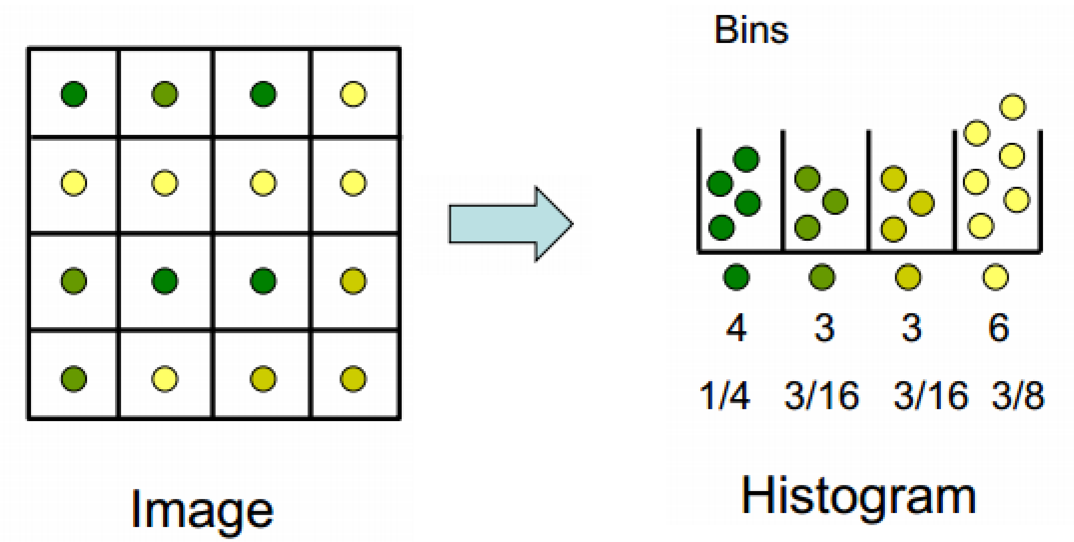
MRI image volume: soft tissue – show presence of a tumour

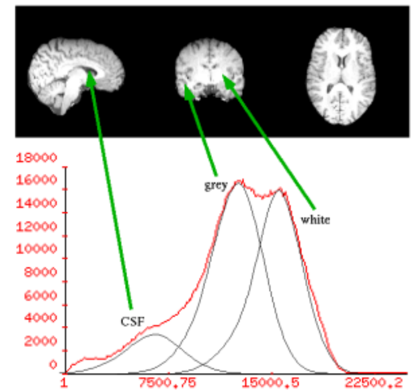


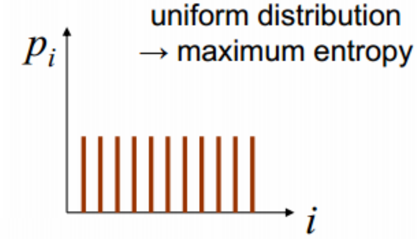
SPECT – MR Registration:
Patient oriented differently in different scanner systems.
Not easy to find landmarks.
NCC would not work in this case.

Information Theoretic Approach towards Registration

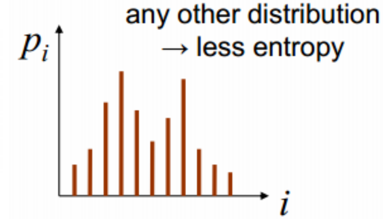
Constructing Image Histograms: Treat image intensities as random variables.



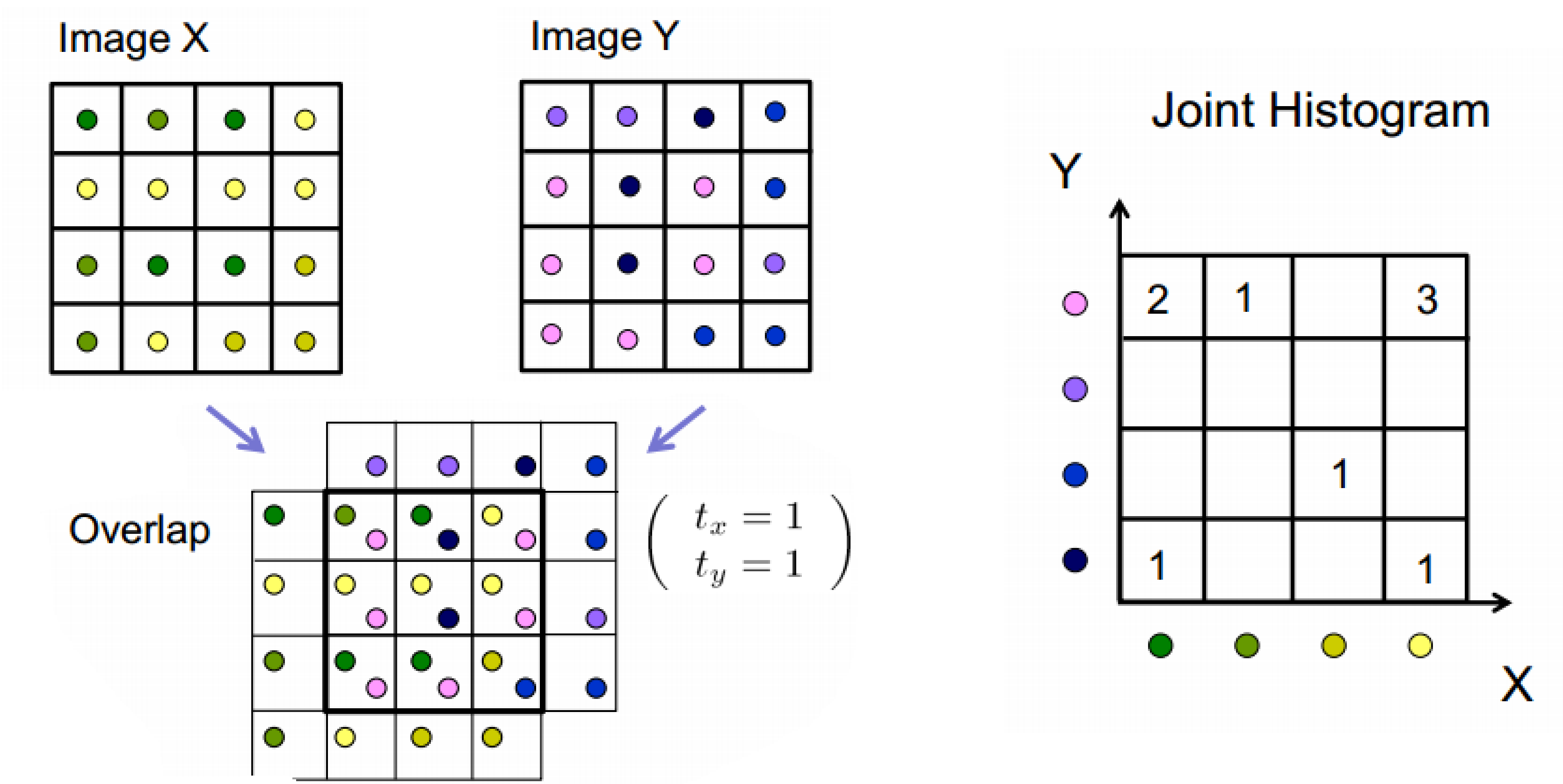




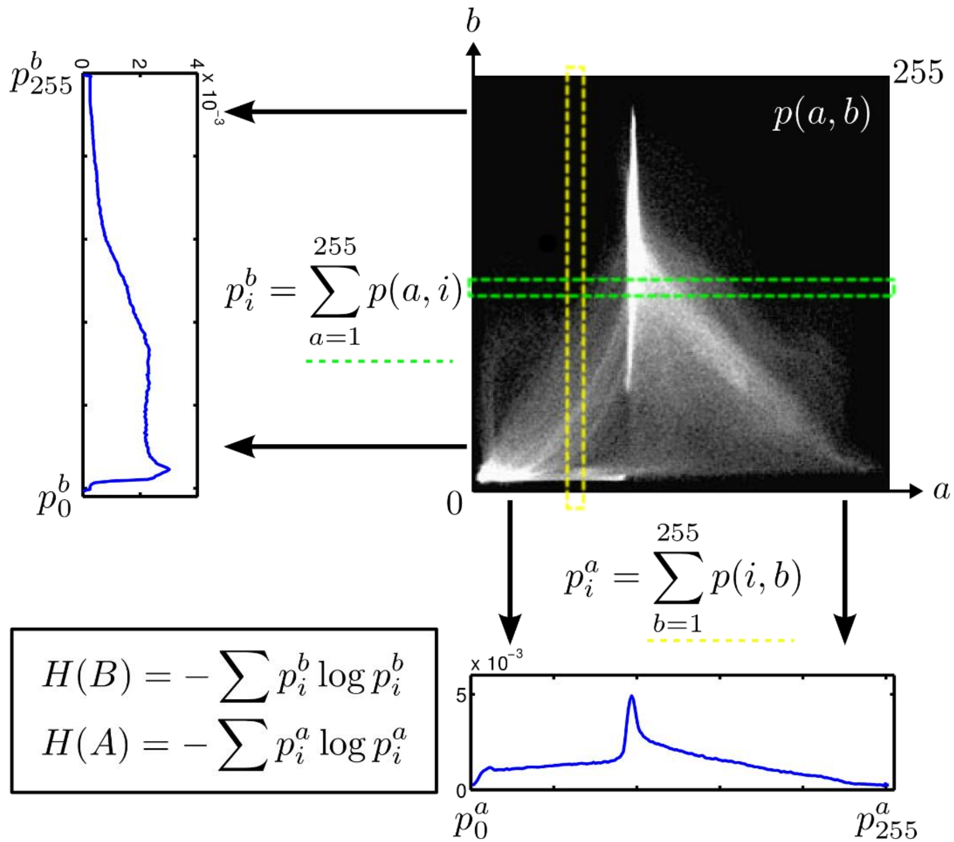
Entropy of Histogram: $$H = -\sum_i p_i \log p_i$$



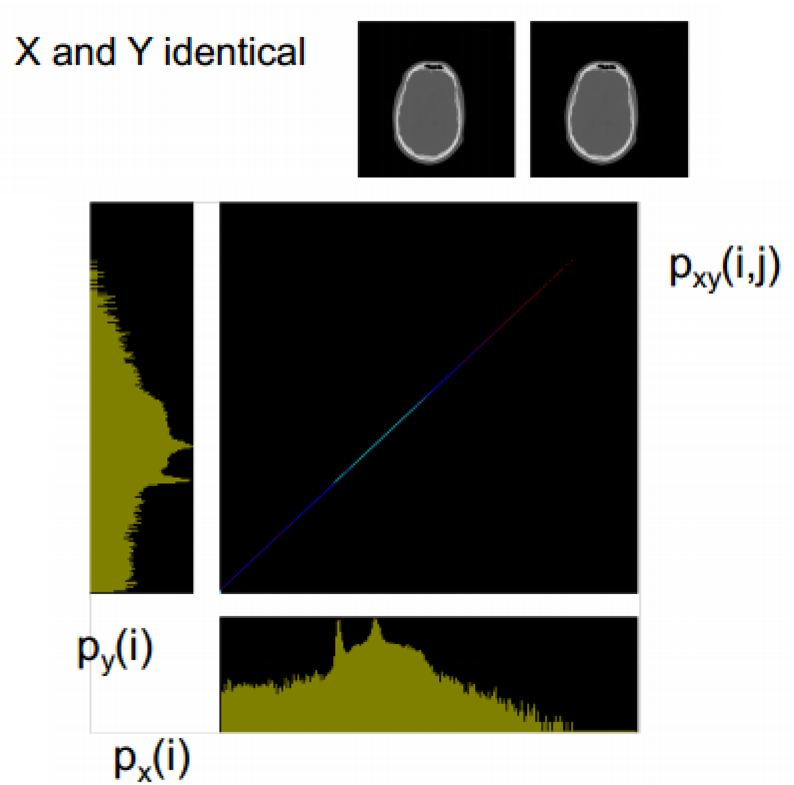
Joint Histogram

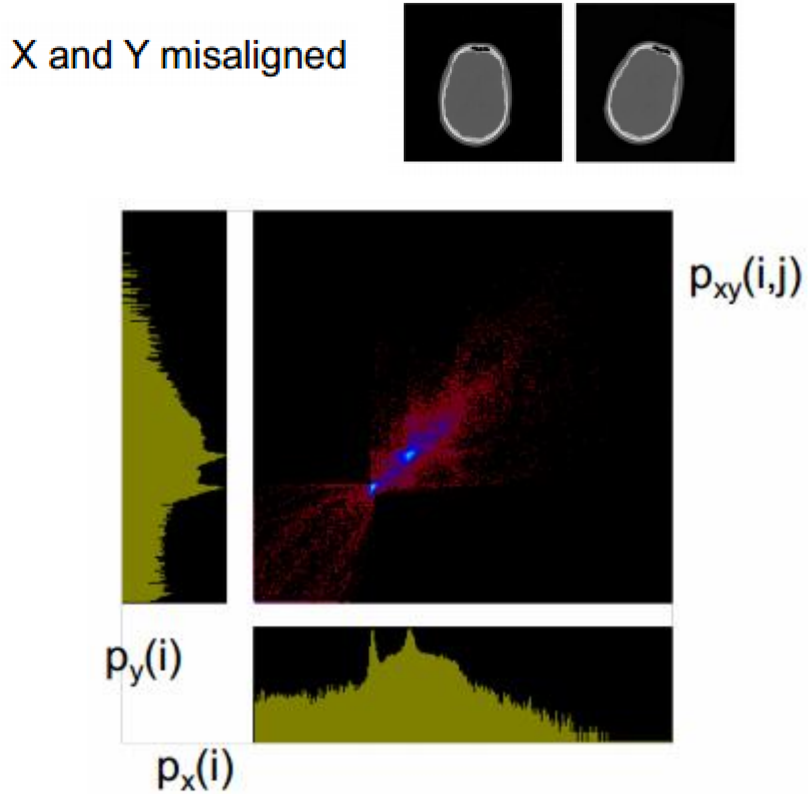


Joint Histogram



Lets see Joint Histogram Construction:

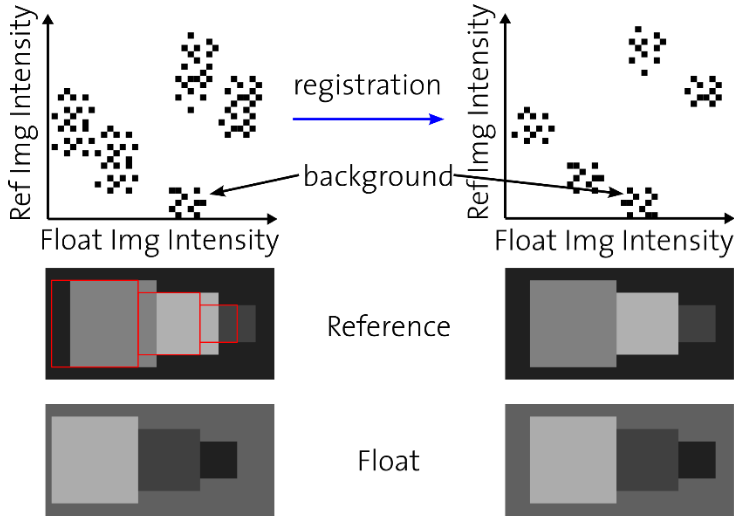


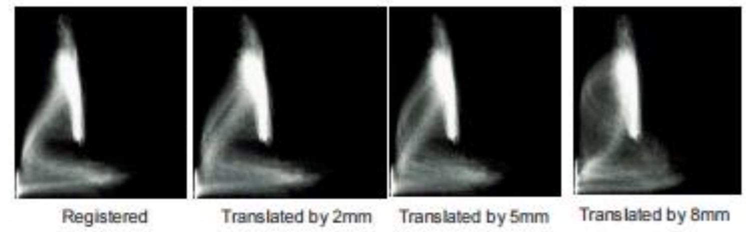


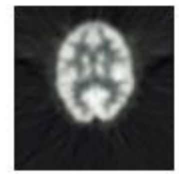
$$p(a,b) = \frac{1}{N} h(a,b)$$

The PDF $p(a,b)$ represents the probability of the pixel pair with intensities a and b to occur in the two images.

Joint Histogram for Multimodal Images







We observe that histogram sharpness can be used as a measure for alignment.

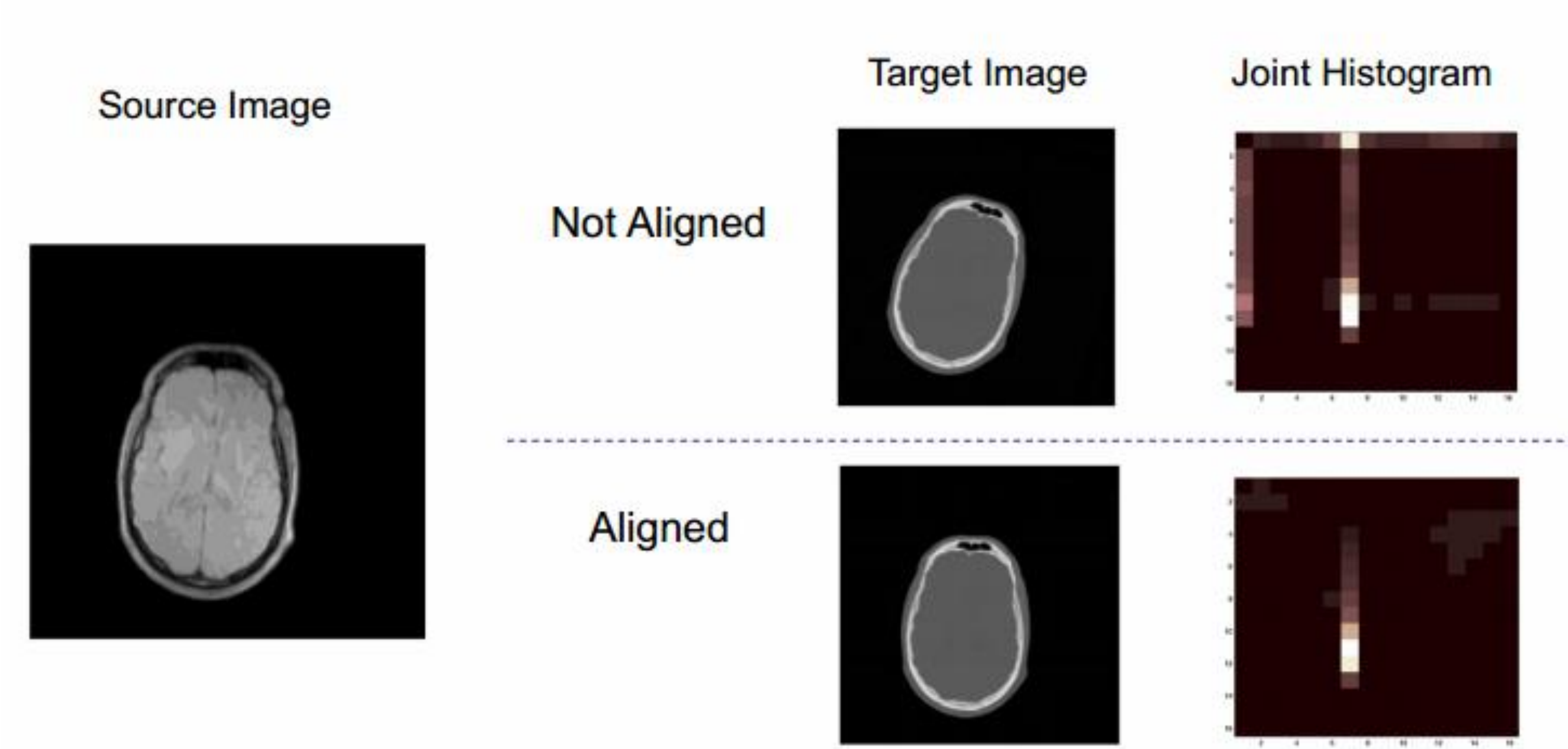
How do we characterize it?

The structure of the joint histogram has to be characterized.
We can use: Joint Shannon Entropy.
Joint Shannon entropy reaches an optimum at highly structured (clustered) histogram.

$$H(A,B) = -\sum_a \sum_b p(a,b) \log p(a,b)$$

Interpretation Entropy of Joint Histogram

$p(a,b)$ **mis-**

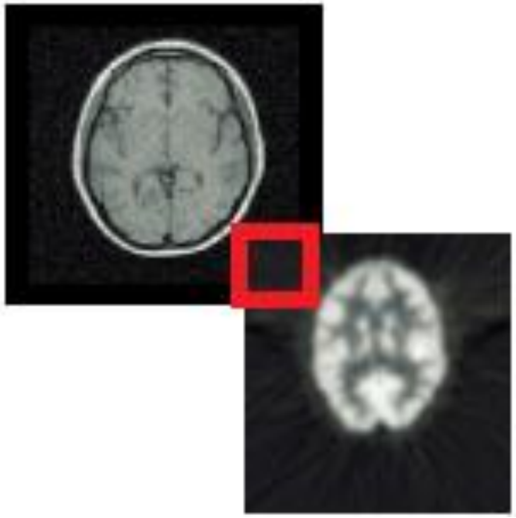


a

Overlap Problem with Joint Entropy

- Joint entropy is calculated in overlapping portions of the image. Consider a case like shown alongside (Air overlaps).
- Joint entropy reaches a maximum and optimisation will be struck at a local optima.
- A registration algorithm that minimises the ***joint entropy*** will thus tend to maximise the amount of air and not necessarily register.
- What is the solution?

- Use Mutual Information instead.



Mutual Information and Normalized MI

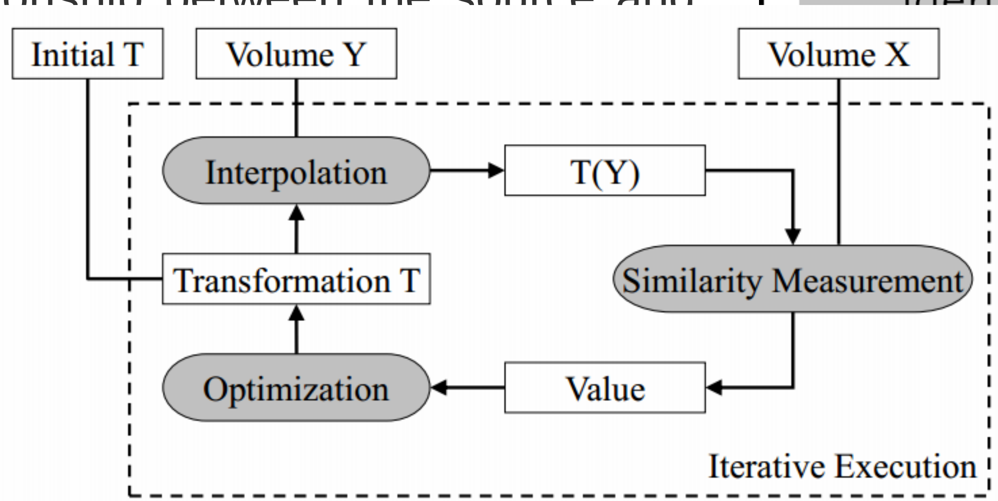
$$\begin{aligned} I(A,B) &= H(A) + H(B) - H(A,B) \\ &= \sum_a \sum_b p(a,b) \log \frac{p(a,b)}{p(a)p(b)} \end{aligned}$$

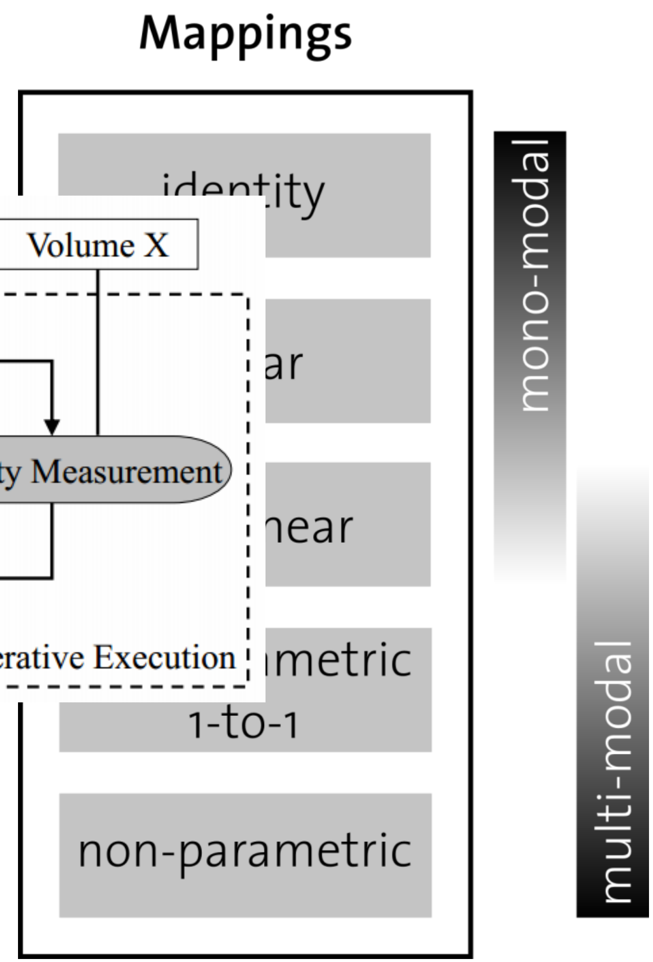
- In ***maximising MI*** we seek for solutions that have ***high marginal entropies*** and a ***low joint entropy***
- ***MI*** is maximised at the optimal alignment and can be thought of as ***a measure*** of ***how well one image explains the other.***
- ***MI*** still has the influence of overlap. To further reduce it, we may use, normalized mutual information.

$$Y(A,B) = \frac{H(A) + H(B)}{H(A,B)}$$

Choosing Similarity Measure

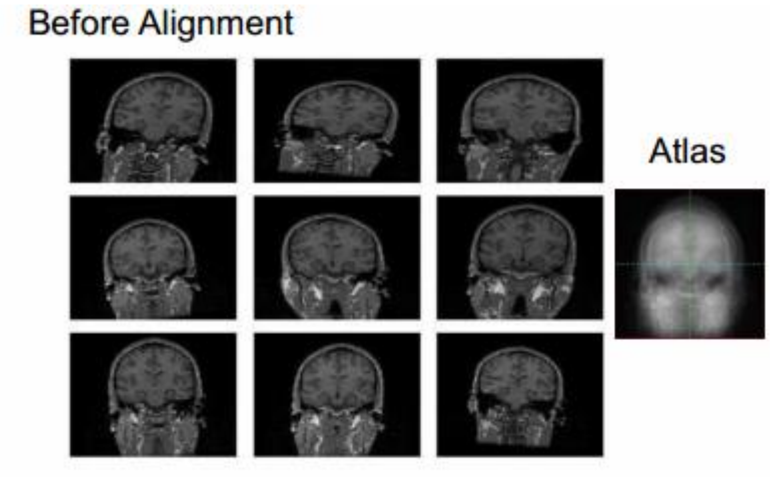
- Similarity measures differ in the assumed intensity relationship between the source and the floating im
- The best crite of the data bei
- Questions to a
  - How differe
  - Which con Statistics et
  - How much
- Looking back:

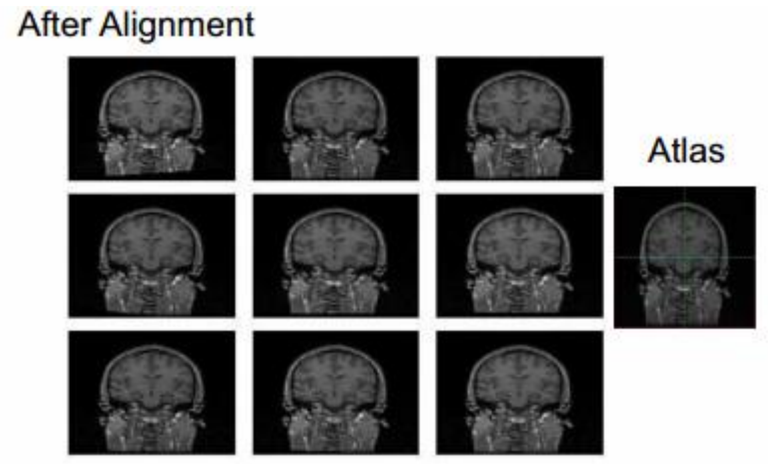




Pairwise and Group-wise Registration

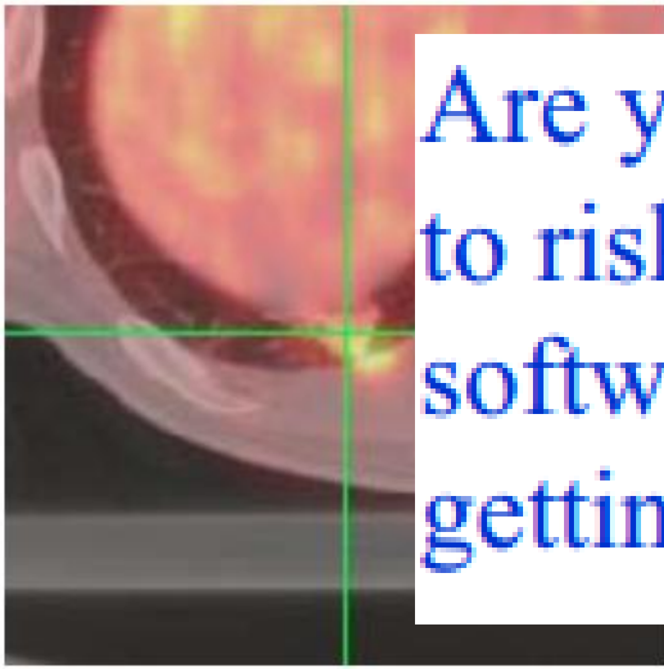
- Depending on the number of images being registered.
- Pairwise: Aligning 2 images.
- Group-wise: Multiple Images. Used for Mosaicking, Population Studies, Atlas Construction.





Courtesy: Christian Wachinger

Limitations of Rigid Registration



Are you prepared to risk your software against getting sued?

Is the tumour in the lungs or the stomach?

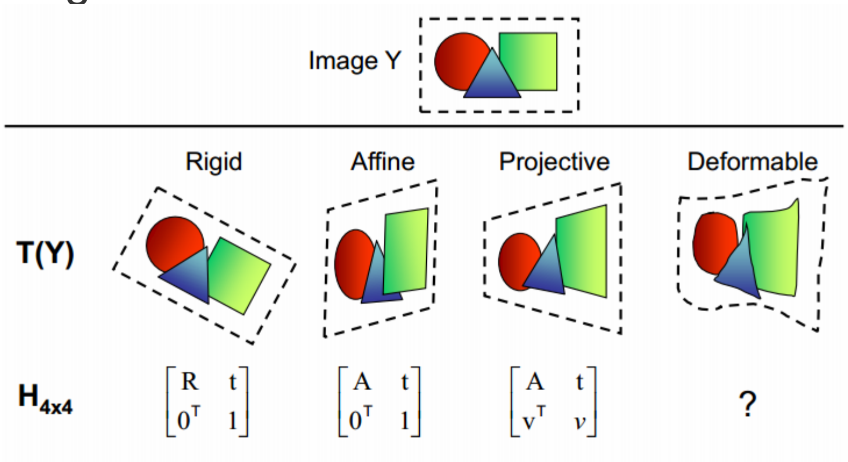
Looks plausible; but how could you be sure?

Courtesy: Michael Brady

Non-Rigid Transformation Model

- Needed for inter-subject registration and distortion correction

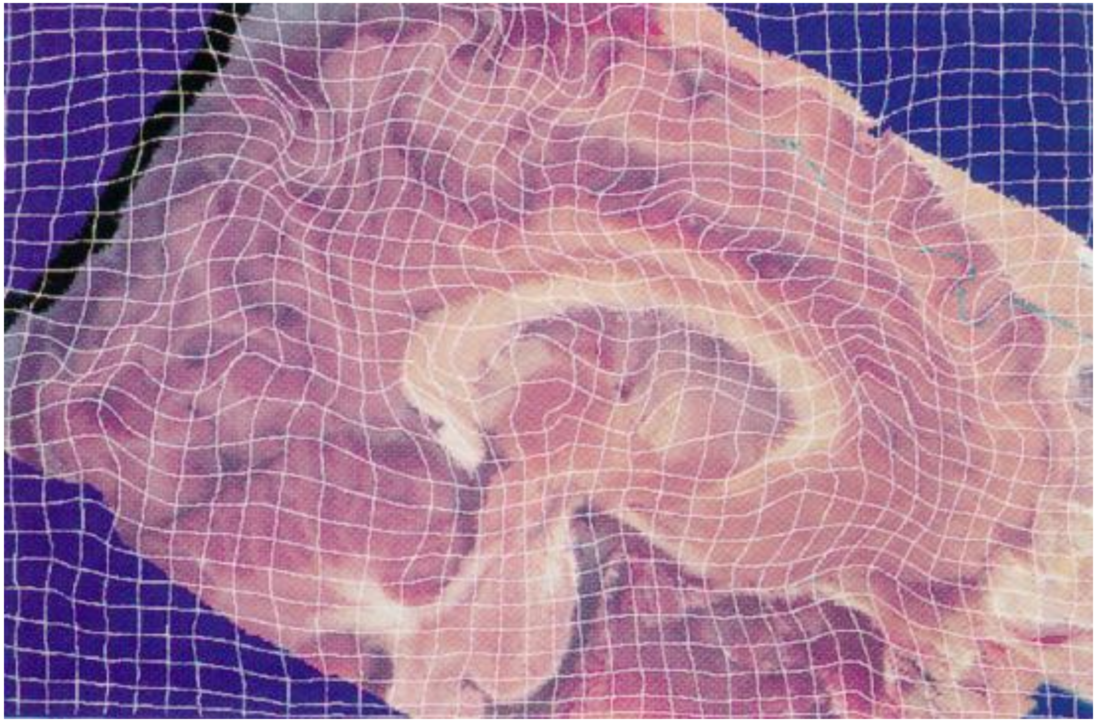
Rigid has only 6 DOF—three shifts and three angles



Important non-rigid transformations

- Similarity: 7 DOF
- Affine: 12 DOF
- Curved: Typically DOF = 100 to 1000.
- Non-linear i.e. no matrix representation
- Many Different Parameterizations e.g.
  - General diffeomorphisms (e.g. fluid models)
  - Spline parameterizations (b-splines, thin-plate splines)
  - Fourier parameterizations (e.g. SPM)

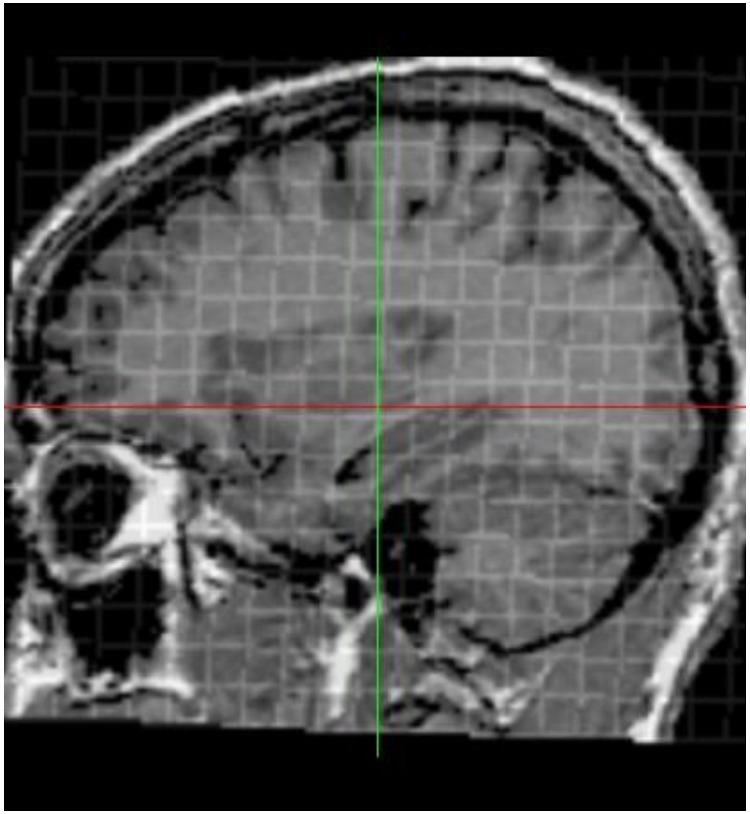
Nonrigid Transformations can be very complex!



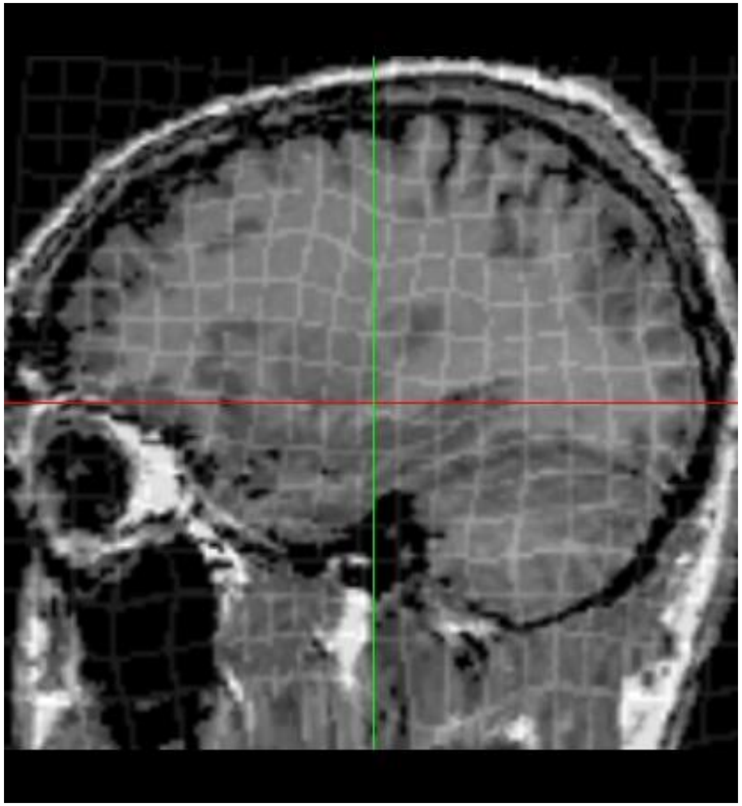
[Thompson, 1996]

Courtesy: Xenious Papademetris

Affine vs Non-Rigid – A Look at the transformation



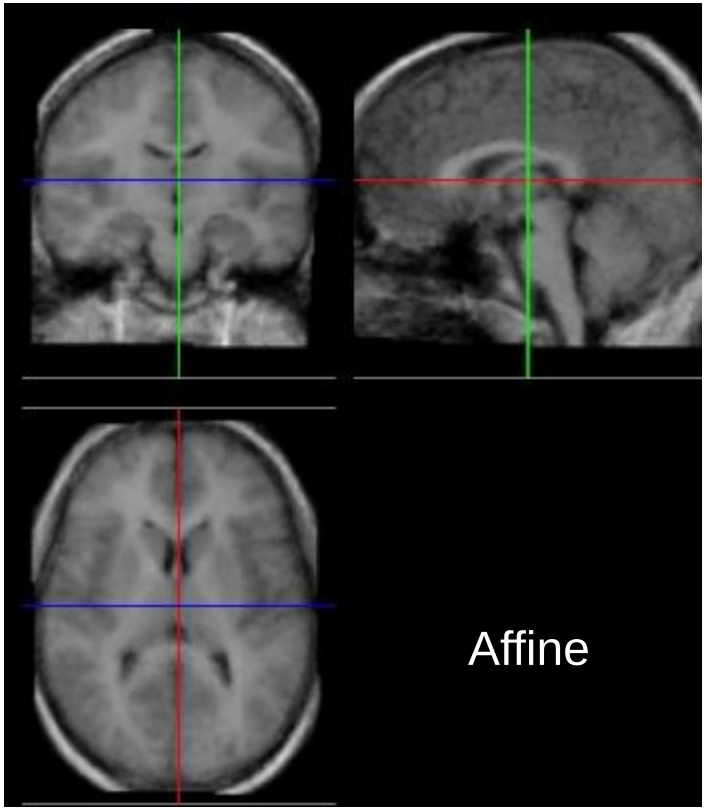
Affine – 12 parameters

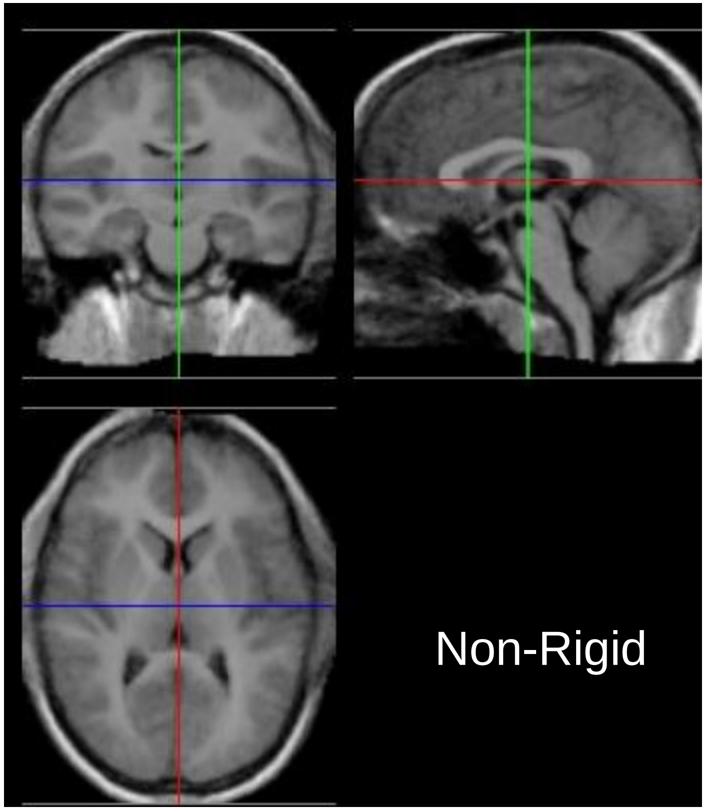


Non-Rigid ~ 2000 parameters

Courtesy: Xenious Papademetris

Affine vs Non-Rigid

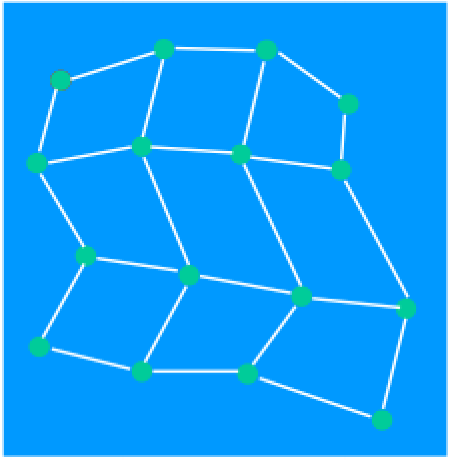




Average Anatomical Images from 10 Subjects displayed at 1.5x1.5x1.5 mm

Courtesy: Xenious Papademetris

Where to use Non Rigid Deformation?



Non-rigid transformations:
- Tissue motion (cardiac cycle/respiratory motion)
- Deformation compensation (intra-operative, soft tissue)
- Longitudinal tissue changes (e.g., tumor growth)
- Inter-subject registration

Courtesy: Niels Chr. Overgaard

Other Interesting Topics In Registration:

- **Non rigid Image Registration**

McInerney, T., & Terzopoulos, D. (1996). Deformable models in medical image analysis: a survey. *Medical image analysis*, *1*(2), 91-108.

Sotiras, A., Davatzikos, C., & Paragios, N. (2013). Deformable medical image registration: A survey. *Medical Imaging, IEEE Transactions on*, *32*(7), 1153-1190.

- **Regularization**

Fischer, B., & Modersitzki, J. (2003). Curvature based image registration.*Journal of Mathematical Imaging and Vision*, *18*(1), 81-85.

Sorzano, C. O., Thévenaz, P., & Unser, M. (2005). Elastic registration of biological images using vector-spline regularization. *Biomedical Engineering, IEEE Transactions on*, *52*(4), 652-663.

- **Optimization in Registration**

Klein, S., Staring, M., & Pluim, J. P. (2007). Evaluation of optimization methods for nonrigid medical image registration using mutual information and B-splines. *Image Processing, IEEE Transactions on*, *16*(12), 2879-2890.

- **Image Interpolation**

Lehmann, T. M., Gonner, C., & Spitzer, K. (1999). Survey: Interpolation methods in medical image processing. *Medical Imaging, IEEE Transactions on*, *18*(11), 1049-1075.

- **Modality Invariance in Registration**

Wachinger, C., & Navab, N. (2012). Entropy and Laplacian images: Structural representations for multi-modal registration. *Medical Image Analysis*, *16*(1), 1-17.

Heinrich, M. P., Jenkinson, M., Bhushan, M., Matin, T., Gleeson, F. V., Brady, M., & Schnabel, J. A. (2012). MIND: Modality independent neighbourhood descriptor for multi-modal deformable registration. *Medical Image Analysis*,*16*(7), 1423-1435.