# Image Registration in Medical Imaging

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## Medical Image Analysis

- Large collection of research fields:
  - developing mathematical algorithms to extract and relate information from medical images
  - For clinical and basic science research
- No “Physics of Medical Image Analysis”
  - Groups of suitable algorithms and mathematical approaches to specific engineering problems
- Historically two key (and related) aspects of research:
  - Image Registration:
    - finding spatial/temporal correspondences between image data and/or models
  - Image Segmentation
    - Extracting/detecting specific features of interest from image data
- Many clinical motivations:
  - one of the key areas has been brain imaging, but many more!



## Medical Image Registration: Overview

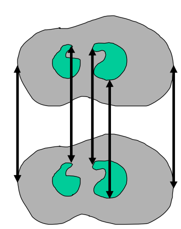
- What is Registration?
  - Definitions
  - Classifications: Geometry, Transformations, Measures
- Motivation for work: Medical Image mis-registration
  - Where is image registration used in medicine and biomedical research?
- Measures of Image Alignment:
  - Landmark/Feature Based Methods
  - Voxel Based Methods:
    - Image Intensity Difference and Correlation
    - Multi-Modality Measures



## Registration

**“the determination of a one-to-one mapping between the coordinates in one space and those in another, such that points in the two spaces that correspond to the same anatomical point are mapped to each other.”**

**Calvin Maurer ‘93**

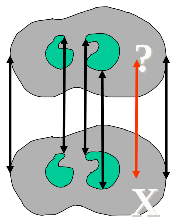


## Image Registration

**"Establishing correspondence, between features**

**in sets of images, and**

**using a transformation model to infer correspondence away from those features."**




**Bill Crum '05**

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## Key Applications I:Change detection

- Look for differences in the same type of images
  Taken at different times, e.g.:
  - Mapping Pre and post contrast agent
    - Digital Subtraction Angiography (DSA)
    - MRI with Gadolinium tracer
  - Mapping Structural Changes
    - Different stages in tumor growth (Before and After treatment)
    - Neuro degenerative disease-> Quantifying tissue loss patterns
  - Detecting Changes due to function
    - Functional MRI (fMRI) Before and After brain stimulus
    - PET imaging: Quantitative tracer uptake measurements
- Problem:
  - Subject scanned multiple times -> removed from scanner
  - We cannot easily fix/know patient location and orientation with respect to imaging system
  - Need to remove differences in patient positioning to detect true differences in patient images

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## Key Applications II:Image Fusion

- Relate contrasting information
  from different types of images
- Multi-Modality Imaging
  - MRI-CT
  - MRI-PET/SPECT
  - structural MRI- functional MRI
  - structural MRI to structural MRI
- Problem:
  - Subject scanned multiple times -> Different scanners
  - We cannot easily fix/know patient location and orientation with respect to different imaging systems
  - Need to remove differences in patient positioning to relate information from different types of images

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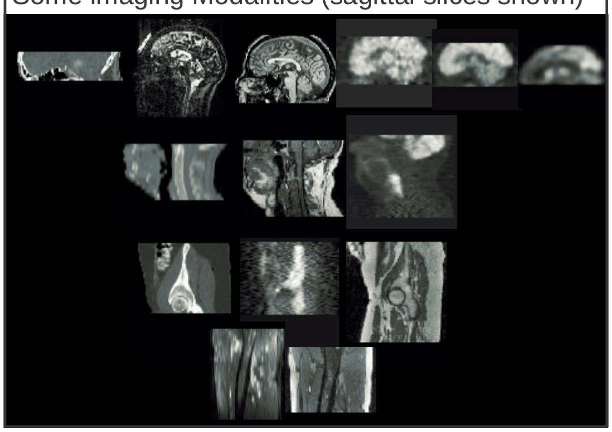
## Some imaging Modalities (sagittal slices shown)

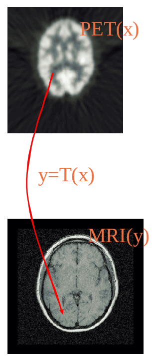


## Components of Image Registration Algorithms

- –Image Data Geometries
  - •2D-2D, 2D-3D, 3D-3D
- •Transformation Type
  - •Rigid/Affine/Non-Rigid

- •Correspondence Criteria/Measure
  - •Feature Based Methods
  - •Voxel Based/Dense Field Methods

- •Optimization Method :
  maximizing/minimizing criteria wrt T()






## Examples of Image Geometries and Transformation Models in Medical Applications



## 2D-2D Inter Modality Image Registration Problem

*Registration and display of the combined bone scan and radiograph in the diagnosis and management of wrist injuries* Hawkes et al, EJNM 1991

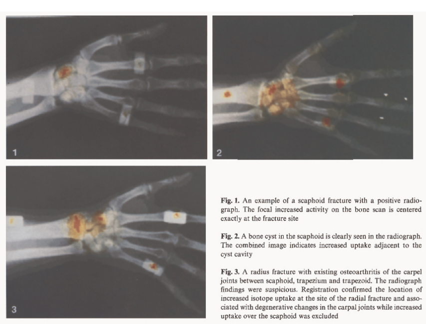


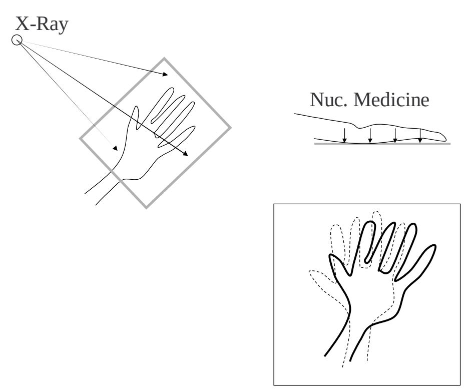
**Fig. 1.** An example of a scaphoid fracture with a positive radiograph. The focal increased activity on the bone scan is centered exactly at the fracture site

**Fig. 2.** A bone cyst in the scaphoid is clearly seen in the radiograph. The combined image indicates increased uptake adjacent to the cyst cavity

**Fig. 3.** A radius fracture with existing osteoarthritis of the carpel joints between scaphoid, trapezium and trapezoid. The radiograph findings were suspicious. Registration confirmed the location of increased isotope uptake at the site of the radial fracture and associated with degenerative changes in the carpal joints while increased uptake over the scaphoid was excluded

Technetium 99m and X-ray radiograph





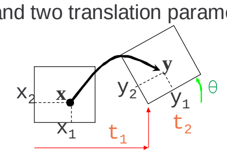
## 2D-2D image transformations

–Simple Case: parallel projection

2 translation (up-down/left-right) and one rotation

e.g. Hand radiographs

Rigid 2D transformation controlled by a rotation θ and two translation parameters t1 and t2:




This is a Linear mapping from $(x_1, x_2)$ to $(y_1, y_2)$

$y_1= \cos\theta . x_1 - \sin\theta . x_2 + t_1$

$y_2= \sin\theta . x_1 + \cos\theta . x_2 + t_2$



## 2D-2D image transformations

$y_1= \cos\theta . x_1 - \sin\theta . x_2 + t_1$

$y_2= \sin\theta . x_1 + \cos\theta . x_2 + t_2$

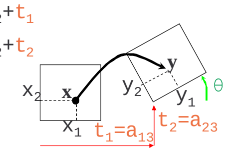
$\downarrow$

$y_1=a_{11}.x_1+a_{12}.x_2+a_{13}$

$y_2=a_{21}.x_1+a_{22}.x_2+a_{23}$

$\downarrow$

$$\begin{bmatrix} y_1 \\ y_2 \\ 1 \end{bmatrix} = \begin{bmatrix} a_{11} & a_{12} & a_{13} \\ a_{21} & a_{22} & a_{23} \\ 0 & 0 & 1 \end{bmatrix} \begin{bmatrix} x_1 \\ x_2 \\ 1 \end{bmatrix}$$




**y=Ax**

Matrix form:

extend to 3x3 Matrix

*Homogeneous coordinate Transformation*

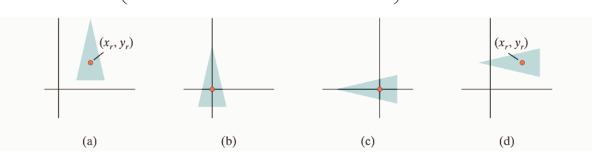


## Rotating around a given location

$$T(x,y)\cdot R(\theta)\cdot T(-x,-y)$$

$$= \begin{pmatrix} 1 & 0 & x \\ 0 & 1 & y \\ 0 & 0 & 1 \end{pmatrix} \cdot \begin{pmatrix} \cos\theta & -\sin\theta & 0 \\ \sin\theta & \cos\theta & 0 \\ 0 & 0 & 1 \end{pmatrix} \cdot \begin{pmatrix} 1 & 0 & -x \\ 0 & 1 & -y \\ 0 & 0 & 1 \end{pmatrix}$$

$$= \begin{pmatrix} \cos\theta & -\sin\theta & x(1-\cos\theta)+y\sin\theta \\ \sin\theta & \cos\theta & y(1-\cos\theta)-x\sin\theta \\ 0 & 0 & 1 \end{pmatrix}$$





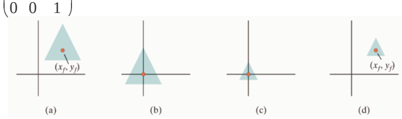

## Image Scaling

- Scaling with respect to a fixed point (x,y)

$$T(x,y)\cdot S(s_x,s_y)\cdot T(-x,-y)$$

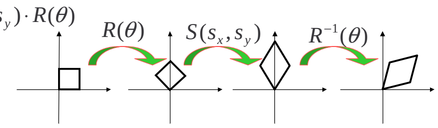
$$= \begin{pmatrix} 1 & 0 & x \\ 0 & 1 & y \\ 0 & 0 & 1 \end{pmatrix} \cdot \begin{pmatrix} s_x & 0 & 0 \\ 0 & s_y & 0 \\ 0 & 0 & 1 \end{pmatrix} \cdot \begin{pmatrix} 1 & 0 & -x \\ 0 & 1 & -y \\ 0 & 0 & 1 \end{pmatrix}$$

$$= \begin{pmatrix} s_x & 0 & (1-s_x)\cdot x \\ 0 & s_y & (1-s_y)\cdot y \\ 0 & 0 & 1 \end{pmatrix}$$




- Scaling Along an Arbitrary Axis:

$$R^{-1}(\theta)\cdot S(s_x,s_y)\cdot R(\theta)$$



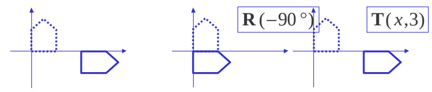
## Influence of Affine Transformations on Images

- Map ***lines*** to ***lines***
- Map ***parallel lines*** to ***parallel lines***
- Preserve ***ratios of distance*** along a line
- Do NOT preserve absolute distances and angles



## Composing Transformations:

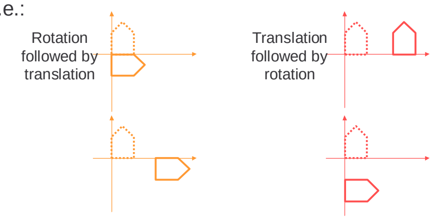
- To Apply: We need to COMPOSE:




- But: Matrix multiplication is not commutative

$$\mathbf{T}(x,3)\cdot\mathbf{R}(-90°)\neq\mathbf{R}(-90°)\mathbf{T}(x,3)$$

- i.e.:






## 2D-3D registration problems

•**Radiotherapy:**
- •**Treatment verification (Portal images)**
- •**Treatment planning (simulator images)**
- •**Treatment guidance (Cyberknife system)**

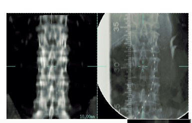
• **Orthopaedic Surgery**
- •**Spinal surgery (Brain Lab, Medtronic)**
- •**Hip or Knee Arthroplasty (ROBODOC)**
  - •**Verification of implant position**

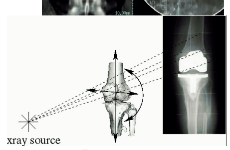
•**Neurointerventions**
- •**Matching MRA to DSA**

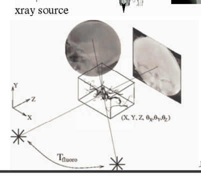
•**Surgical Microscope**
- •**MRI/CT neurosurgery guidance**

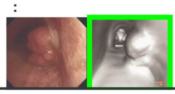
•**Virtual Endoscopy**

:





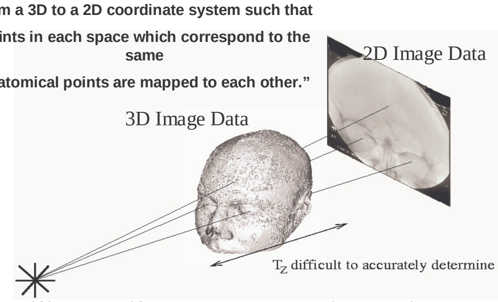







## 2D-3D Registration Geometry

**"the determination of a projection mapping, from a 3D to a 2D coordinate system such that points in each space which correspond to the same anatomical points are mapped to each other."**



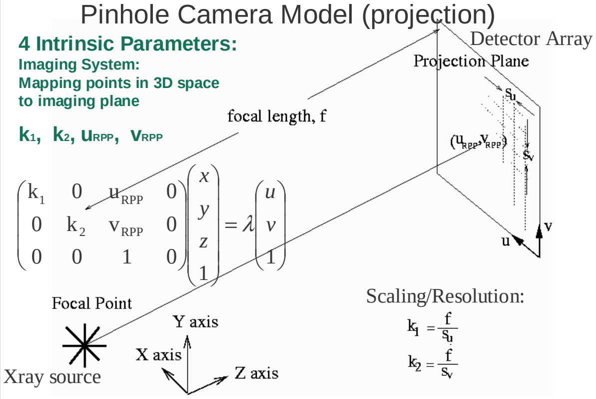

•(A) Imaging/Acquisition Parameters ( intrinsic )
•(B) Subject Parameters (extrinsic)

## 2D-3D Acquisition parameters: Pinhole Camera Model (projection)

**4 Intrinsic Parameters:**

**Imaging System:**
**Mapping points in 3D space to imaging plane**

**$k_1$, $k_2$, $u_{RPP}$, $v_{RPP}$**




$$\begin{pmatrix} k_1 & 0 & u_{RPP} & 0 \\ 0 & k_2 & v_{RPP} & 0 \\ 0 & 0 & 1 & 0 \end{pmatrix} \begin{pmatrix} x \\ y \\ z \\ 1 \end{pmatrix} = \lambda \begin{pmatrix} u \\ v \\ 1 \end{pmatrix}$$

$$k_1 = \frac{f}{s_u} \qquad k_2 = \frac{f}{s_v}$$

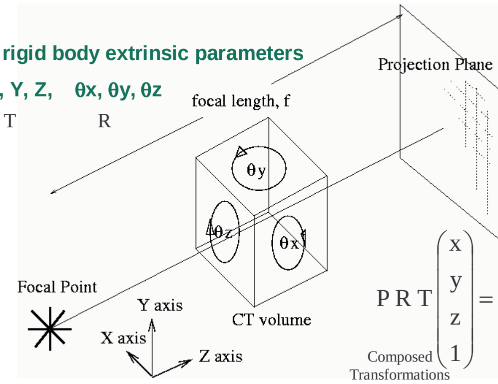


## 2D-3D: Subject (extrinsic) parameters

**6 rigid body extrinsic parameters**

**X, Y, Z, θx, θy, θz**

T R




$$P\,R\,T \begin{pmatrix} x \\ y \\ z \\ 1 \end{pmatrix} = \lambda \begin{pmatrix} u \\ v \\ 1 \end{pmatrix}$$



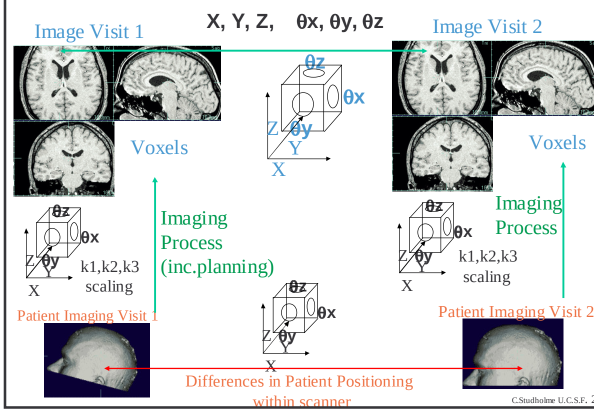
## 3D to 3D image registration

- Many different 3D clinical imaging modalities
  - MRI probably still the least common
- Images used in many different clinical settings
  - diagnosis
  - treatment planning
  - treatment guidance
  - clinical research: studying disease
- Transformation types:
  - Rigid positioning of subject: still most common
  - Non rigid deformations to describe
    - tissue deformation
    - imaging distortion
    - differences between subjects



## 3D-3D Registration

**X, Y, Z, θx, θy, θz**



## 3D Rigid Transformations

3 Translations x,y,z

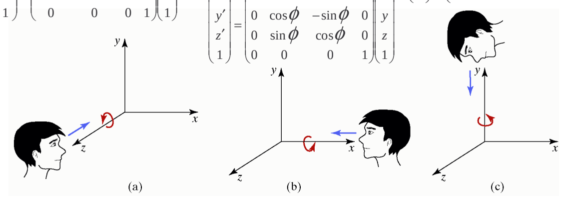
3 Rotations:

$$T(\mathbf{p}) = \begin{pmatrix} \mathbf{M}_{3\times3} & \mathbf{T}_{3\times1} \\ 0 & 1 \end{pmatrix} \begin{pmatrix} \mathbf{p}_{3\times1} \\ 1 \end{pmatrix}$$

$$\begin{pmatrix} x' \\ y' \\ z' \\ 1 \end{pmatrix} = \begin{pmatrix} \cos\theta & -\sin\theta & 0 & 0 \\ \sin\theta & \cos\theta & 0 & 0 \\ 0 & 0 & 1 & 0 \\ 0 & 0 & 0 & 1 \end{pmatrix} \begin{pmatrix} x \\ y \\ z \\ 1 \end{pmatrix}$$

$$\begin{pmatrix} x' \\ y' \\ z' \\ 1 \end{pmatrix} = \begin{pmatrix} 1 & 0 & 0 & 0 \\ 0 & \cos\phi & -\sin\phi & 0 \\ 0 & \sin\phi & \cos\phi & 0 \\ 0 & 0 & 0 & 1 \end{pmatrix} \begin{pmatrix} x \\ y \\ z \\ 1 \end{pmatrix}$$

$$\begin{pmatrix} x' \\ y' \\ z' \\ 1 \end{pmatrix} = \begin{pmatrix} \cos\omega & 0 & -\sin\omega & 0 \\ 0 & 1 & 0 & 0 \\ \sin\omega & 0 & \cos\omega & 0 \\ 0 & 0 & 0 & 1 \end{pmatrix} \begin{pmatrix} x \\ y \\ z \\ 1 \end{pmatrix}$$




(a) (b) (c)



## Feature Based Registration

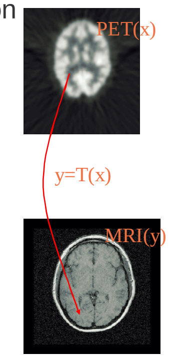
–Image Data Geometries
- •2D-2D, 2D-3D, 3D-3D

•Transformation Type
- •Rigid/Affine/Non-Rigid

•Correspondence Criteria/Measure
- •Feature Based Methods
- •Voxel Based/Dense Field Methods

•Optimization Method :
- Maximizing/minimizing Measure wrt T()

1. Extract Features From Images
2. Evaluate Physical Distance Between Features
3. Minimize Distance






## Feature Based Approaches

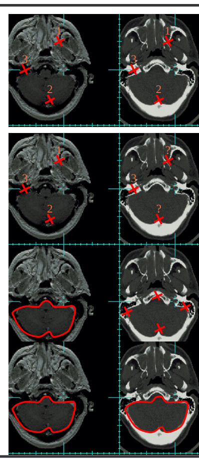
–Point set->Point set
(homologous)

–Point set->Point set
(non homologous..
so need to find order)

–Point set -> Surface

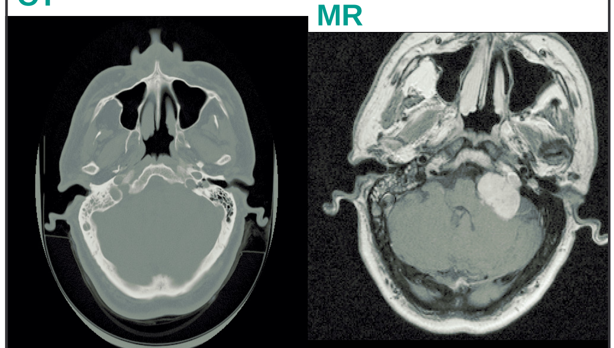
–Surface -> Surface

(also [space] Curve -> Surface)



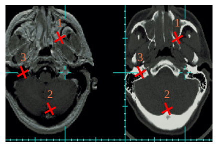


**CT** **MR**



M & UMDS

## MR-CT REGISTRATION



- Manual point landmark identification (around 12 points) in MR and CT
- Accuracy of 1mm at center, and around 2 mm at the edge
- Relates soft tissue structures such as enhancing tumor and blood flow to bone features in CT

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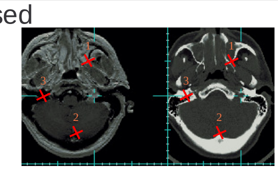
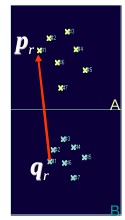
## Homologous Feature Based Alignment



•General case of two lists of *corresponding* feature locations
$[\boldsymbol{p}_1, \boldsymbol{p}_2 \ldots \boldsymbol{p}_N]$ and
$[\boldsymbol{q}_1, \boldsymbol{q}_2 \ldots \boldsymbol{q}_N]$
both with N points
•We want to Find:
Transformation $T(\boldsymbol{q})$ that Minimizes **squared distance** between corresponding points:

$$E= \sum_r ||\boldsymbol{p}_r - T(\boldsymbol{q}_r)||^2$$




•Where one set of points, q, is transformed by T()

-> Extrapolate Transformation for all image voxels/pixels

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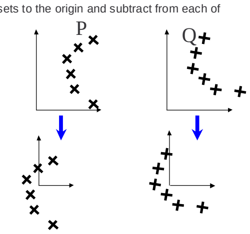
## Procrustes Point Alignment

[Golub&VanLoan, *Matrix Computations*, 1989]

- Remove Translational differences:
  Calculate translation that brings each of the point sets to the origin and subtract from each of the point sets to create centered point sets:
  $\boldsymbol{q}'_i = \boldsymbol{q}_i - 1/N \sum_i \boldsymbol{q}_i$
  $\boldsymbol{p}'_i = \boldsymbol{p}_i - 1/N \sum_i \boldsymbol{p}_i$

  Re-write centered point lists as matrices




$$P=\begin{bmatrix} p_1 \\ p_2 \\ p_3 \\ \vdots \\ p_N \end{bmatrix} = \begin{bmatrix} x_1, y_1 & z_1 \\ x_2, y_2 & z_2 \\ x_3, y_3 & z_3 \\ \vdots & \\ x_N, y_N & z_N \end{bmatrix} \quad Q=\begin{bmatrix} q_1 \\ q_2 \\ q_3 \\ \vdots \\ q_N \end{bmatrix} = \begin{bmatrix} x'_1, y'_1 & z'_1 \\ x'_2, y'_2 & z'_2 \\ x'_3, y'_3 & z'_3 \\ \vdots & \\ x'_N, y'_N & z'_N \end{bmatrix}$$

- Estimate Rotations: we want to find the rotation matrix R such that
  - $P^T = R.Q^T$

The system $P^T = R.Q^T$ is over-determined and there is noise, thus we want to find the rotation matrix *R* such that

$$\min_R = ||P^T - R.Q^T||^2$$

K. S. Arun, T. S. Huang, and S. D. Blostein. Least square fitting of two 3-d point sets. IEEE Transactions on Pattern Analysis and Machine Intelligence, 9(5):698 - 700, 1987.

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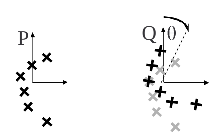
## Procrustes Point Alignment

- Scale (procrustes normally includes estimate of scaling)
  - But can assume scanner voxel dimensions are accurate
- Rewrite expression $P^T = R.Q^T$
  $Q^T P^T = R.(Q^T Q)$
- Now can decompose symmetric matrix $Q^T Q$ using singular value decomposition (SVD):
  $(Q^T Q) \rightarrow (USV^T)$
- Here S is a diagonal matrix and $VU^T$ is the rotation matrix.
  For 2D:
  $$VU^T = \begin{bmatrix} \cos(\theta) & -\sin(\theta) \\ \sin(\theta) & \cos(\theta) \end{bmatrix}$$




K. S. Arun, T. S. Huang, and S. D. Blostein. Least square fitting of two 3-d point sets. IEEE Transactions on Pattern Analysis and Machine Intelligence, 9(5):698 - 700, 1987.

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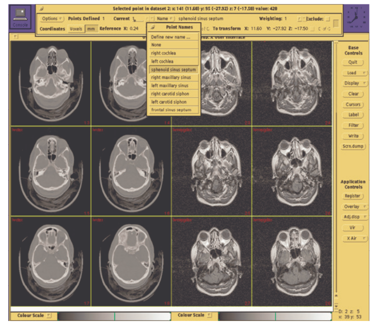
## Alternatives to SVD alignment

Alternative transformation decompositions and parameterizations can be used eg:

- Quaternion methods:
  - B. K. P. Horn. Closed-form solution of absolute orientation using unit quaternions. *Journal of the Optical Society of America A*, 4(4):629 - 642, April 1987.
- Orthonormal matrices:
  - B. K. P. Horn, H. M. Hilden, and Sh. Negahdaripour. Closed-form solution of absolute orientation using orthonormal matrices. *Journal of the Optical Society of America A*, 5(7):1127 - 1135, July 1988.
- Dual quaternions:
  - M. W. Walker, L. Shao, and R. A. Volz.Estimating 3-d location parameters using dual number quaternions. *CVGIP: Image Understanding*, 54:358 - 367, November 1991.
- These algorithms generally show similar performance and stability with real world noisy data:
  - A. Lorusso, D. Eggert, and R. Fisher. A Comparison of Four Algorithms for Estimating 3-D Rigid Transformations. In *Proceedings of the 4th British Machine Vision Conference (BMVC '95)*, pages 237 - 246, Birmingham, England, September 1995.

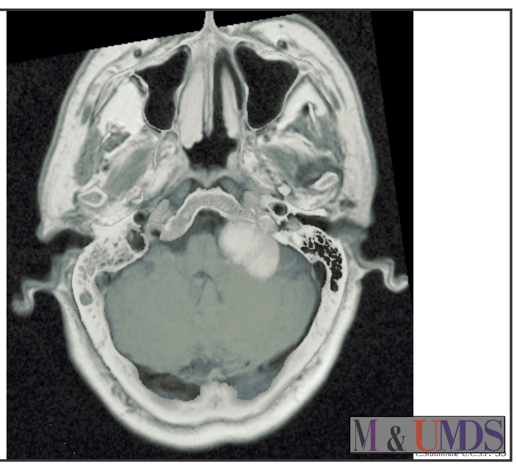


## Manual Landmark Based Registration



D.L.G. Hill, et al, Accurate Frameless Registration of MR and CT Images of the Head: Applications in Surgery and Radiotherapy Planning, Radiology, 191, 1994, pp 447-454

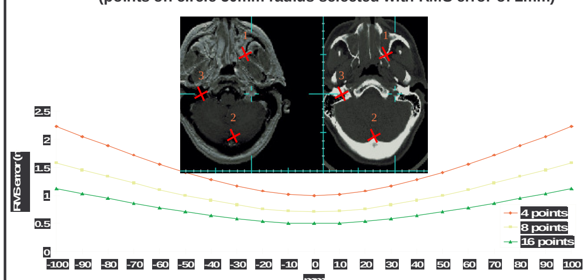







## Extrapolating Transformations: THEORETICAL POINT BASED REGISTRATION ERROR

**(points on circle 50mm radius selected with RMS error of 2mm)**




Important factor: registration error lowest where 3D landmarks can be found

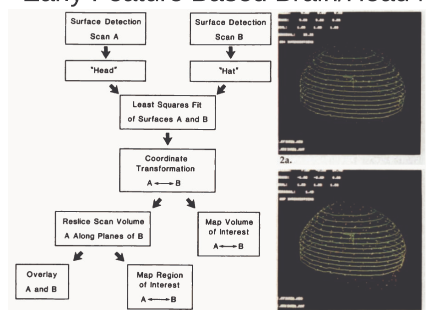
**The distribution of target registration error in rigid-body point-based registration**
Fitzpatrick, J.M.; West, J.B. Medical Imaging, IEEE Transactions on
Volume 20, Issue 9, Sep 2001 Page(s):917 - 927

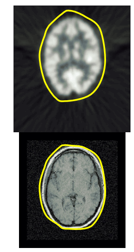
## Approaches to Landmark/Feature Extraction and Matching

- Markers Attached to Subject (rigid bone attachment?)
  - Need to be visible in different types of Images
  
  [Hawkes et al *Registration and display of the combined bone scan and radiograph in the diagnosis and management of wrist injuries*, EJNM 1991]
- Manual Landmark identification
  - Time consuming, introduce errors, difficult to find true consistent 3D landmarks: But VERY flexible and can adapt to data.
  
  [D.L.G. Hill, et al, Accurate Frameless Registration of MR and CT Images of the Head: Applications in Surgery and Radiotherapy Planning, Radiology, 191, 1994, pp 447-454.]
- Automated Landmark Identification: geometric models of local anatomy:
  - Need to be true unique 3D points in intensity map: tip-like, saddle-like, and sphere-like structures.
  - Need to be consistent in different subjects and image types
  
  [Stefan Wörz, Karl Rohr Localization of anatomical point landmarks in 3D medical images by fitting 3D parametric intensity models, Medical Image Analysis Volume 10, Issue 1, Page 41-58, Feb 2006.]
- Non-Homologous Landmarks/ 3D Structures:
  - Easier to automatically find general features: for example points on a surface using edge detection.
  - But: Which point maps to which point?
  - Need to then find correspondence and alignment: Point Cloud Fitting



## Early Feature Based Brain/Head Matching



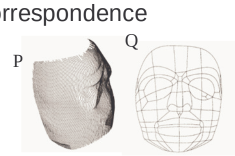
•"Head-hat" matching of Head surfaces.

Retrospective Geometric Correlation of MR, CT and PET Images, Levin, Pelizzari, Chen, Chen Cooper, Radiology, 1988

•Chamfer Distance Matching: Borgefors 1986 Jiang 1992

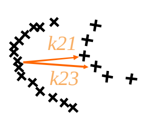


## Alignment of non-Homologous Feature Locations: fuzzy correspondence




General case of two lists of point locations $P=[\mathbf{p}_1, \mathbf{p}_2 \ldots \mathbf{p}_N]$ and $Q=[\mathbf{q}_1, \mathbf{q}_2 \ldots \mathbf{q}_M]$ with $N$ and $M$ points respectively,

and a list of weights $[k_{ij}]$ to describe the fuzzy correspondence between every possible point pair:




Registration error can then be expressed as.

$$E(R,\boldsymbol{t}) = \sum_i \sum_j k_{ij} \| \boldsymbol{p}_i - (\mathbf{R}\boldsymbol{q}_j + \boldsymbol{t}) \|^2$$

But… need to estimate both $\mathbf{R}$, $\boldsymbol{t}$ and correspondence $[k_{ij}]$.



## Iterative Closest Point Algorithm

Approximates correspondence matrix $[k_{ij}]$ by assigning each point to the current closest point.

- Applying current transformation $\mathbf{R}$ and $\boldsymbol{t}$ to $Q=[\boldsymbol{q}_1, \boldsymbol{q}_2 \ldots \boldsymbol{q}_M]$
  
  So that
  
  $Q' = RQ_i + \boldsymbol{t}$
- Take each point $P_i=[\boldsymbol{p}_1, \boldsymbol{p}_2 \ldots \boldsymbol{p}_N]$ and search list $Q'_i$ to find the nearest point $Q^i_i$ to create a new list with $N$ points.
- Apply Least Squares fit of current nearest points (eg using Procrustes point matching) to estimate R and $\boldsymbol{t}$
- Repeat Until Change in transformation falls below threshold.

P. Besl and N. McKay. A method for Registration of 3-D Shapes. *IEEE Transactions on Pattern Analysis and Machine Intelligence (PAMI)*, 14(2): 239 256, February 1992.

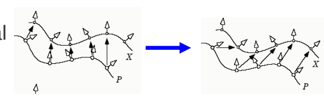
## I.C.P. advantages and disadvantages

- Can be applied to both discrete landmarks, lines, surfaces etc
- But: Highly dependent on starting estimate!
  - Only finds a local optima
  - Can use multi-start to improve search
- Search for closest point in large point lists or surfaces can be computationally expensive

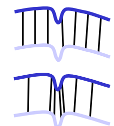


## Improvements/Adaptations in ICP

•Orientation driven ICP: Matches location and local boundary/surface orientation
[Godin 2001,Schutz 1998]




•Subsampling: Choosing only meaningful points
•Eg points on curved parts of surface



•Optimized Searching Techniques to find closest point
Multi-resolution Matching
•Outlier rejection: to handle outliers and also incomplete overlap

[S. Rusinkiewicz, M. Levoy, Efficient Variants of the ICP Algorithm, Proc 3rd international conference on 3D digital Imaging 2001]



## Fuzzy Correspondence and Point Matching

Now a very large field in both computer vision and medical image analysis, with many different approaches proposed

H. Chui and A. Rangarajan, A New point Matching Algorithm for non-rigid registration, Computer Vision and Image Understanding, vol 89, Issue 2-3, 2003.

Z. Xue, D. Shen, E Khwang Teoh, An Efficient fuzzy algorithm for aligning shapes under affine transformations, Pattern Recognition, Volume 34, Issue 6, June 2001.



## Validation of Rigid Body Registration

- Between Modality validation a difficult problem:
  - Need to introduce corresponding features visible in different imaging systems
  - That can be found accurately in each modality
  - That have fixed relationship with underlying anatomy

  Calvin R. Maurer, J. Michael Fitzpatrick, Matthew Y. Wang, Student Member, Robert L. Galloway, Robert J. Maciunas, George S. Allen, **Registration of Head Volume Images Using Implantable Fiducial Markers (1997)** IEEE Transactions on Medical Imaging
- This successfully used to evaluate MRI-CT, MRI-MRI and MRI-PET registration using bone implanted markers

  J. West, J.M. Fitzpatrick, M.Y. Wang, B.M. Dawant, C.R. Maurer, R.M. Kessler, R.J. Maciunas, C. Barillot, D. Lemoine, A. Collignon, F. Maes, P. Suetens, D. Vandermeulen, P.A. van den Elsen,S. Napel,T.S. Sumanaweera, B. Harkness, P.F. Hemler, D.L.G. Hill, D.J. Hawkes, C. Studholme, J.B.A Maintz, M.A. Viergever, G. Malandain, X. Pennec, M.E. Noz,G.Q. Maguire, M. Pollack, C.A. Pelizzari, R.A. Robb,D. Hanson, R.P. Woods, **Comparison and Evaluation of Retrospective Intermodality Brain Image Registration Techniques**, J. Comp. Assist. Tomog. Vol 21(4), 1997, pp 554-566.

## Challenges in Automating medical image registration

–Finding suitable features
  –e.g. true 3D landmarks
–Finding the same feature in different types of images
  –Not computer vision!
  –no nice edges/corners and man made scenes
–Variable/limited anatomical coverage
  –No scanner images the whole body
    –truncated: part of head or at neck
  –Makes using global methods
–Variable/low contrast to noise

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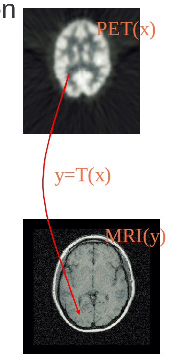
## Feature Based Registration

–Image Data Geometries
  •2D-2D, 2D-3D, 3D-3D
•Transformation Type
  •Rigid/Affine/Non-Rigid
•Correspondence Criteria/Measure
  •Feature Based Methods
  •Voxel Based/Dense Field Methods
•Optimization Method :
  •Maximizing/minimizing Measure wrt T()




1. Define Suitable Image Similarity Measure
2. Optimise Similarity wrt Transform T()

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## Pixel/Voxel Based Registration

- History: Template Matching
  – Detecting an object or feature based on pixel/voxel values
- Avoid the need to automatically extract corresponding landmarks or surfaces
- Similarity Measures for Image Registration can Assume:
  – linear intensity mapping
  – non-parametric 1-to-1 intensity mapping
  – non-parametric many-to-1 intensity mapping
- Simplest: Image Intensity Difference

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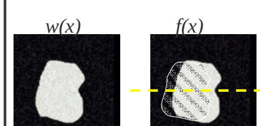
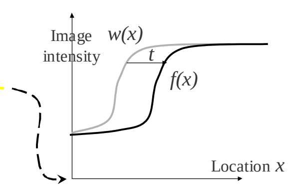
## Iterative Refinement of Transformation Parameters: small displacements




Consider 1D case:
for no noise, assume
*w(x)* is some exact translation of *f(x)*

$w(x)= f(x+t)$

and image 'mis match' or error for given displacement *t* can simply be

**Local Difference in intensity:**

$e(t)=f(x+t)-w(x)$

[Lucas and Kanade, An Iterative Image Registration Technique with an Application to Stereo Vision Proc Image Understanding Workshop, P121-130, 1981]

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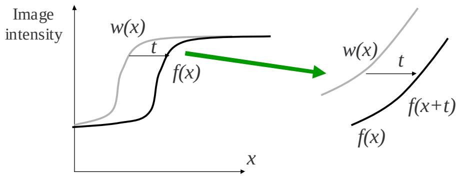
## Iterative Refinement of Transformation Parameters: small displacements AT A POINT




At one point $x$, for small $t$

$f'(x) \approx (f(x+t)-f(x))/t$

Which, taking from above, is

$= (w(x)-f(x))/t$

So, translation $t$ to align image $f$ with w at point $x$ is then

$t \approx [w(x)-f(x)]/f'(x)$

[Lucas and Kanade, An Iterative Image Registration Technique with an Application to Stereo Vision Proc Image Understanding Workshop, P121-130, 1981]

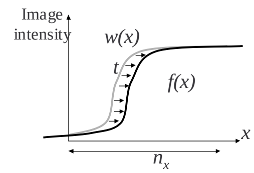


## Iterative Refinement of Transformation Parameters: small displacements OVER ALL x

$t(x) \approx [w(x)-f(x)]/f'(x)$

so average over $x$ is

$t \approx \sum_x t(x) / n_x$




**But:** Because of Local Approximations
**First estimate of t does not get you to the optimal solution: Just gets you nearer to it.**

**Need multiple steps: Iterative Registration:**

if $t_0=0$ then $t_{n+1}=t_n+\sum_x t(x) / n_x$

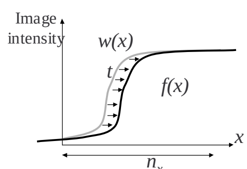


## Iterative Refinement of Transformation Parameters: small displacements OVER ALL x

$t(x) \approx [w(x)-f(x)]/f'(x)$

so average over $x$ is

$t \approx \sum_x t(x) / n_x$




**Weighted average:**
Use contributions where linear approximation to $f'(x)$ is better.
i.e. weight to points where $|f''(x)|$ closer to zero.
Possible weight $k(x)$ for where (w'(x)-f'(x))/t at point x is:

$k(x)=1/|w'(x)-f'(x)|$ Giving $t= \frac{\sum_x k(x)t(x)}{\sum_x k(x)}$

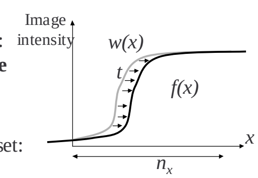
so if $t_0=0$ then $t_{n+1}=t_n+ \frac{\sum_x k(x)t(x)}{\sum_x k(x)}$



## Minimizing Sum of Squared Intensity Difference

If we use an alternative form for the intensity 'mis match' or error:
The **squared intensity difference**

$E(t)= \sum_x [f(x+t)-w(x)]^2$




To find optimal transformation $t$ set:

$0= \frac{\partial E}{\partial t}$ *so:*

$0=\frac{\partial}{\partial t} \sum_x [f(x+t)-w(x)]^2= \frac{\partial}{\partial t} \sum_x [f(x)+t\, f'(x)-w(x)]^2$

$= \sum_x 2f'(x)\, (f(x)+t\, f'(x)-w(x))$

*Giving:*

$t \approx \frac{\sum_x f'(x)\, (w(x)-f(x))}{\sum_x f'(x)^2}$ so if $t_0=0$ then $t_{n+1}=t_n+ \frac{\sum_x f'(x)\, (w(x)-f(x))}{\sum_x f'(x)^2}$

[Lucas and Kanade, Proc Image Understanding Workshop, P121-130, 1981]

## Extension to N dimensional Images

The squared intensity difference can be extended to the case where location $\boldsymbol{x}$ and translation $\boldsymbol{t}$ are vectors of N dimensions:

$E(\mathbf{t})= \sum_{\mathbf{x}\in \mathbf{R}} [f(\mathbf{x}+\mathbf{t})-w(\mathbf{x})]^2$

As for 1D, we can then use a linear approximation for small $\boldsymbol{t}$ so that

$$f(\mathbf{x}+\mathbf{t})=f(\mathbf{x})+\mathbf{t}\ \frac{\partial}{\partial \mathbf{x}} f(\mathbf{x})$$

*We can then set*

$$0= \frac{\partial E}{\partial \mathbf{t}} \quad \text{so:}$$

$$0=\frac{\partial}{\partial \mathbf{t}} \sum_{\mathbf{x}\in \mathbf{R}} [f(\mathbf{x})+t\ \frac{\partial f(\mathbf{x})}{\partial \mathbf{x}} -w(\mathbf{x})]^2 = \sum_{\mathbf{x}\in \mathbf{R}} 2\ \frac{\partial f(\mathbf{x})}{\partial \mathbf{x}}\ [f(\mathbf{x})+t\ \frac{\partial f(\mathbf{x})}{\partial \mathbf{x}}-w(\mathbf{x})]$$

and then

$$\mathbf{t}=[\ \sum_{\mathbf{x}\in \mathbf{R}} [\partial f(\mathbf{x})/\partial x]^T[w(\mathbf{x})-f(\mathbf{x})]\ ][\sum_{\mathbf{x}\in \mathbf{R}} (\partial f(\mathbf{x})/\partial x)^T (\partial f(\mathbf{x})/\partial x)\ ]^{-1}$$

[Lucas and Kanade, Proc Image Understanding Workshop, P121-130, 1981]



## Other forms of Linear Spatial Transformations

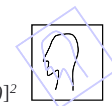
Mapping from One space to the other can be described by a Linear 3x3 transformation matrix **A** and a translation vector $\boldsymbol{t}$

So, we assume at the correct transformation:

$$w(\mathbf{x})=f(\mathbf{x}\mathbf{A}+\mathbf{t})$$

and intensity error is

$$E(\mathbf{A},\mathbf{t})= \sum_{\mathbf{x}\in \mathbf{R}} [f(\mathbf{x}\mathbf{A}+\mathbf{t})-w(\mathbf{x})]^2$$



To minimize this, one approach is to use a linear approximation to changes in transformation

$$f(\mathbf{x}(\mathbf{A}+\Delta\mathbf{A})+(\mathbf{t}+\Delta\mathbf{t}))$$
$$\approx f(\mathbf{x}\mathbf{A}+\mathbf{t}) + (\mathbf{x}\Delta\mathbf{A}+\Delta\mathbf{t})\ \frac{\partial}{\partial \mathbf{x}} f(\mathbf{x})$$

[Lucas and Kanade, Proc Image Understanding Workshop, P121-130, 1981]

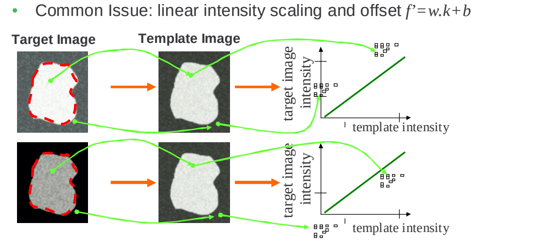


## Alternative Image Similarity Measures for Image Alignment



## Global Intensity Variations

- Many Medical Images have ‘uncalibrated’ intensities
  - Gain or illumination changes
- Common Issue: linear intensity scaling and offset $f' = w.k + b$




- Absolute difference will not tend to zero at correct match:
  - *OR Worse: minimum does not correspond to correct match*

## Sum of Squared Difference and Correlation

(2) $$D = \sum_{t=1}^{J}\sum_{s=1}^{K}(f(x+s, y+t) - w(s,t))^2$$

This can be expanded to:

$$D = \sum_{t=1}^{J}\sum_{s=1}^{K} f(x+s,y+t)^2 + \sum_{t=1}^{J}\sum_{s=1}^{K} w(s,t)^2 - 2\sum_{t=1}^{J}\sum_{s=1}^{K} f(x+s,y+t).w(s,t)$$

- Will be Small when last term is large or first two terms are small.
- First two terms are the summed intensities within the template region
- Neglecting the first two terms and the factor $-2$ gives us a simple commonly used measure of template match to be MAXIMIZED :

(3) $$c(x,y) = \sum_{t=1}^{J}\sum_{s=1}^{K} f(x+s,y+t)w(s,t)$$

this sum of the products of the intensity pairs at each pixel is the Correlation between template and target image intensities

[Pratt, 1974], [Pratt Digital Image Processing 1978]
[Rosenfeld,Kak, Digital Picture Processing 1976]

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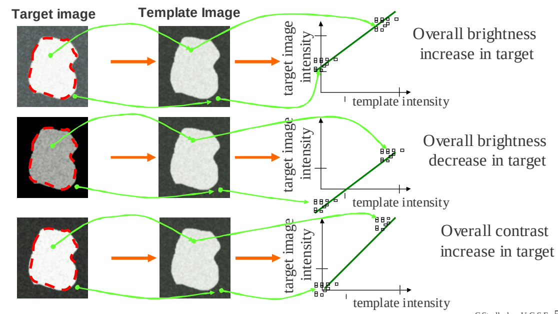
## Correlation

- Correlation is measuring the residual errors between the data and a best fit of a line to that data
- Allows relationship to have different slope and offset
- So: Robust to global linear changes in Brightness/Contrast

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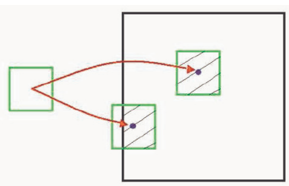
## Normalised Correlation: Boundary overlap



(5) $$c(x,y) = \sum_{t=1}^{J}\sum_{s=1}^{K} f(x+s,y+t)w(s,t)$$

- At image boundaries the overlap of template and target image may be limited: Match will be reduced by number of pixels not overlapping
- Can Normalize Measure by Number of overlapping pixels:

(6) $$c'(x,y) = \frac{1}{N_t}\sum_{t=1}^{J}\sum_{s=1}^{K} f(x+s,y+t)w(s,t)$$

- Where $N_t$ is the number of template pixels overlapping with target image at template location $x, y$

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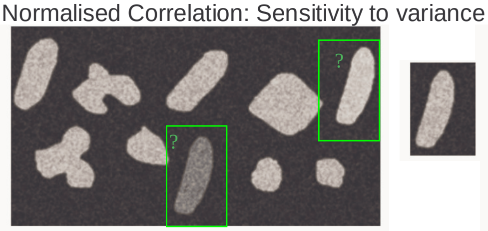
## Normalised Correlation: Sensitivity to variance




- Correlation is still a function of the overall energy or brightness of the image and template
- So.... Can Still End up picking Brightest Target
- One Option: Can normalize by the Summed Brightness of the target image:

(7) $$c'(x,y) = \frac{1}{E}\sum_{t=1}^{J}\sum_{s=1}^{K} f(x+s,y+t)w(s,t)$$

where:

(8) $$E = \sum_{t=1}^{J}\sum_{s=1}^{K} f(x+s,y+t)$$

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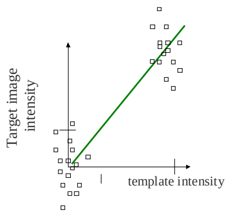
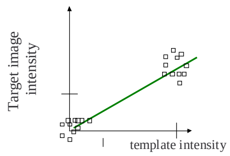
## Variance?

- Problem: Match may still be biased by variance in Target/Template



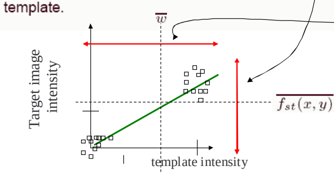



## Correlation Coefficient

- Normalise Correlation by the summed residuals around mean in template and target overlap:

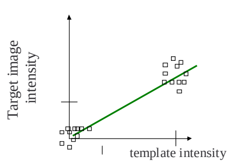
(9) $$\gamma(x,y) = \frac{\sum_{t=1}^{J}\sum_{s=1}^{K}[f(x+s,y+t) - \overline{f_{st}(x,y)}][w(s,t) - \overline{w}]}{\sum_{t=1}^{J}\sum_{s=1}^{K}[f(x+s,y+t) - \overline{f_{st}(x,y)}]^2 \sum_{t=1}^{J}\sum_{s=1}^{K}[w(s,t) - \overline{w}]^2}$$

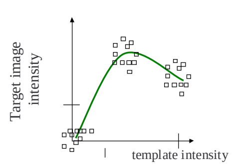
- Here:
  $\overline{w}$ is the mean intensity in the template image
  $\overline{f_{st}(x,y)}$ is the mean intensity of target image in the region overlapping with the template.






## What about non-linear intensity mappings?





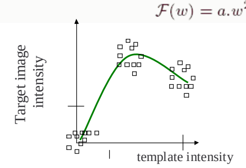

## Non-Linear Intensity Mapping

- Minimize Square Difference Between Target and some Function $\mathcal{F}()$ of Template Intensity:

(5) $$CR = \sum_{t=1}^{J}\sum_{s=1}^{K}(f(x+s,y+t) - \mathcal{F}(w(s,t)))^2$$

- $\mathcal{F}()$ is generally a low order polynomial (for speed)

$$\mathcal{F}(w) = a.w^2 + b.w + c$$




Now need to estimate the location of the template and the parameters of the function $\mathcal{F}()$

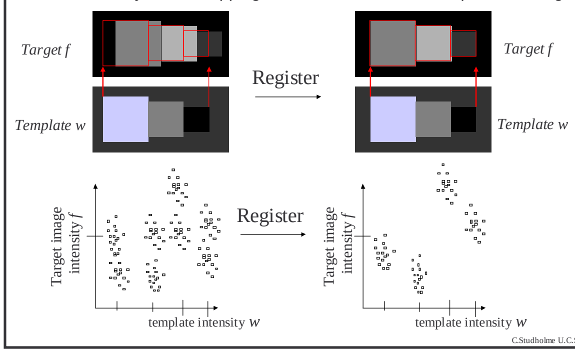
Multi Modality Similarity Measures

Matching Images with Different Tissue Contrast Properties

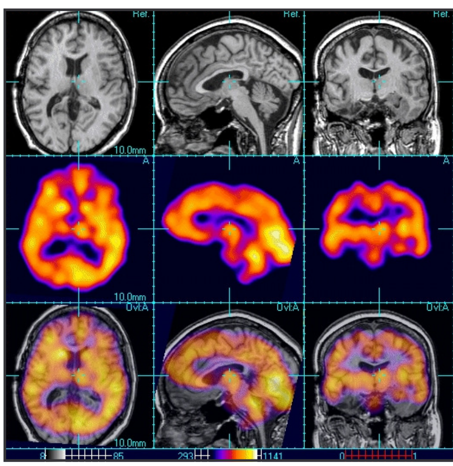


## Non-parametric 1-to-1 mapping

- But Intensity mapping is not usually smooth or easily parameterized (e.g. discrete because of different tissue classes)
- Assume only 1-to-1 mapping of intensities between template and target:



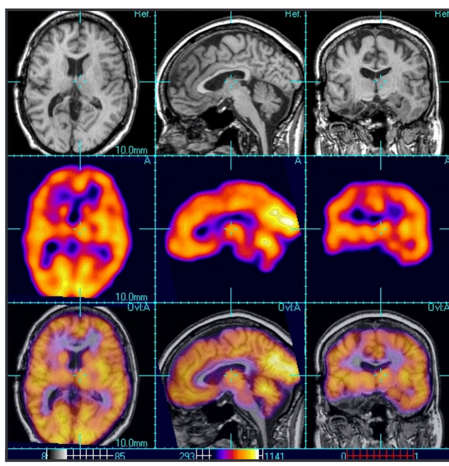


SPECT-MRI registration: Patient orientated differently with respect to scanner coordinates:

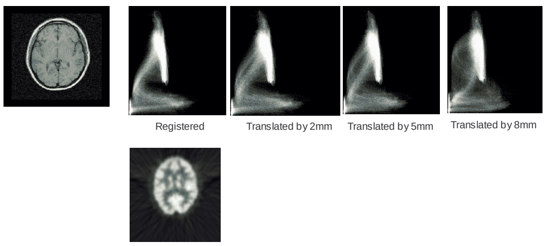
1.Head rest design
2.Gantry angle limitations
3. No easy to find 3D landmarks





SPECT-MRI registration

## The Effects of Misregistration in Intensity Feature Space

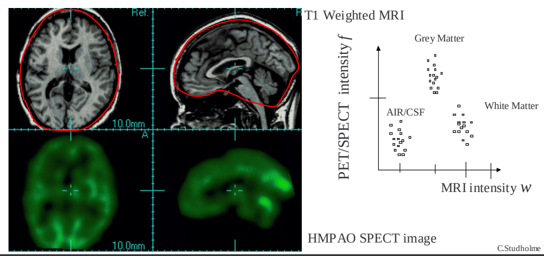





## Partitioned Image Uniformity

[Woods et al JCAT 93]

- Used for MRI-PET/SPECT registration
  - MRI scan scalp edited-> Only consider intra-cranial tissues
  - Grey-white-CSF values in cranial region differ
    - Non-monotonic mapping
    - Approx 1-to-1






## Partitioned Image Uniformity

[Woods et al JCAT 93]

- Divide up the template image intensities $w$ into bins $b \in B$
- The partitioned image uniformity of target image $f$, is given by the weighted summation of normalised standard deviations of $f$ in each bin:

$$PIU_f = \sum_{b \in B} \frac{n_b}{J.K} \frac{\sigma_b(f)}{\mu_b(f)} \quad (7)$$

where

$$\mu_b(f) = \frac{1}{n_b} \sum_{t=1}^{J} \sum_{s=1}^{K} f(x+s, y+t).\psi_b(w)$$

and

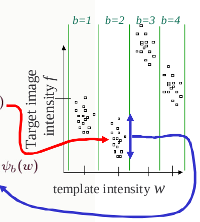
$$\sigma_b^2(f) = \frac{1}{n_b} \sum_{t=1}^{J} \sum_{s=1}^{K} (f(x+s, y+t) - \mu_b(f))^2.\psi_b(w)$$

where

$$\psi_b(w) = \begin{cases} 1 & \text{if } w \text{ is in bin } b \\ 0 & \text{otherwise} \end{cases}$$

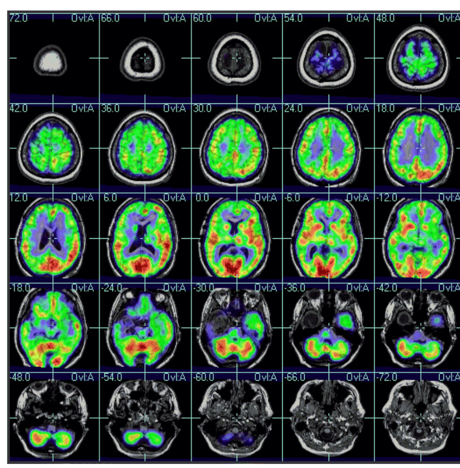
is the intensity binning and $n_b$ is the number of pixels falling in bin $b$

$$n_b = \sum_{t=1}^{J} \sum_{s=1}^{K} \psi_b(w)$$




- This definition can also be reversed to evaluate $PIU_w$





Functional/ Structural Fusion:

MRI-SPECT

## Correlation Ratio

*[A. Roche et al MICCAI 98]*

- For a given bin $b$ of template intensity $w$, evaluate the expected value of $f$:

$$\mu_b(f) = \frac{1}{n_b} \sum_{t=1}^{J} \sum_{s=1}^{K} f(x+s, y+t).\psi_b(w)$$

where $n_b$ is the number of pixels in bin $b$, and $\psi_b(w)$ is the binning function.

- Evaluate the variance of the difference between this expected and the actual values of $f$:

$$\sigma_b^2 = \frac{1}{n_b} \sum_{t=1}^{J} \sum_{s=1}^{K} (f(x+s, y+t) - \mu_b(f))^2.\psi_b(w)$$

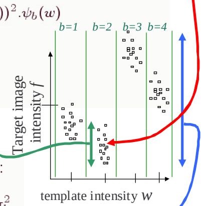
- Evaluate the weighted sum of these over the bins:

$$\eta'(f|w) = \sum_b \frac{n_b}{J.K} \sigma_b^2$$

•Need to avoid picking region with small variance:

- Divide by the variance of $f$, $\sigma(f)$ over the overlap region:

Correlation Ratio: $$\eta(f|w) = 1 - \frac{1}{\sigma(f)} \sum_b \frac{n_b}{J.K} \sigma_b^2$$

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## MR-CT Registration in the Skull Base

- CT (and MR) image volume often targeted with limited axial extent.
- Automated segmentation or identification of features is difficult.
- Axial resolution limited.

Need to make best use of all shared features in the images.

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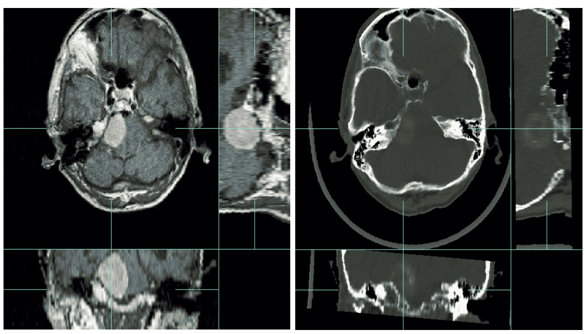
## MR and CT



Manual Registration Estimate
(Using Corresponding Anatomical Landmarks)

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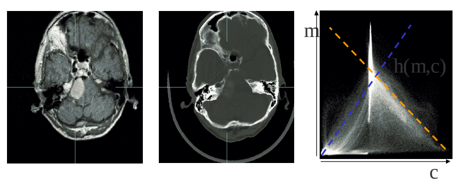
## Correlation Coefficient




Assumes Linear Relationship between MR and CT intensity.

Improved by using only modified soft tissue or bone intensities from CT. (Van den Elsen, 1994).

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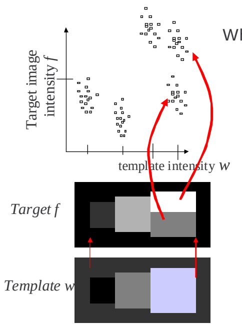
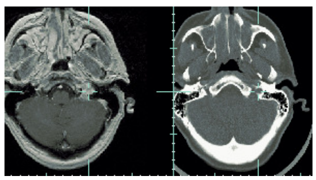
## Many-to-1 Intensity Mapping ?




Where one image type can detect sub classes of tissue, while the other sees one.
(e.g. T1 weighted MRI vs CT)

**Multiple soft tissue intensities** | **One/few soft tissue intensities**



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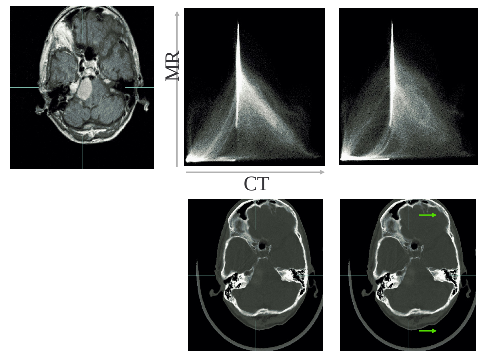
## Changes in 2D Histogram with Alignment

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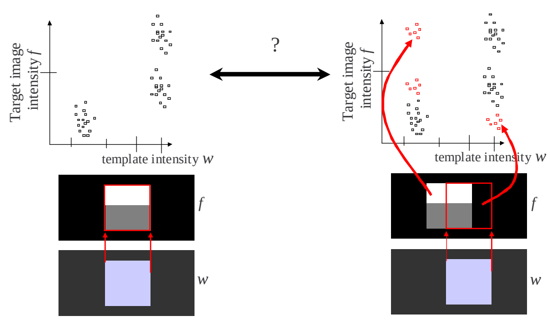
## How to Characterize Alignment?
## -> 'Histogram Sharpness'

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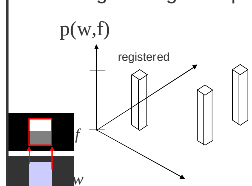
## Information and Entropy

[Collignon, CVRMED 95]

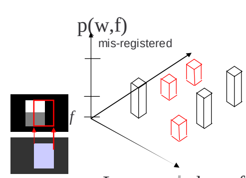
If guessing what pair of values *(w,f)* a pixel will have...




Small number of high-probability pairs

Less Uncertainty

Overall: Image Pair Provides Less Information...
'Less Complex'




Larger number of lower-probability pairs

More Uncertainty

Overall: Image Pair Provides More Information..
'More Complex'

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## Information and Entropy

[Collignon, CVRMED 95]

- Average Uncertainty or Joint Entropy of the sets of co-occurring template $w \in W$ and target $f \in F$ intensities:

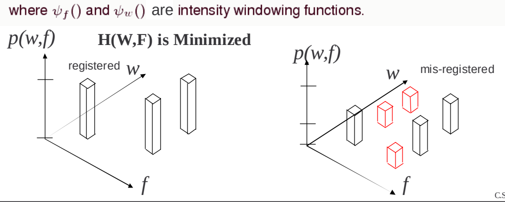
$$H(W,F) = \sum_{w \in W} \sum_{f \in F} -p(w,f) \log p(w,f)$$

where $p(w,f)$ is an estimate of the joint probability of $w$ and $f$ occurring together.

- $p(w,f)$ can be estimated by intensity windowed summation of voxels:

$$p(w,f) = \frac{1}{J.K} \sum_{t=1}^{J} \sum_{s=1}^{K} \psi_f(f(x+s, y+t)) \psi_w(w(x,y))$$

where $\psi_f()$ and $\psi_w()$ are intensity windowing functions.






## Mutual Information

[Viola and Wells: ICCV 95, Collignon et al: IPMI 95]

- Joint entropy, like correlation and correlation ratio, is influenced by the image structure in the image overlap
  - The changing transformation modifies the information provided by the images

- Instead: form a measure of the relative information in the Target image with respect to Template using Mutual information:
  - difference between marginal and joint entropies

*I(F,W)=H(F)+H(W)-H(F,W)*

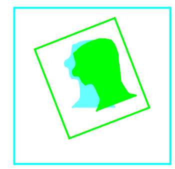
**to be Maximized**

*where*

$$H(F) = \int_f -p(f) \log(p(f))$$

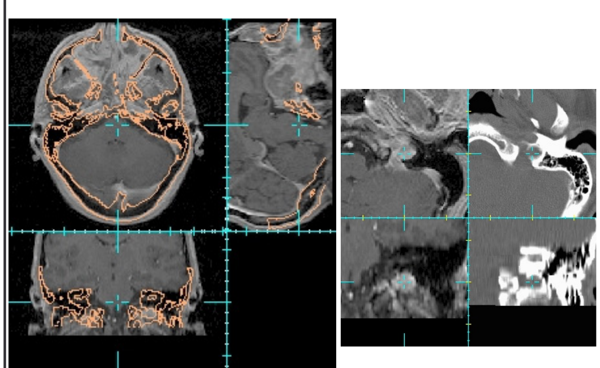
$$H(W) = \int_w -p(w) \log(p(w))$$

$$H(F,W) = \int_f \int_w -p(f,w) \log(p(w,w))$$

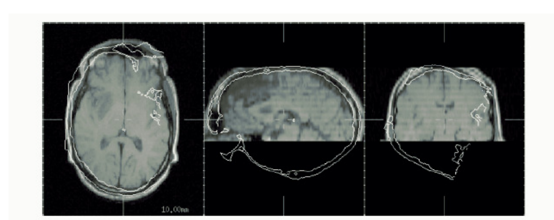


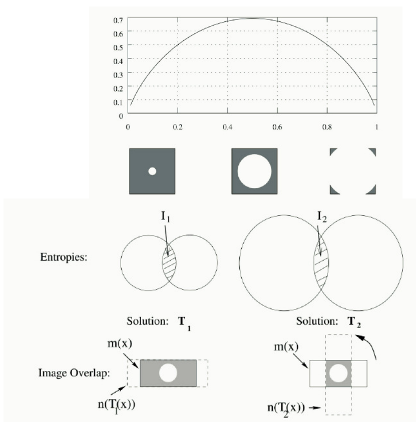


## MRI-CT for skull base surgery planning





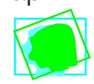


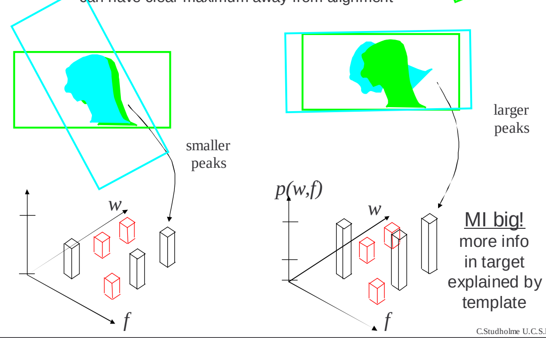





## Information Measures and Overlap

- MI behavior varies
- MI Behavior Depends of Field of View:
  - can have clear maximum away from alignment



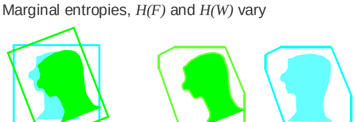





## Normalised Mutual Information

[Studholme et al, 1998]

- When mutual information is used to evaluate the alignment of two finite images: overlap still has an confound:
  - Both Marginal entropies, $H(F)$ and $H(W)$ vary

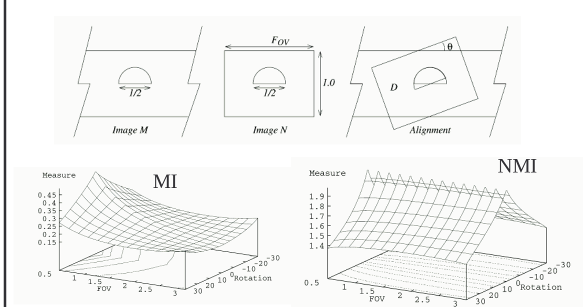


- Alignment can be driven by choosing overlap that has large $H(F)$ and $H(W)$.
  - e.g. overlap with equal area of background and foreground intensities
- Rather than look for difference in joint and marginal entropies, use their ratio (like correlation coefficient):

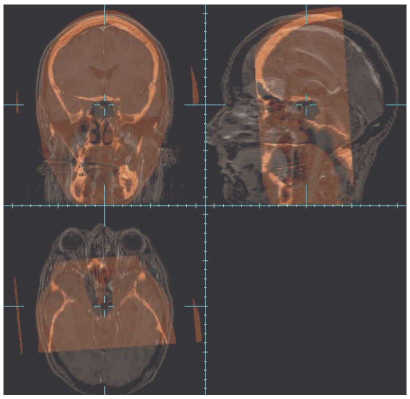
$$Y(F,W)=\frac{H(F)+H(W)}{H(F,W)}$$ **to be Maximized**

But.... Does not solve all problems!





## MRI-CT Registration



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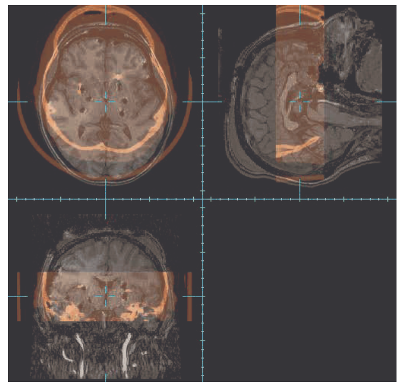
## MRI-CT Registration



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## 3D Rigid MR-CT Registration in the Skull Base

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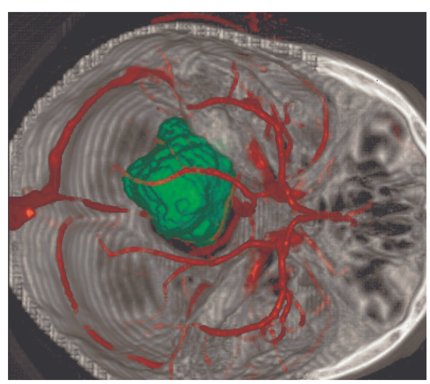
## Image Fusion for Skull Base Surgery Planning
Hawkes et al, 1993



CT: Bone
MR Gadolinium: Tumor
MRA: Blood Vessels

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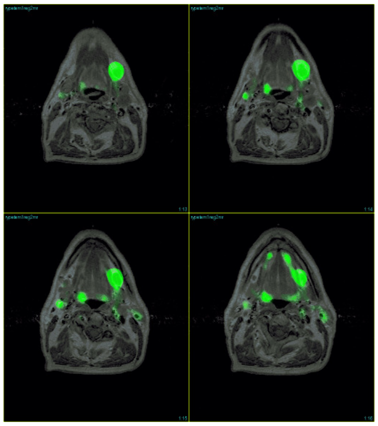
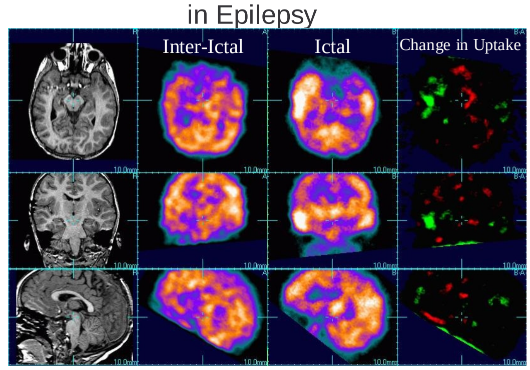


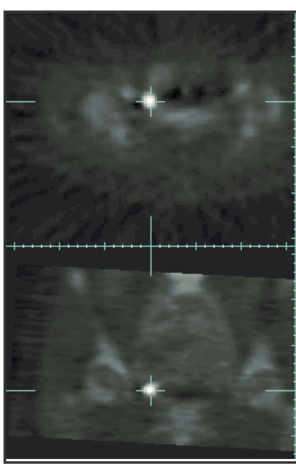
Registered MR+PET



## Subtraction SPECT Imaging in Epilepsy





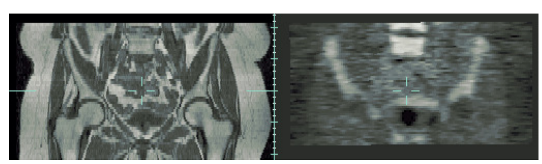



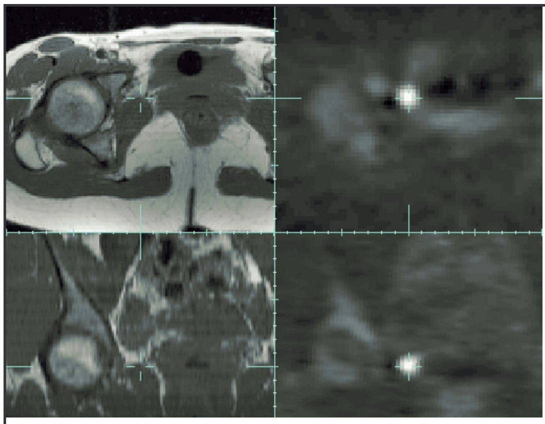
- High Contrast F.D.G. Uptake in Regions of Interest.
- Some Soft Tissue Detail.
- F- Tracer Added to Highlight Bone Structure.



## Shared Features in MR and PET Images of the Pelvis

- Bone Features
  - PET: F- Uptake.
  - MR: Marrow White.
- Soft Tissue
  - Some Boundaries in PET: Very Low Contrast.
  - Deformed by Different Bed Shapes.





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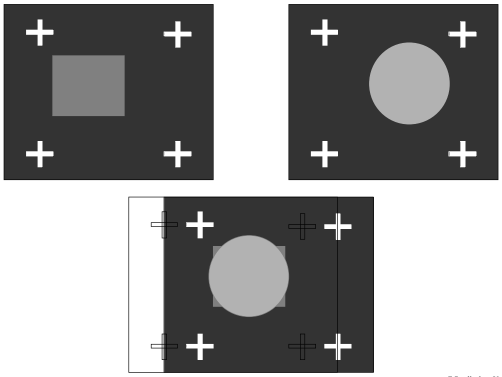
Its still only overlaps of intensities…
The biggest overlaps drive the registration



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## Summary

- A range of medical alignment measures have been developed in the last 15yrs
- These vary in the assumptions they make about the relationship between intensities in the two images being matched
- Many other criteria not covered!
- Many ways of modifying the criteria:
  - Evaluation at multi resolution/scale
  - Edge/boundary/geometric feature extraction: modify contrast
  - Spatial windowing and encoding can localize the criteria
- Best criteria will depend on the type of data you have:
  - How different the information provided and what contrast is shared
  - How much they overlap

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