PRESENTATION

MEDICAL IMAGE REGISTRATION BY MAXIMIZATION OF MUTUAL INFORMATION

Dissertation Defense

by

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Why and What

Why medical image registration?

- Medical image registration has been applied to the diagnosis of breast cancer, cardiac studies, and a variety of neurological disorders including brain tumors.

Why maximization of mutual information?

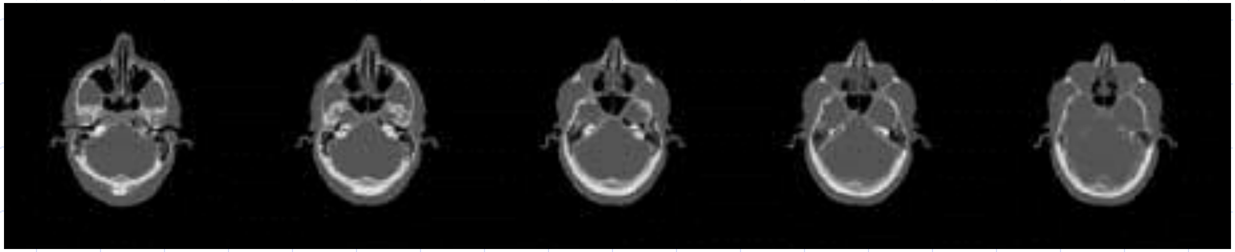
- Maximization of mutual information of voxel intensities has been proved to be one of the most popular registration methods for three-dimensional multimodal medical image registration.

What's the goal of this thesis?

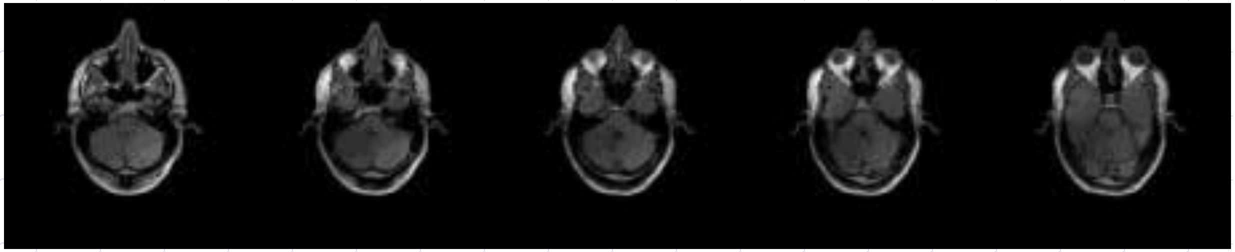
- To develop a registration software.
- To implement new approaches for multimodality medical image registration.
- Improve accuracy and/or speed.
- The result could be used in clinical cases.

Modalities Involved in Registration

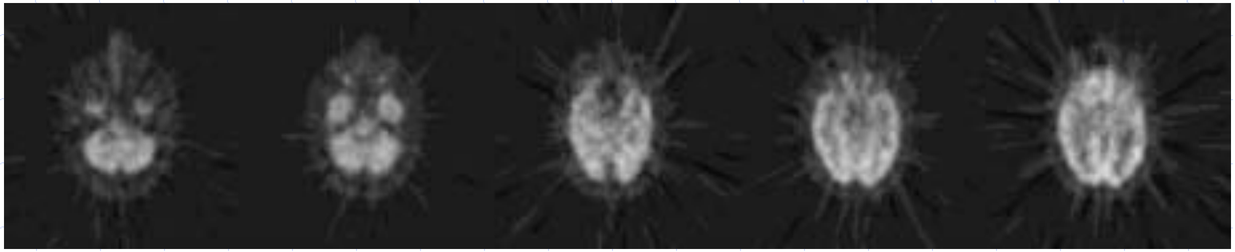
- Computed Tomography (CT) gives anatomical information



- Magnetic Resonance (MR) imaging gives anatomic information



- Positron Emission Tomography (PET) gives functional information



Why Registration?

- **Monomodality:**
  - A series of same modality images (MR with MR....).
  - A wider range of sequence types may be required.
  - Images may be acquired weeks or months apart.
  - Aligning images in order to detect subtle changes in intensity or shape

- **Multimodality:**
  - A combination of MR and CT with SPECT or PET.
  - Complementary anatomic and physiological information can be obtained for the precise diagnosis and treatment.
  - Examples:PET and SPECT (low resolution, functional information) need MR or CT to get structure information.
  - In future, medical images (such as PET, SPECT and CT, MR) will be acquired in a single machine.

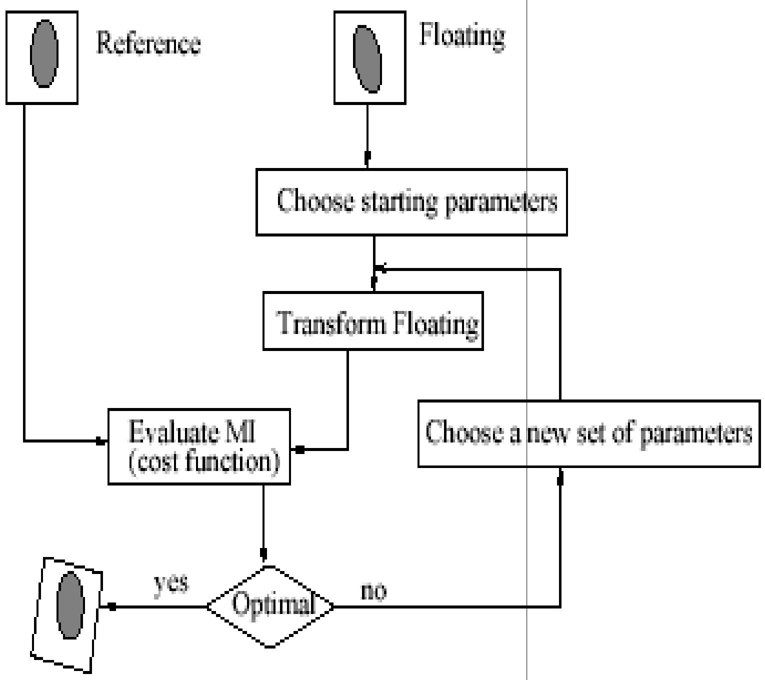
Registration Methods

- Landmark-based:
  - Based on identification of corresponding point landmarks or fiducial marks in two images.
  - Accurate, but inconvenient, and cannot applied retrospectively.
  - Labor-intensive and their accuracy depends on the accurate indication of corresponding landmarks in all modalities.
- Surface-based:
  - Corresponding surfaces are delineated and a transformation computed that minimizes some measure of distance between the two surfaces.
  - Segmentation needed, and surfaces are not easily identified in functional modalities(PET).
- Voxel-based:
  - Use the intensities in the two images alone without any requirement to segment or delineate corresponding structure.
  - It includes sum of squared intensity difference (SSD), correlation coefficient (CC), variance of intensity ratio (VIR), and mutual information (MI).
  - Mutual information is widely used in multimodality registration.

Mutual Information Criterion

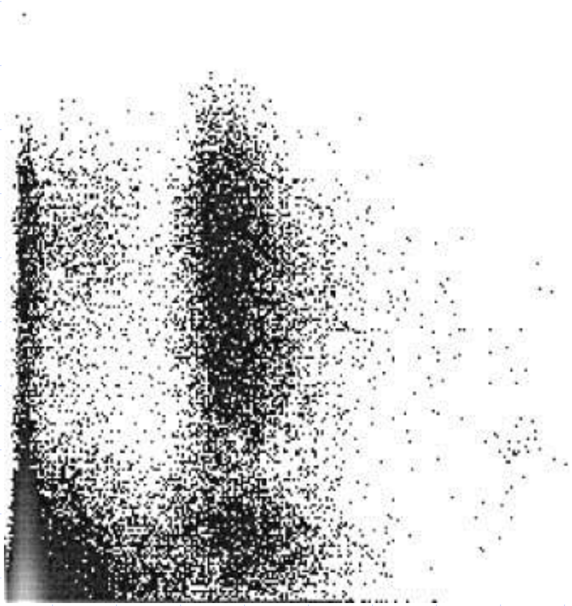
- Mutual information is applied to measure the statistic dependence between the image intensities of corresponding voxels in both images, which is assumed to be maximal if the images are geometrically aligned.

$$MI(A,B) = \sum_a \sum_b P_{AB}(a,b) \log \frac{P_{AB}(a,b)}{P_A(a)P_B(b)}$$
$$= H(A) + H(B) - H(A,B)$$
$$= H(A) - H(A \mid B)$$
$$= H(B) - H(B \mid A)$$

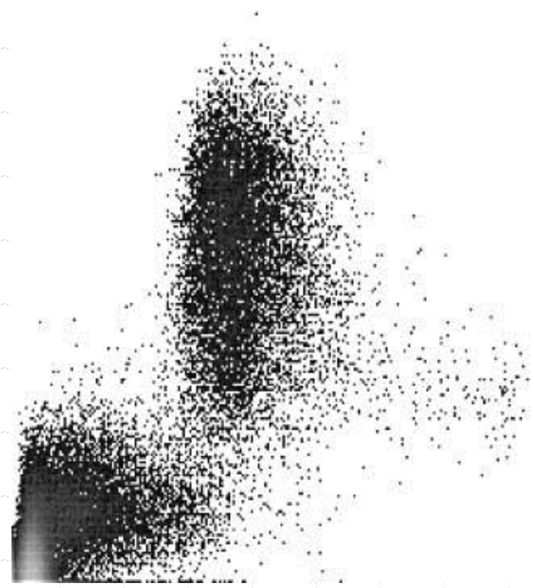


Joint Histogram Comparison

- A typical joint probabilities distributions of intensities for MR(x-axis) and PET(y-axis) before and after registration.



Before registration
MI(A,B)=0.636287
(more diffusion)



After registration
MI(A,B)=0.805367
(less diffusion)

Normalized Mutual Information

- Extension of Mutual Information

Maes et. al.:

$$NMI(A,B) = H(A,B) - MI(A,B)$$

$$NMI(A,B) = \frac{2 \times MI(A)}{H(A) + H(B)}$$

Studholme et. Al.:

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

- Compensate for the sensitivity of MI to changes in image overlap

Geometry Transformation

Description:

- The features (dimension, voxel size, slice spacing, gantry tilt, orientation) of images, which are acquired from different modalities, are not the same.

Image coordinate Transform:

- From voxel units (column, row, slice spacing) to millimeter units with its origin in the center of the image volume. $\vec{c} = (c_x, c_y, c_z) = (\vec{d} - 1)/2$ where $\vec{d} = (d_x, d_y, d_z)$
- The formula is:

$$\vec{n} = (O * G * V * C) \cdot \vec{p}$$

$$\vec{n} = T_{image} \cdot \vec{p}$$

Affine Transform:

- The affine transformation that transforms new coordinates $\vec{n}_1$ in image 1 into new coordinates $\vec{n}_2$ in image 2 is defined by matrix A.

$$\vec{n}_2 = A \cdot \vec{n}_1$$

$$A = T * R * K * S$$

Corresponding Points Transform:

$$\vec{n}_2 = A \cdot \vec{n}_1$$

$$T_{image2} \cdot \vec{p}_2 = A * T_{image1} \cdot \vec{p}_1$$

$$\vec{p}_2 = (T_{image2}^{-1} * A * T_{image1}) \cdot \vec{p}_1$$

$$\vec{p}_2 = T_{mapping} \cdot \vec{p}_1$$

Implementation Specifics

Data Set:

- Involved 1 patient: contains 12 pairs of brain images,which were provide by Philip Medical System at OH, USA.
- Involved 9 patients: containing 76 pairs of brain images, which were provided by Vanderbilt University, Nashville, TN, USA.

Interpolation:

- Nearest-neighbor method.
- Tri-linear method.
- Tri-linear partial volume method.

Optimization:

- Powell's direction set method.
- Downhill simplex method.

Registration:

- By maximization of mutual information or normalized mutual information.
- Software was developed using Microsoft Visual C++, and Interactive-Data-Language (IDL).
- Rigid body transformation.

Multiresolution and Subsampling:

- Subsampling: Takes one out of every n voxels in x, y, z dimension.
- Averaging approach: The voxels values within a sampling volume are averaged.

Implementation Specifics
Data Set (9 patients)

- Data set from **The Retrospective Registration Evaluation Project** database by Vanderbilt University.
- Images for 9 patients.
- 76 image pairs were available to be registered.
  - 41 CT-MR pairs of 7 out of 9 patients.

	P_01	P_02	P_03	P_04	P_05	P_06	P_07	P_08	P_09
CT	√	√	√	√	√	√	√		
MR_PD	√	√	√	√	√	√	√	√	√
MR_T1	√	√	√	√	√	√	√	√	√
MR_T2	√	√	√	√	√	√	√	√	√
MR_T1-rect.	√	√	√	√	√		√		
MR_PD-rect.	√	√	√	√	√	√	√		
MR_T2-rect.	√	√	√	√	√	√	√		
PET	√	√			√	√	√	√	√

Implementation Specifics
Data Set (cont.)

- Image characteristics (9 patients)

Image	Size	Voxels(mm)
CT	$512^2 \times (28-34)$	$0.653595^2 \times 4.0$
MR_PD	$256^2 \times (20-26)$	$1.25^2 \times 4.0$
MR_PD_Rectified	$256^2 \times (20-26)$	$(1.250876-1.267106)^2 \times (4.0492-4.1136)$
MR_T1	$256^2 \times (20-26)$	$1.25^2 \times 4.0$
MR_T1_Rectified	$256^2 \times (20-26)$	$(1.252254-1.26762)^2 \times (4.0468-4.1288)$
MR_T2	$256^2 \times (20-26)$	$1.25^2 \times 4.0$
MR_T2_Rectified	$256^2 \times (20-26)$	$(1.252003-1.271)^2 \times (4.0436-4.1596)$
PET	$128^2 \times 15$	$(1.943042-2.590723)^2 \times 8.0$

Multi-resolution

- Why Multi-resolution?
  - Methods for detecting optimality can not guarantee that a global optimal value will be found.
  - Time to evaluate the registration criterion is proportional to the number of voxels.
- The result at coarser level is used as the starting point for the finer level.
- Currently multi-resolution approaches:
  - Sub-sampling.
  - Averaging.

Three New Registration Approaches Based on NMI

- A Binarization Approach:
  - Background segmentation.
  - Linear binning size.
  - Using sub-sampling multi-resolution.
  - For CT-MR registration.
- A Non-linear Binning Approach:
  - Background segmentation.
  - K-means clustering.
  - Nonlinear binning size.
  - Using sub-sampling multi-resolution.
  - For CT-MR registration.
- A Wavelet-Based Multi-resolution Approach:
  - Linear binning size.
  - Using wavelet-based multi-resolution.
  - For CT-MR and PET-MR registration.

A Binarization Approach

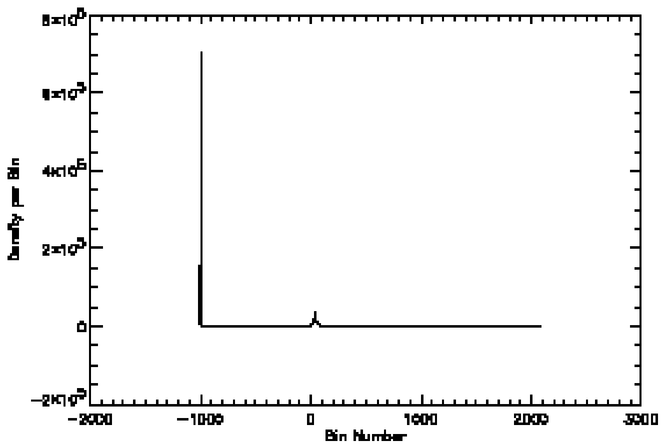
- Two stages:

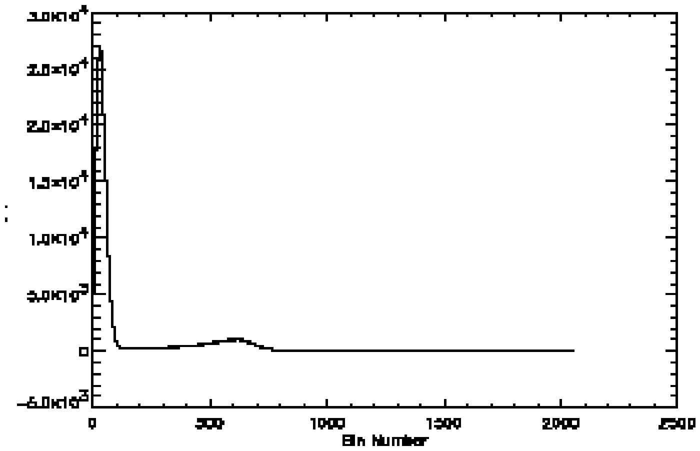
1. Region Growing:
   Segmentation into Background and Foreground.
2. Two levels Registration:
   Binarized 2-bin images are input to the lower level.

- Down-sampled binarized images as the input to the first level.
- Result of the first level as the initial estimate for the second level.
- The second level performs the registration of full images, using Maximization of Normalized Mutual Information.

A Binarization Approach
Region Growing Implementation

- Finding Starting Points:
  Easy to select a point as seed for background.
- Similarity Criteria:
  Threshold T can be extracted from the histogram



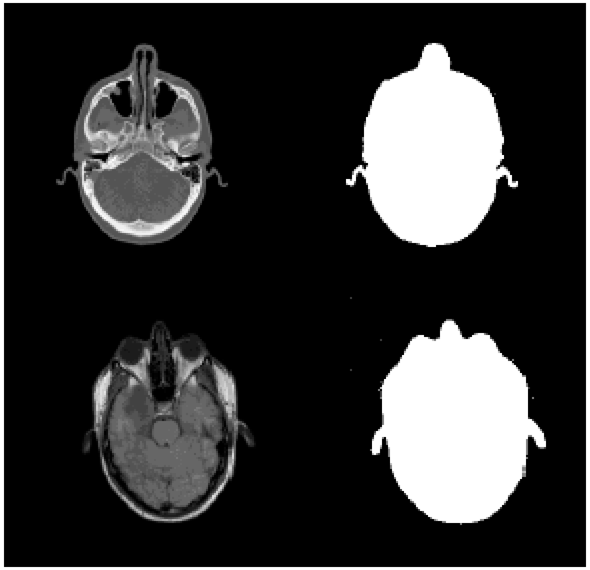


Typical histogram for CT image (left) & MR image (right)

A Binarization Approach

Region Growing Implementation

- Connectivity:
  - 8-adjacency.
- Stopping Rule:
  - No more new pixels to be included in that region.



Upper row: CT image.

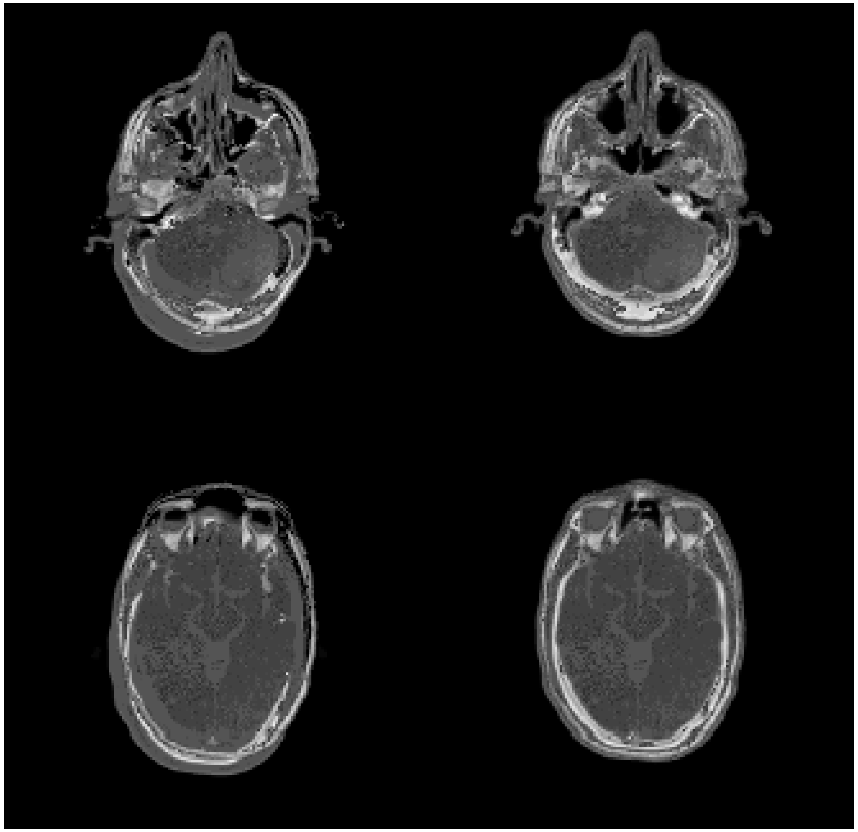
Lower row: MR image.

Left: original.

Right: binarized.

A Binarization Approach

- Result



A typical superposition of CT-MR images.

Left : before registration
Right: after registration.

A Binarization Approach

- Median and maximum error between the prospective gold-standard and several retrospective registration techniques. Ours is labeled as LO1.
  - Median Error

	BA	CO	EL	HA	HE	HI	MAI	MAL	NO	PE	RO1	LO1
CT-T1	1.6	1.5	1.6	3.4	1.4	1.2	5.1	4.3	3.3	2.7	4.2	1.26
CT-PD	1.9	1.5	2.0	3.1	2.4	1.9	4.1	4.0	7.8	1.9	4.5	1.67
CT-T2	2.5	1.5	1.6	4.2	4.7	1.5	3.9	5.0	3.9	2.5	4.5	1.64
CT-T1-rect.	1.4	0.7	0.9	3.3	1.0	0.7	4.9	5.4	3.4	2.2	5.9	0.65
CT-PD-rect.	1.7	0.8	1.1	3.0	1.7	0.7	3.0	4.0	4.6	2.1	5.9	0.85
CT-T2-rect.	2.1	0.8	1.6	3.5	1.6	0.8	4.3	5.3	4.2	2.9	5.5	0.81

  - Maximum Error

	BA	CO	EL	HA	HE	HI	MAI	MAL	NO	PE	RO1	LO1
CT-T1	6.4	6.7	6.0	51.8	11.0	2.8	12.8	61.4	10.4	7.3	26.0	3.15
CT-PD	6.9	3.6	6.6	49.6	10.4	4.1	19.0	59.0	13.9	4.3	25.9	3.64
CT-T2	9.1	3.4	4.1	50.6	13.6	4.2	6.3	59.5	9.7	7.2	26.7	3.64
CT-T1-rect.	5.8	3.8	2.6	48.2	2.1	2.3	14.2	60.9	9.6	5.9	27.8	1.98
CT-PD-rect.	5.9	2.5	5.3	45.9	3.7	2.3	9.9	62.7	11.5	4.6	27.5	2.13
CT-T2-rect.	7.4	4.3	5.2	49.1	14.3	3.0	6.5	63.2	10.2	9.0	27.1	2.65

Non-Linear Binning Approach

- Description
  - Background Segmentation (Region Growing)
  - K-means Clustering
  - Registration Using Maximization of NMI

Non-Linear Binning Approach

- Background segmentation
- Segmented image as input to K-means Clustering
  1. Initially partition the image voxels into k bins where
     k = 256.
     1a. Put all the background voxels into bin 0.
     1b. Calculate the step size for the other k-1 bins using $\frac{MaxIntensity - MinIntensity}{k-1}$

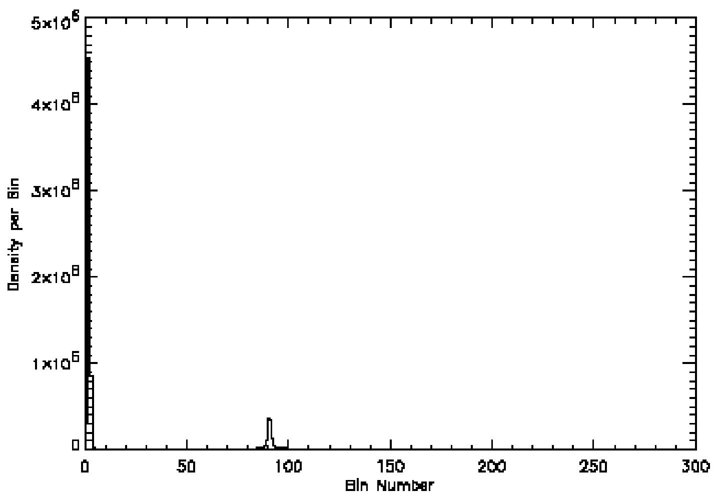
     Each bin will be assigned all voxels whose intensity falls within the range of its boundary.
     1c. Calculate the centroid of each bin.

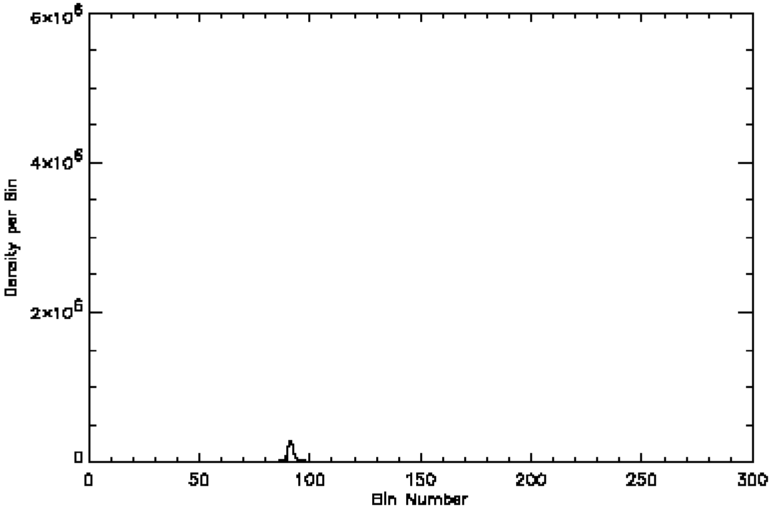
Non-Linear Binning Approach

- K-means Clustering (cont.)
  2. For each voxel in the image, compute the distances to the centroids of its current,previous, and next bin, if exists; if it is not currently in the bin with the closest centroid, switch it to that bin, and update the centroids of both bins.
  3. Repeat step 2 until convergence is achieved; that is, continue until a pass through all the voxels in the image causes no new assignments or until a maximization iterations is reached where the maximization iterations = 500.
- Two-level Registration

Non-Linear Binning Approach

- Histogram variance:





Histograms of a typical CT image (256 bins).

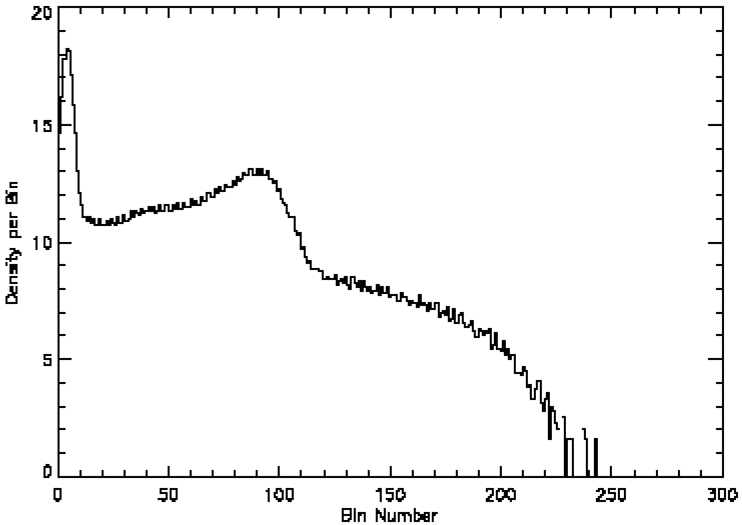
Left: The intensities are scaled to [0,255] using linear binning method;

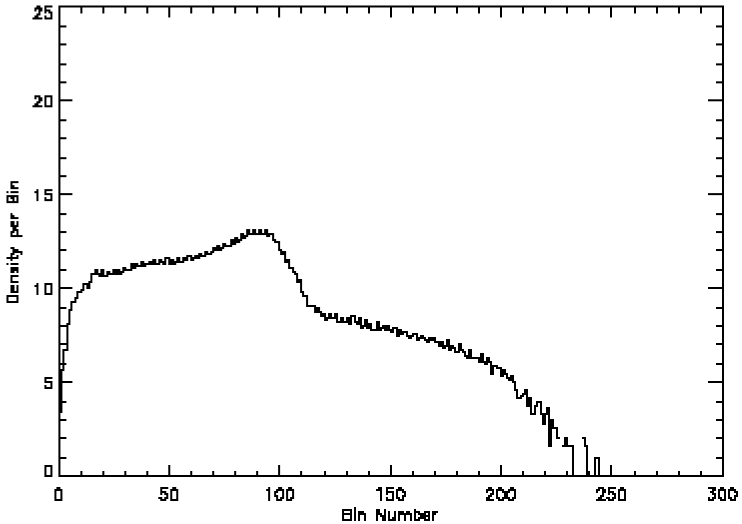
Right: Background voxels map to bin 0, the remaining voxels to bins[1,255].

Minimizing the variance of intensities within each bin.

Non-Linear Binning Approach

- Histogram variance (cont.):





Logarithmic histograms of a typical MR image (256 bins)

Left: The intensities are scaled to [0,255] using linear binning method;

Right: Background voxels map to bin 0, the remaining voxels to bins[1,255].

Minimizing the variance of intensities within each bin.

Non-Linear Binning Approach

- Median and maximum error between the prospective gold-standard and several retrospective registration techniques. Ours is labeled as LO2.
  - ✓ Median Error

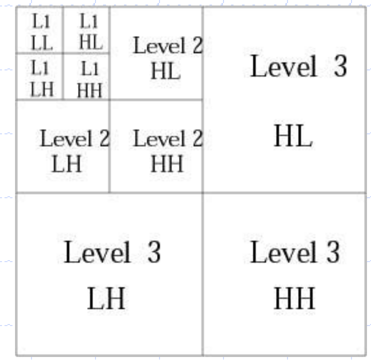
	BA	CO	EL	HA	HE	HI	MAI	MAL	NO	PE	RO1	LO2
CT-T1	1.6	1.5	1.6	3.4	1.4	1.2	5.1	4.3	3.3	2.7	4.2	1.24
CT-PD	1.9	1.5	2.0	3.1	2.4	1.9	4.1	4.0	7.8	1.9	4.5	1.90
CT-T2	2.5	1.5	1.6	4.2	4.7	1.5	3.9	5.0	3.9	2.5	4.5	1.47
CT-T1-rect.	1.4	0.7	0.9	3.3	1.0	0.7	4.9	5.4	3.4	2.2	5.9	0.96
CT-PD-rect.	1.7	0.8	1.1	3.0	1.7	0.7	3.0	4.0	4.6	2.1	5.9	0.90
CT-T2-rect.	2.1	0.8	1.6	3.5	1.6	0.8	4.3	5.3	4.2	2.9	5.5	0.89

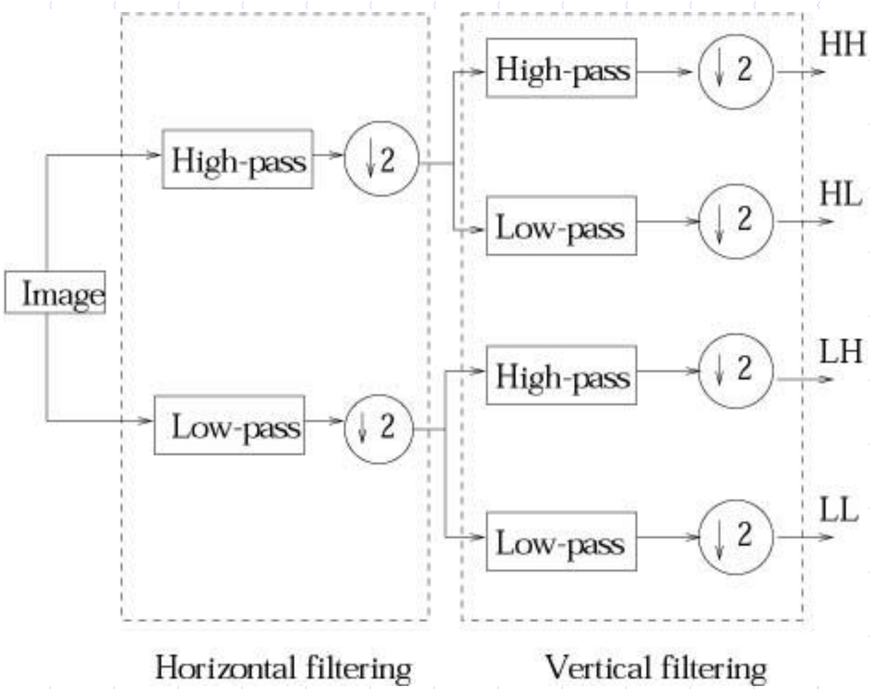
  - ✓ Maximum Error

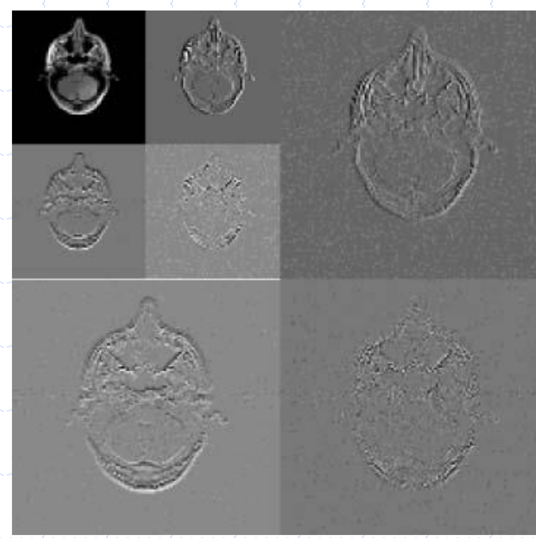
	BA	CO	EL	HA	HE	HI	MAI	MAL	NO	PE	RO1	LO2
CT-T1	6.4	6.7	6.0	51.8	11.0	2.8	12.8	61.4	10.4	7.3	26.0	2.76
CT-PD	6.9	3.6	6.6	49.6	10.4	4.1	19.0	59.0	13.9	4.3	25.9	3.91
CT-T2	9.1	3.4	4.1	50.6	13.6	4.2	6.3	59.5	9.7	7.2	26.7	4.64
CT-T1-rect.	5.8	3.8	2.6	48.2	2.1	2.3	14.2	60.9	9.6	5.9	27.8	1.95
CT-PD-rect.	5.9	2.5	5.3	45.9	3.7	2.3	9.9	62.7	11.5	4.6	27.5	1.81
CT-T2-rect.	7.4	4.3	5.2	49.1	14.3	3.0	6.5	63.2	10.2	9.0	27.1	2.05

Wavelet-based multi-resolution Approach

- Description:
  - Multi-resolution: Improve optimization speed and capture range.
  - The wavelet intends to transform images into a multi-scale representation.
  - A wavelet can be created by passing the image through a series of filter bank stages.







Wavelet-based multi-resolution Approach

- Implementation:
  - Daubechies Wavelet filter coefficients (DAUB4)

$$c_0 = (1+\sqrt{3})/4\sqrt{2} \approx 0.4829629131445341$$

$$c_1 = (3+\sqrt{3})/4\sqrt{2} \approx 0.8365163037378079$$

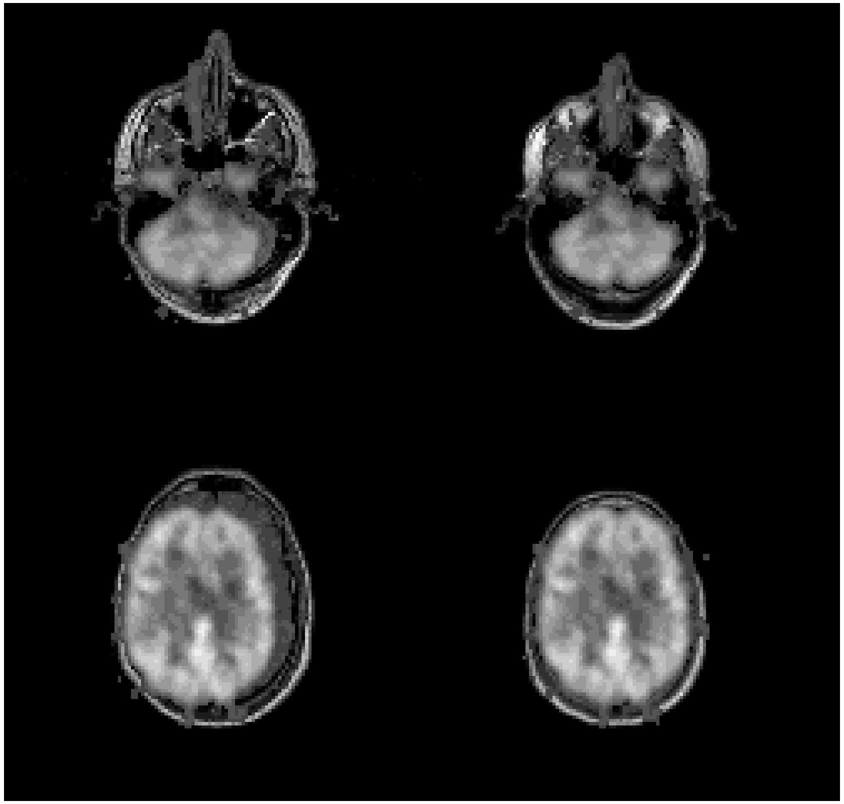
$$c_2 = (3-\sqrt{3})/4\sqrt{2} \approx 0.2241438680420134$$

$$c_3 = (1-\sqrt{3})/4\sqrt{2} \approx -0.1294095225512604$$

  - Four-level WT on 41 CT-MR pairs registration.
  - Three-level WT on 35 PET-MR pairs registration.

Wavelet-based multi-resolution Approach

- Result (cont.)



A typical superposition of PET-MR images.

Left : before registration
Right: after registration.

Wavelet-based multi-resolution Approach

- Median and maximum error between the prospective gold-standard and several retrospective registration techniques. Ours is labeled as LO3.
  - Median Error

	BA	CO	EL	HA	HE	HI	MAI	MAL	NO	PE	RO1	LO3
CT-T1	1.6	1.5	1.6	3.4	1.4	1.2	5.1	4.3	3.3	2.7	4.2	1.2
CT-PD	1.9	1.5	2.0	3.1	2.4	1.9	4.1	4.0	7.8	1.9	4.5	1.7
CT-T2	2.5	1.5	1.6	4.2	4.7	1.5	3.9	5.0	3.9	2.5	4.5	1.5
CT-T1-rect.	1.4	0.7	0.9	3.3	1.0	0.7	4.9	5.4	3.4	2.2	5.9	1.0
CT-PD-rect.	1.7	0.8	1.1	3.0	1.7	0.7	3.0	4.0	4.6	2.1	5.9	0.8
CT-T2-rect.	2.1	0.8	1.6	3.5	1.6	0.8	4.3	5.3	4.2	2.9	5.5	0.9

  - Maximum Error

	BA	CO	EL	HA	HE	HI	MAI	MAL	NO	PE	RO1	LO3
CT-T1	6.4	6.7	6.0	51.8	11.0	2.8	12.8	61.4	10.4	7.3	26.0	2.0
CT-PD	6.9	3.6	6.6	49.6	10.4	4.1	19.0	59.0	13.9	4.3	25.9	3.4
CT-T2	9.1	3.4	4.1	50.6	13.6	4.2	6.3	59.5	9.7	7.2	26.7	3.1
CT-T1-rect.	5.8	3.8	2.6	48.2	2.1	2.3	14.2	60.9	9.6	5.9	27.8	2.0
CT-PD-rect.	5.9	2.5	5.3	45.9	3.7	2.3	9.9	62.7	11.5	4.6	27.5	2.2
CT-T2-rect.	7.4	4.3	5.2	49.1	14.3	3.0	6.5	63.2	10.2	9.0	27.1	3.7

Wavelet-based multi-resolution Approach

- Median and maximum error between the prospective gold-standard and several retrospective registration techniques. Ours is labeled as LO3.
  - ✓ Median Error

	BA	CO	HA	HI	MAI	MAL	NO	PE	RO3	RO4	WO1	LO3
PET-T1	4.6	3.6	2.8	3.2	3.5	4.2	3.6	2.9	4.0	3.4	2.3	3.2
PET-PD	5.2	2.9	4.2	3.1	4.7	4.0	4.1	3.3	4.3	3.3	2.9	2.7
PET-T2	4.7	2.8	2.7	2.4	5.3	4.9	4.6	3.3	4.0	3.6	3.6	2.8
PET-T1-rect.	3.2	2.8	3.6	2.5	3.9	3.6	3.9	2.8	3.8	3.6	2.0	1.7
PET-PD-rect.	4.5	3.0	3.2	3.0	4.7	3.6	4.4	2.8	3.6	4.1	2.5	2.4
PET-T2-rect.	3.9	2.0	3.3	2.2	4.0	3.6	5.2	2.9	3.8	3.4	2.5	2.4

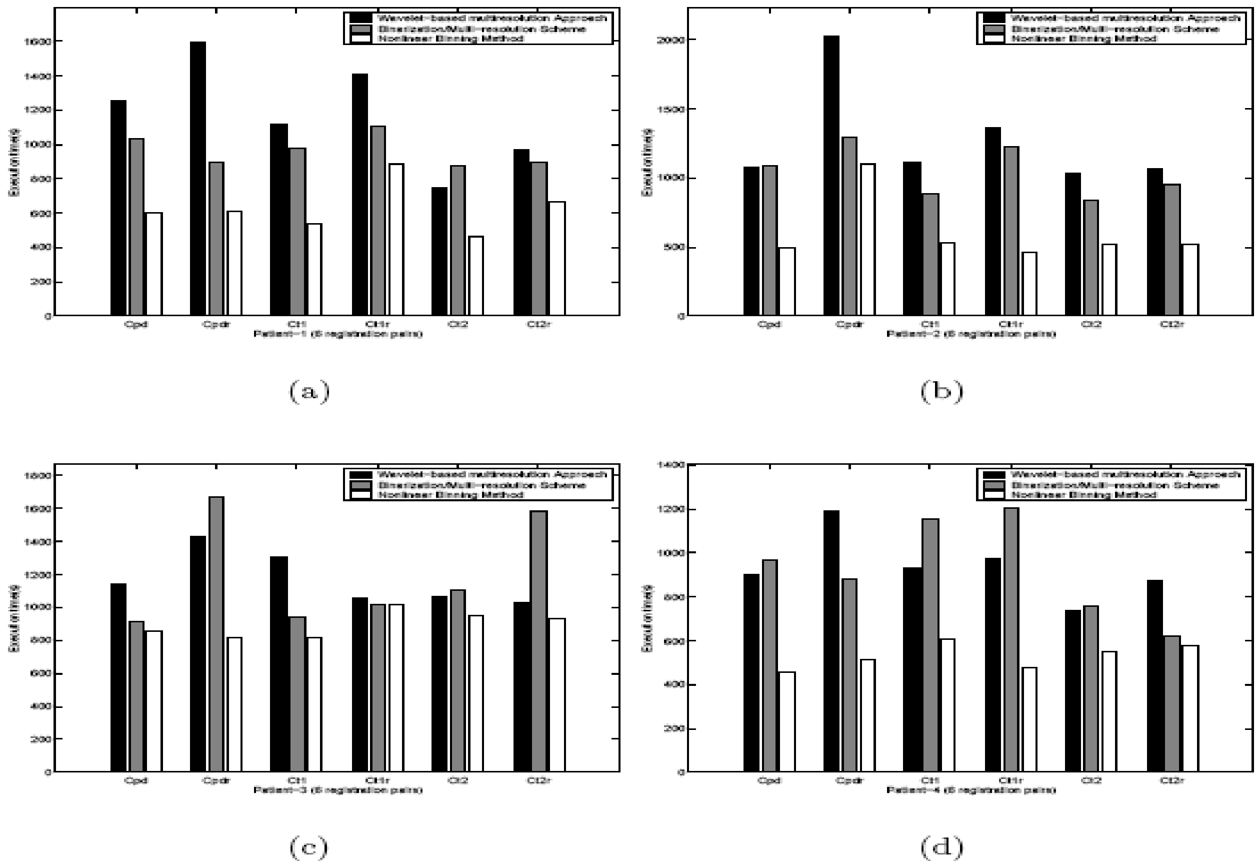
  - ✓ Maximum Error

	BA	CO	HA	HI	MAI	MAL	NO	PE	RO3	RO4	WO1	LO3
PET-T1	11.5	12.7	12.1	9.3	10.6	8.5	11.4	10.0	9.4	5.9	5.8	9.1
PET-PD	11.2	9.2	10.3	8.1	9.8	9.3	8.9	11.3	8.8	7.1	6.9	6.2
PET-T2	12.3	7.5	17.4	8.3	15.0	12.3	7.3	13.4	9.0	7.3	8.4	5.1
PET-T1-rect.	6.0	3.7	17.7	6.0	7.7	8.4	14.2	7.9	7.3	8.9	4.2	4.6
PET-PD-rect.	11.0	7.3	10.1	7.5	9.2	9.4	7.4	11.0	6.6	6.6	5.5	4.7
PET-T2-rect.	9.8	7.1	10.2	9.3	10.9	12.4	11.2	15.2	5.8	7.1	6.0	4.7

Three New Approaches Based on NMI

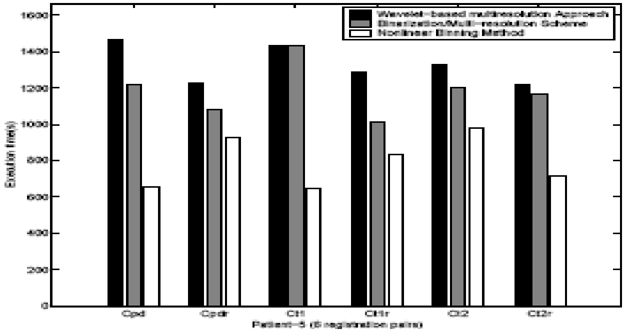
Registration Time Comparison

- Registration time required for three approaches:

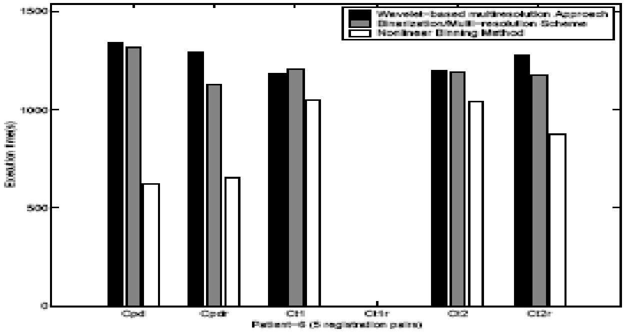


Three New Approaches Based on NMI
Registration Time Comparison

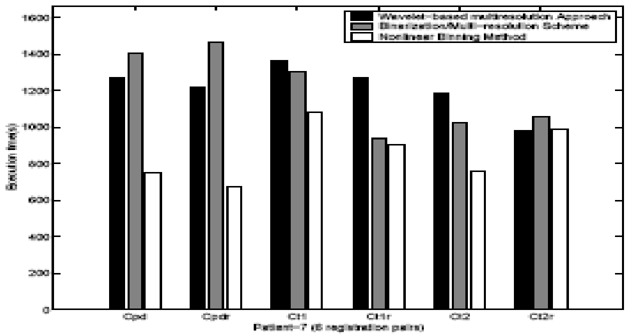
- Registration time required for three approaches:



(a)



(b)



(c)

Conclusion

- Binarization Approach:
  - ✓ Improve capture range.
  - ✓ Reach a subvoxel accuracy without loss speed.
  - ✓ For CT-MR registration.
- Non-linear Binning approach:
  - ✓ Less dispersion in join-histogram.
  - ✓ Improve accuracy and speed.
  - ✓ For CT-MR registration.
- Wavelet based multi-resolution approach:
  - ✓ Accurate subvoxel registration.
  - ✓ For CT-MR and PET-MR registration.
- Can be used in clinical cases.

Results are accessible via:
http://www.vuse.vanderbilt.edu/~image/registration/results.html

Future Work

- Other approaches derived from our new approaches:
  - Coherence.
  - Alternative bin size & other clustering method.
  - More Wavelet filters & other sub-bands.

- Approaches derived from registration by mutual information:
  - the influence of implementation parameters of registration of CT and MR brain image.

- Extension to non-rigid body registration:
  - non-rigid transformation needs more parameters
  - rigid registration can be the basis for non-rigid
  - hierarchical strategy used in non-rigid registration

Thank you