New Software for PET/MR Image Registration

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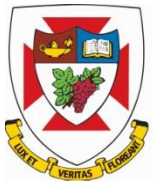
CAP Congress 2014
Sudbury, ON



THE UNIVERSITY OF WINNIPEG

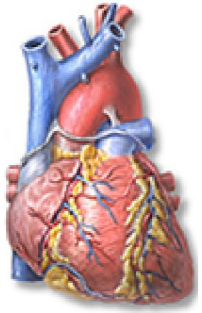
Contents

- Biomedical Application
  - Stem Cell Therapy
  - Rat Infarct Heart Model
- Imaging Techniques
  - Positron Emission Tomography (PET)
  - Magnetic Resonance Imaging (MRI)
- Image Registration
  - Affine Image Registration
- Work in progress

Biomedical Application: Statistics

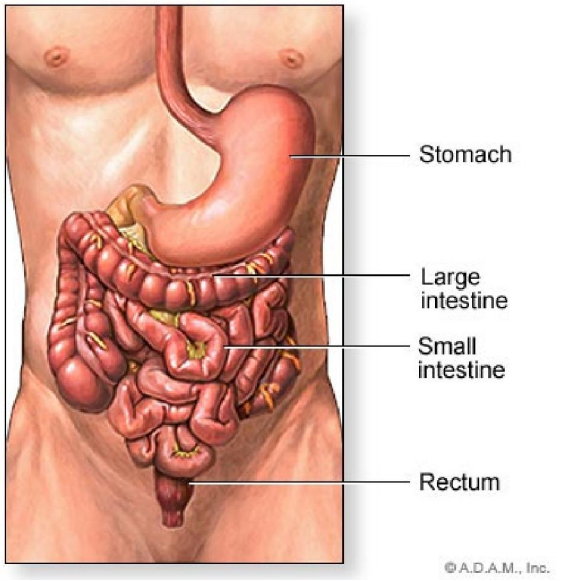
- 30% of Canadian deaths are due to cardiovascular disease
  - 50% of deaths in the United States
- Costs Canadian economy ~20 billion every year
  - Due to hospital costs, physician services, lost wages, and decreased productivity
- How can we reduce the number of deaths due to cardiovascular disease?

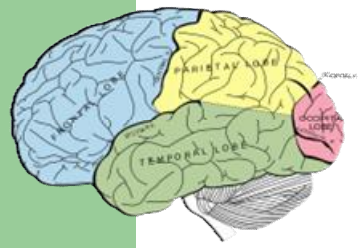
Biomedical Application: Stem Cell Therapy



Stem cell therapy may be able to treat several diseases and disorders such as:

- Cardiovascular Diseases
  - Ischemic Heart Disease
  - Acute Myocardial Infarction
- Digestive Disease
  - Crohn's Disease
- Neurological Disorders
  - Temporal Lobe Epilepsy



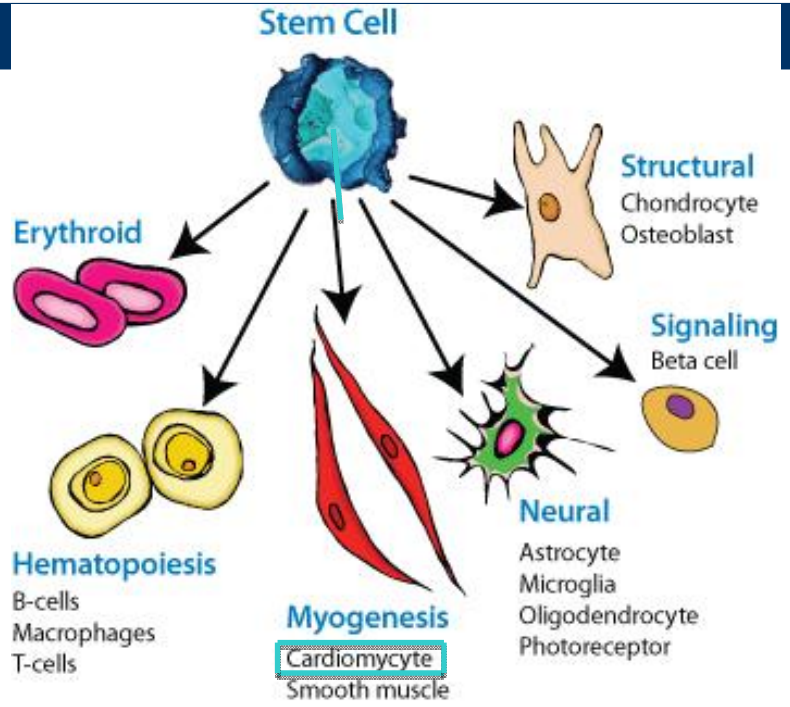


http://www.nlm.nih.gov/medlineplus/heartdiseases.html

http://en.wikipedia.org/wiki/Human_brain

http://www.healthcentral.com

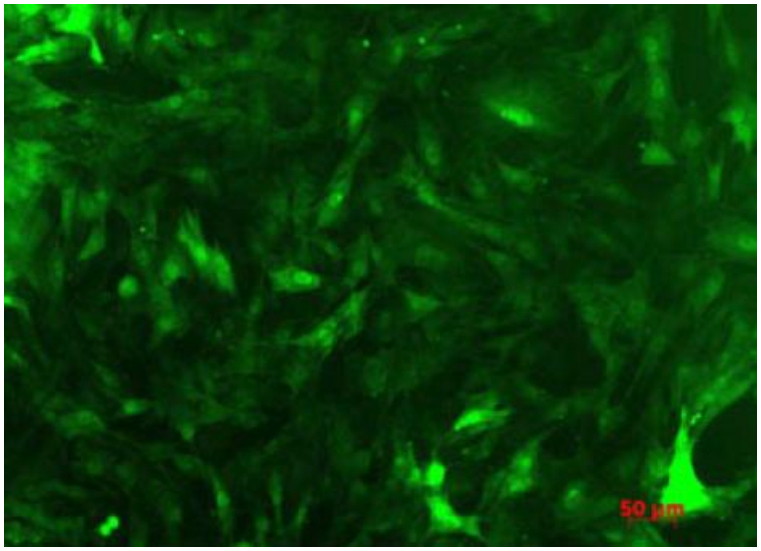
Biomedical Application: Stem Cell Therapy



Two main categories of stem cells:
- Somatic (Adult) Stem Cells
- Embryonic Stem Cells

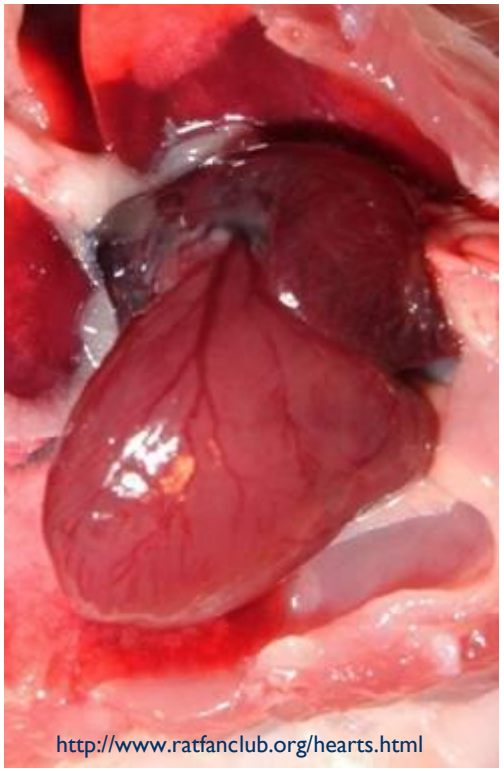
Adipose derived stem cells are multipotent, meaning they have the ability to differentiate into several different cells

Stem cells have the ability to differentiate into cardiomyocytes

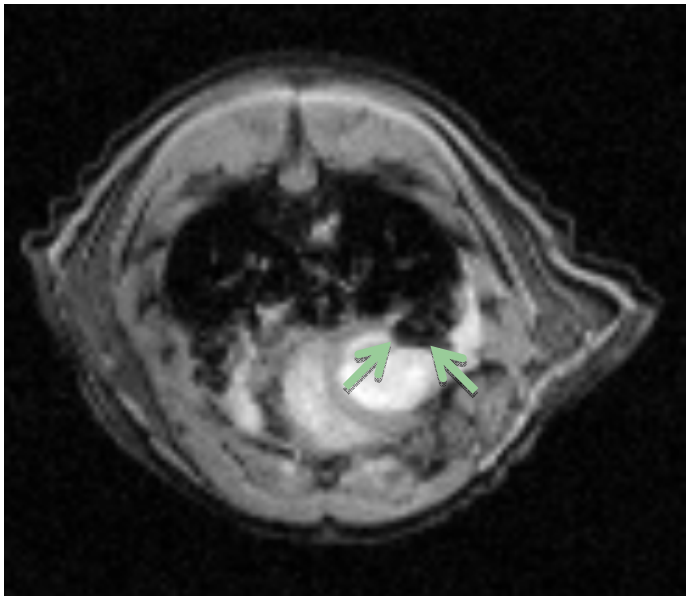


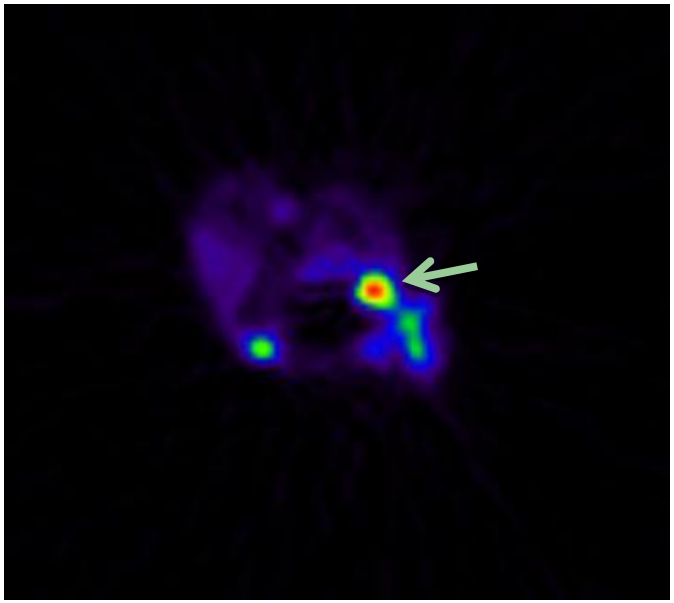
Biomedical Application: Rat Model of Heart Infarction

- Rat model heart failure
  - Heart attack induced by occluding the artery supplying oxygenated blood to the heart muscle
- Inject stem cells directly into myocardial tissue
- Repair damaged heart muscle with stem cells

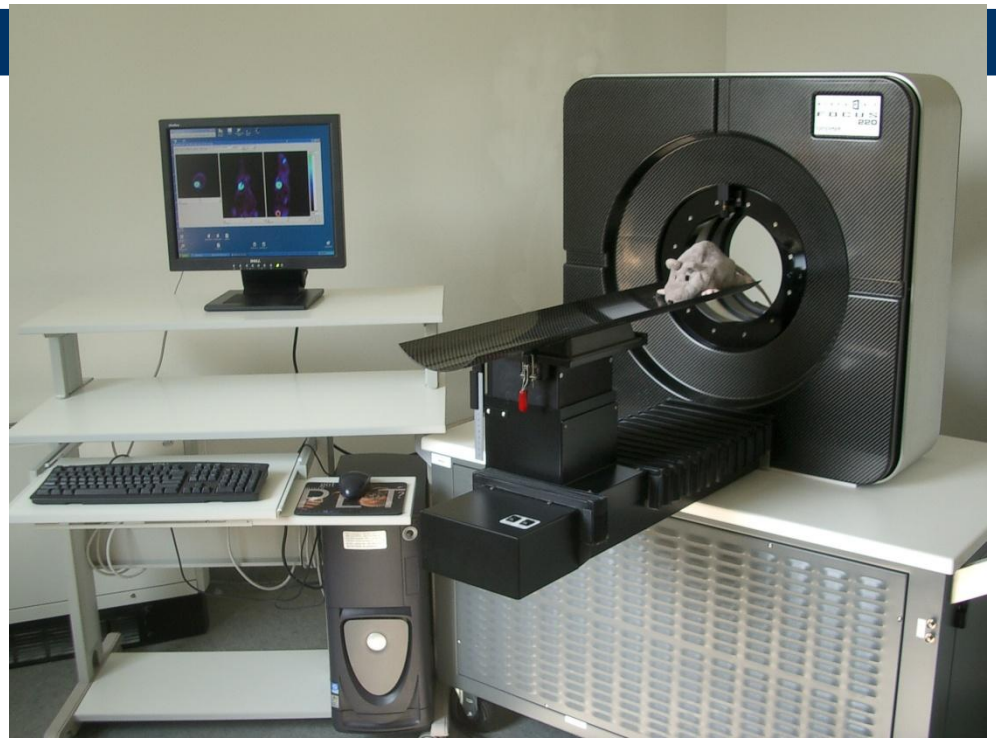


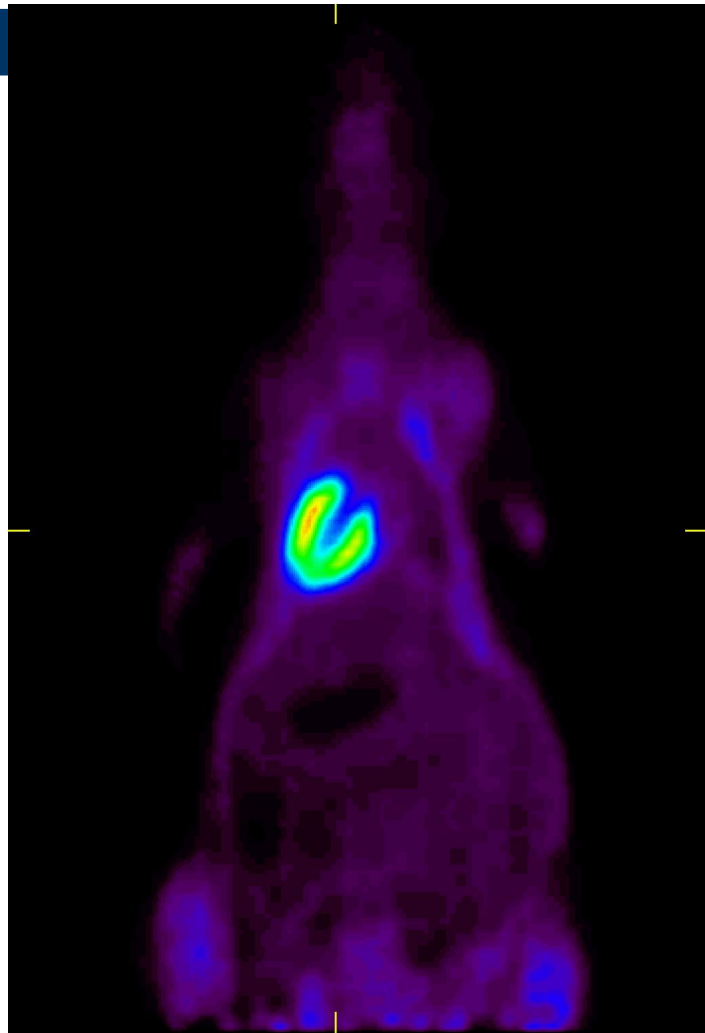
- Stem cells are combined with:
  - ^{18}F-FDG (Fluoro-2-deoxy-D-glucose)
    - Shows up in PET images
  - SuperParamagnetic Iron Oxide (SPIO) particles
    - Shows up as dark regions in MR image





Imaging Techniques
Positron Emission Tomography

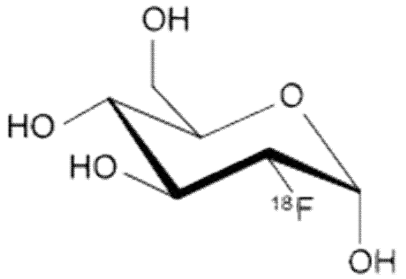




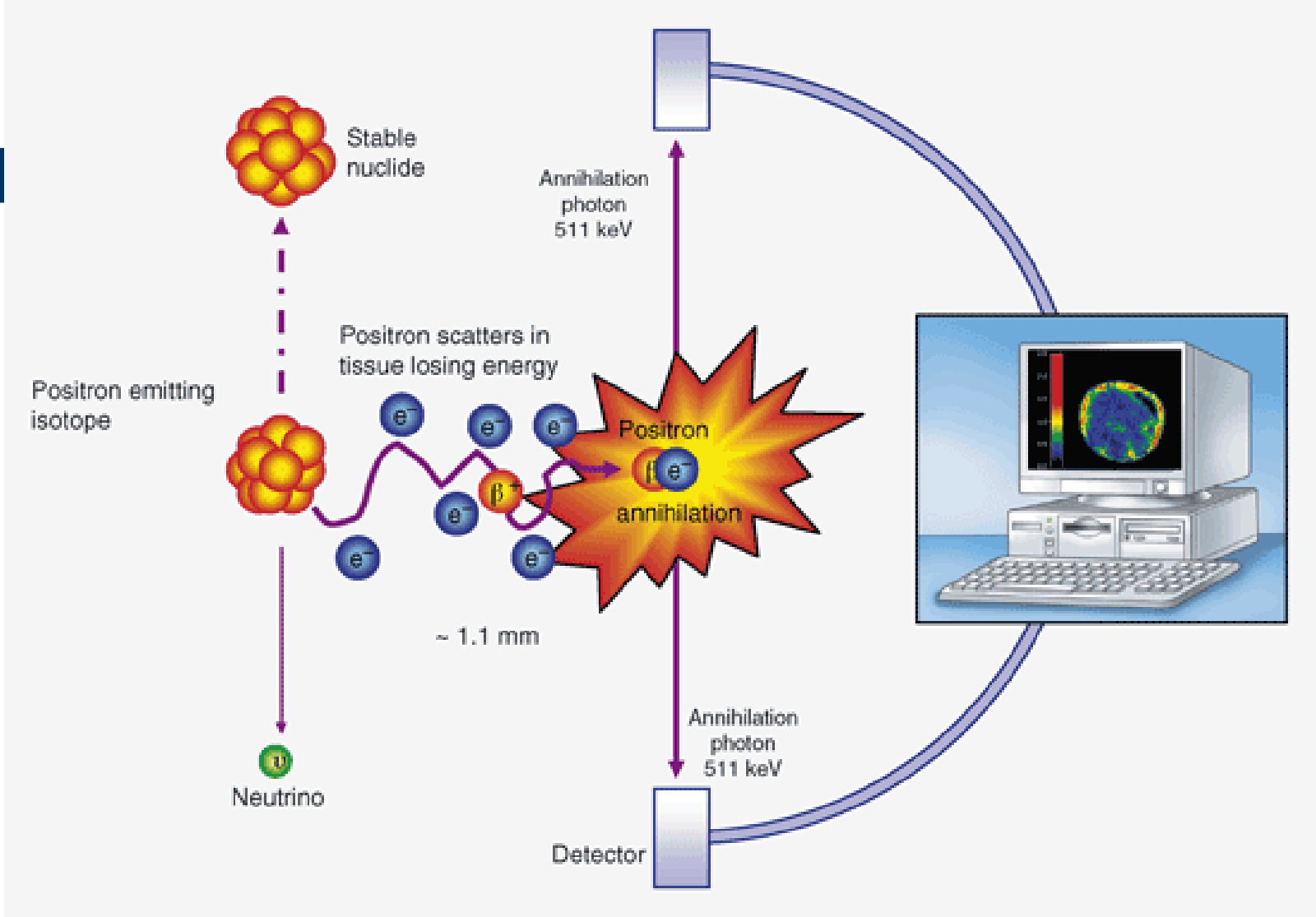
Imaging Techniques
Positron Emission Tomography

- PET is a functional imaging modality
  - Images are of physiological processes
  - Most common example is glucose uptake

- Radiopharmaceuticals
  - Radionuclide attached to a chemical tracer
  - ^{18}F-FDG (Fluoro-2-deoxy-D-glucose)
  - Administered intravenously

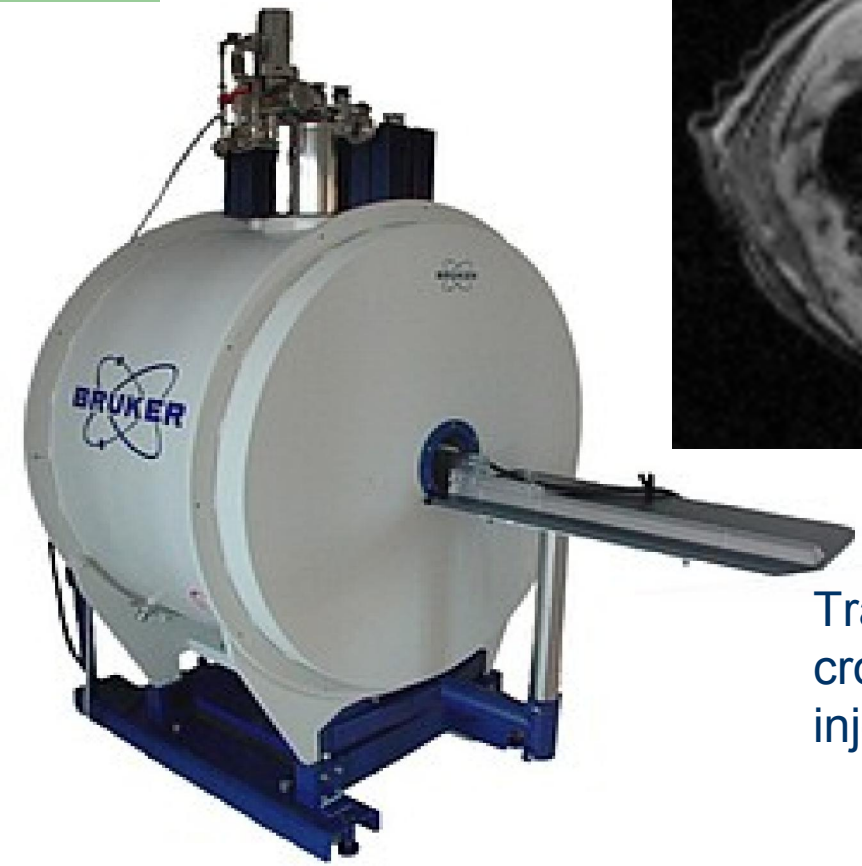


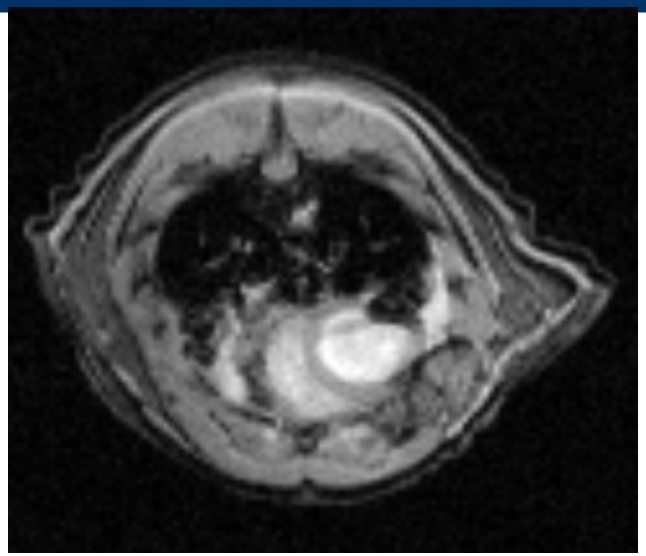
http://en.wikipedia.org/wiki/Fludeoxyglucose_(18F)



http://vefir.mh.is/emjul/efni/nemverk/nemverkv09/SPG/eldsneyti.htm

Imaging Techniques
Magnetic Resonance Imaging

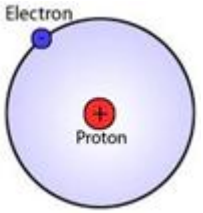




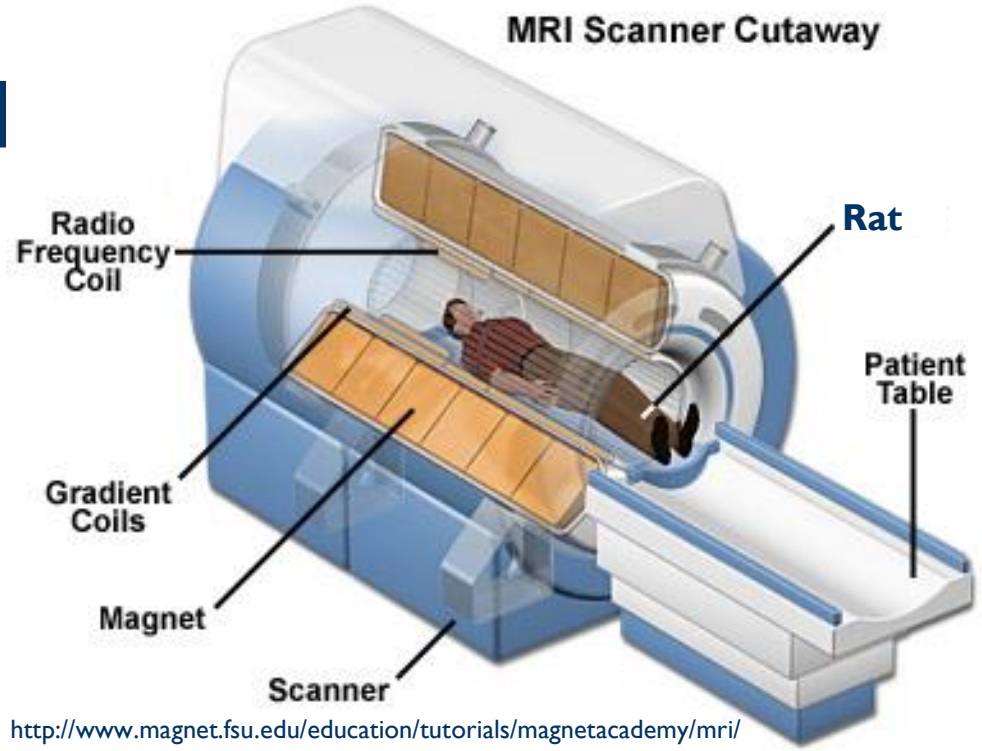
Transverse and Coronal cross sections of a rat injected with stem cells

- MRI is an anatomical imaging modality
  - Creates detailed image of object

- MRI creates images by utilizing the nuc properties of matter (Hydrogen)
  - Hydrogen contains 1 proton & 1 electron



- Humans made up of 75% H_2O
  - H_2O contains 2 H atoms (2 protons)



http://www.magnet.fsu.edu/education/tutorials/magnetacademy/mri/

MRI scanner has a submillimeter resolution

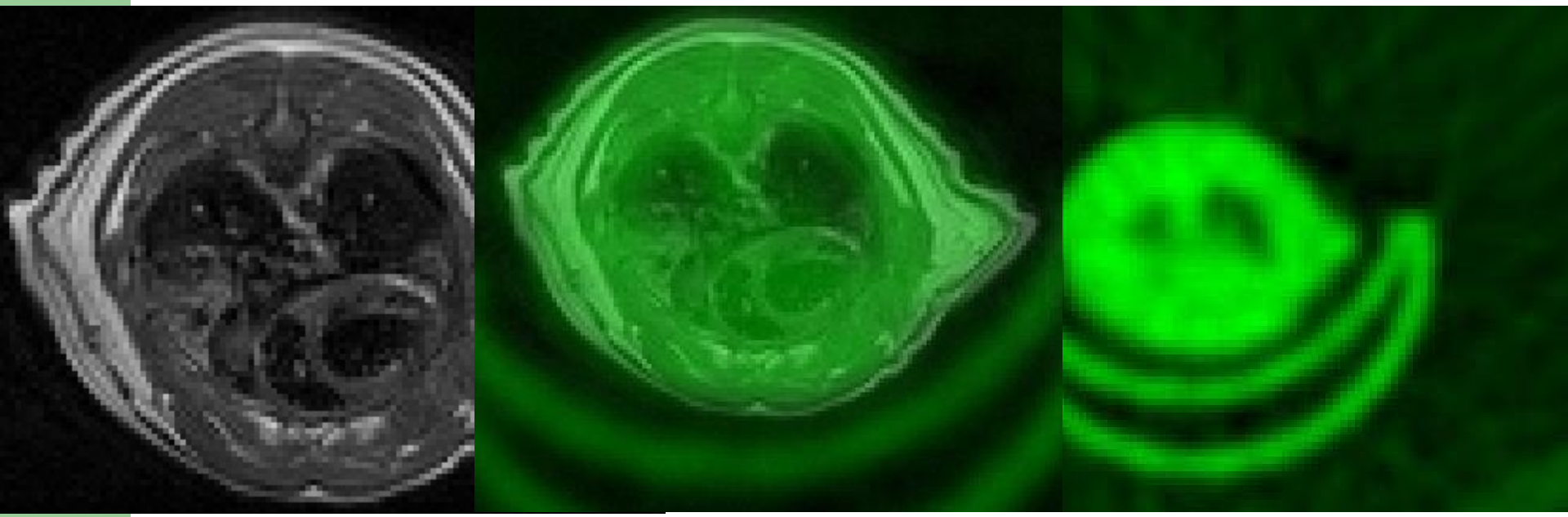
Large magnet aligns protons

RF coil sends energy to protons

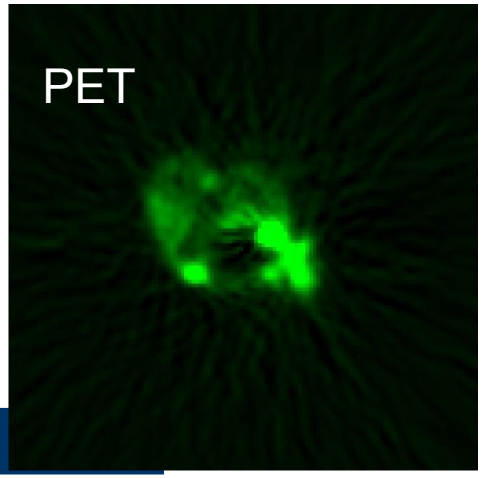
As protons relax they release energy, which is detected by RF coil

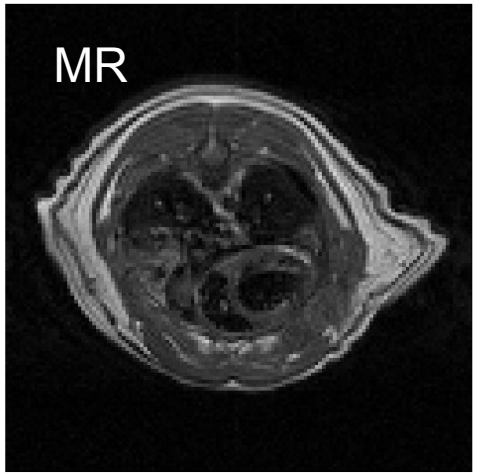
Gradient coils allow for localization of the signal, by creating a gradual change in the x, y, and z axis fields.

Image Registration



- PET images contain functional information, which is used to determine the stem cell location and proliferation
- Anatomical MRI images show detailed information of the structure, but not stem cell location (except injection site)
- Combining these two imaging modalities, is essential for quantification





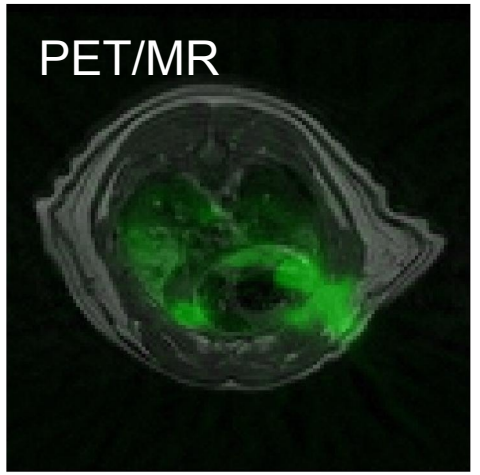
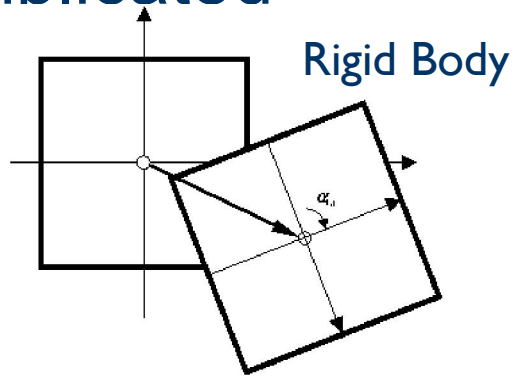
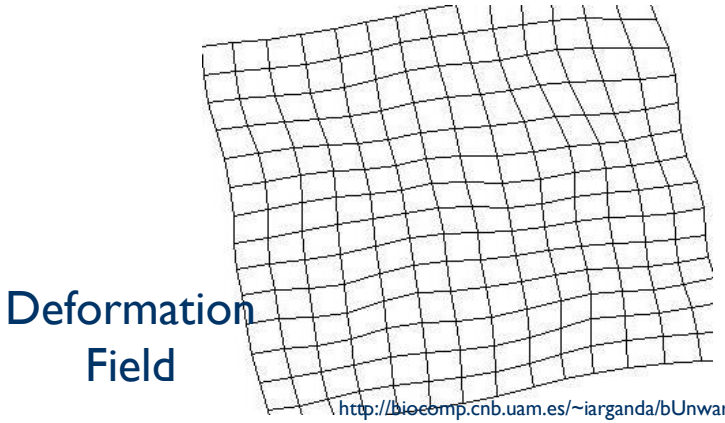


Image Registration Algorithm

- Several image transformations exist
  - Rigid Body (3 DOF – 6 DOF)
  - Affine (6 DOF – 9 DOF)
  - Deformation Field (non-linear: ∞ DOF)
- Rigid body too simple and non-linear too complicated

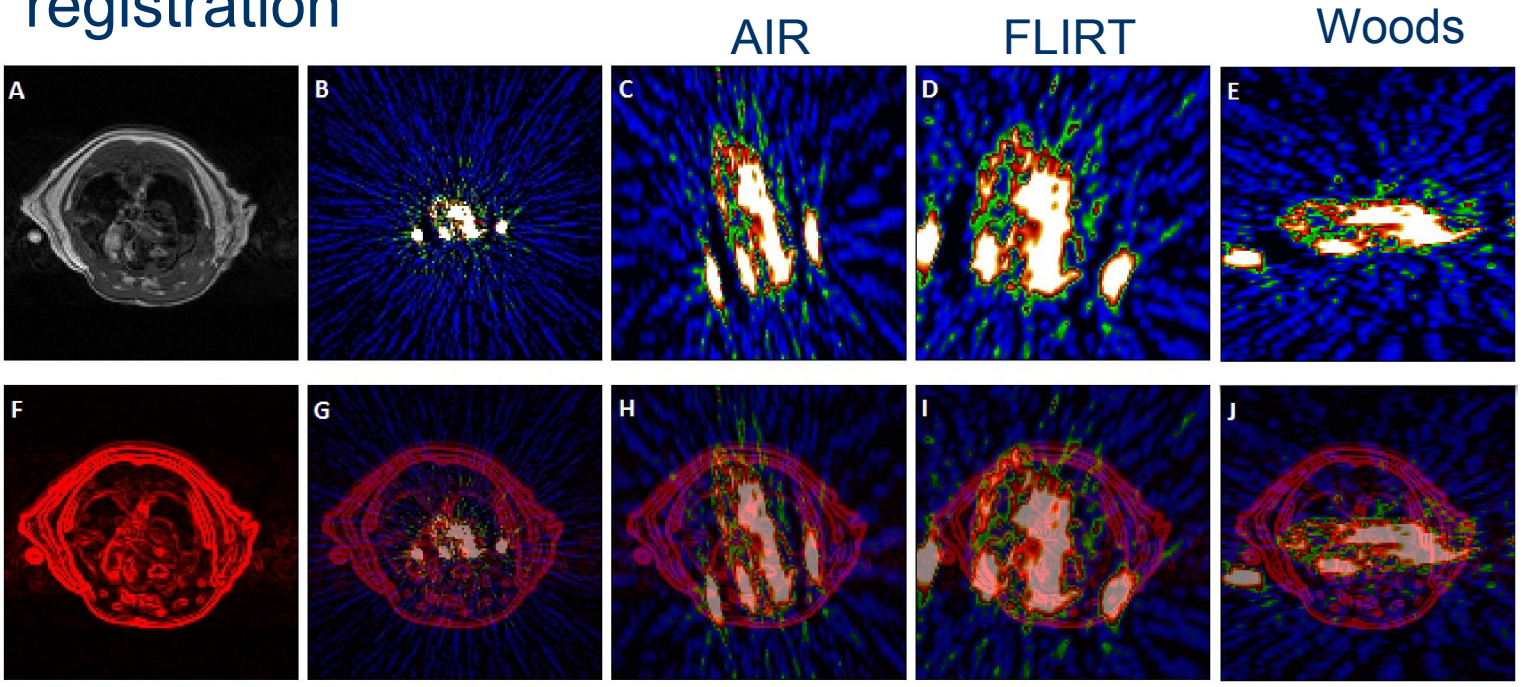




- Automated image registration programs
  - Automatic Image Registration (AIR),
  - FMRIB's Linear Image Registration Tool (FLIRT),
  - Medical Image Processing, Analysis, and visualization (MIPAV),
- Various Cost Functions for image registration (minimization of the cost ft.)
  - correlation ratio (CR)
  - normalized cross correlation (NCC)
  - mutual information (MI)
  - normalized mutual information (NMI)
  - Woods algorithm (Woods)

Application to Animal Images

- Due to the fact that the cardiac region of the PET and MRI images are not similar, automated image registration software did not produce accurate registration



Affine Image Registration

- An affine transformation is any transformation in which parallel lines remain parallel (preservation of collinearity)
  - Transformations include:
    - Translation
    - Rotation
    - Skew
    - Scale
    - Any combination of the above

- Some math:

$$y_i = a_{ij} x_j + t_j \qquad i, j = 1,2,3$$

$$\begin{pmatrix} y_1 \\ y_2 \\ y_3 \\ 1 \end{pmatrix} = \begin{pmatrix} a_{11} & a_{12} & a_{13} & t_x \\ a_{21} & a_{22} & a_{23} & t_y \\ a_{31} & a_{32} & a_{33} & t_z \\ 0 & 0 & 0 & 1 \end{pmatrix} \begin{pmatrix} x_1 \\ x_2 \\ x_3 \\ 1 \end{pmatrix}$$

- The 3x3 a_{ij} matrix includes:
  - Rotation, Skew, & Scale
- t_x, t_y, & t_z are translation variables

- Scale Matrix

$$Sc = \begin{pmatrix} Sc_x & 0 & 0 & 0 \\ 0 & Sc_y & 0 & 0 \\ 0 & 0 & Sc_z & 0 \\ 0 & 0 & 0 & 1 \end{pmatrix}$$

- Skew Matrix

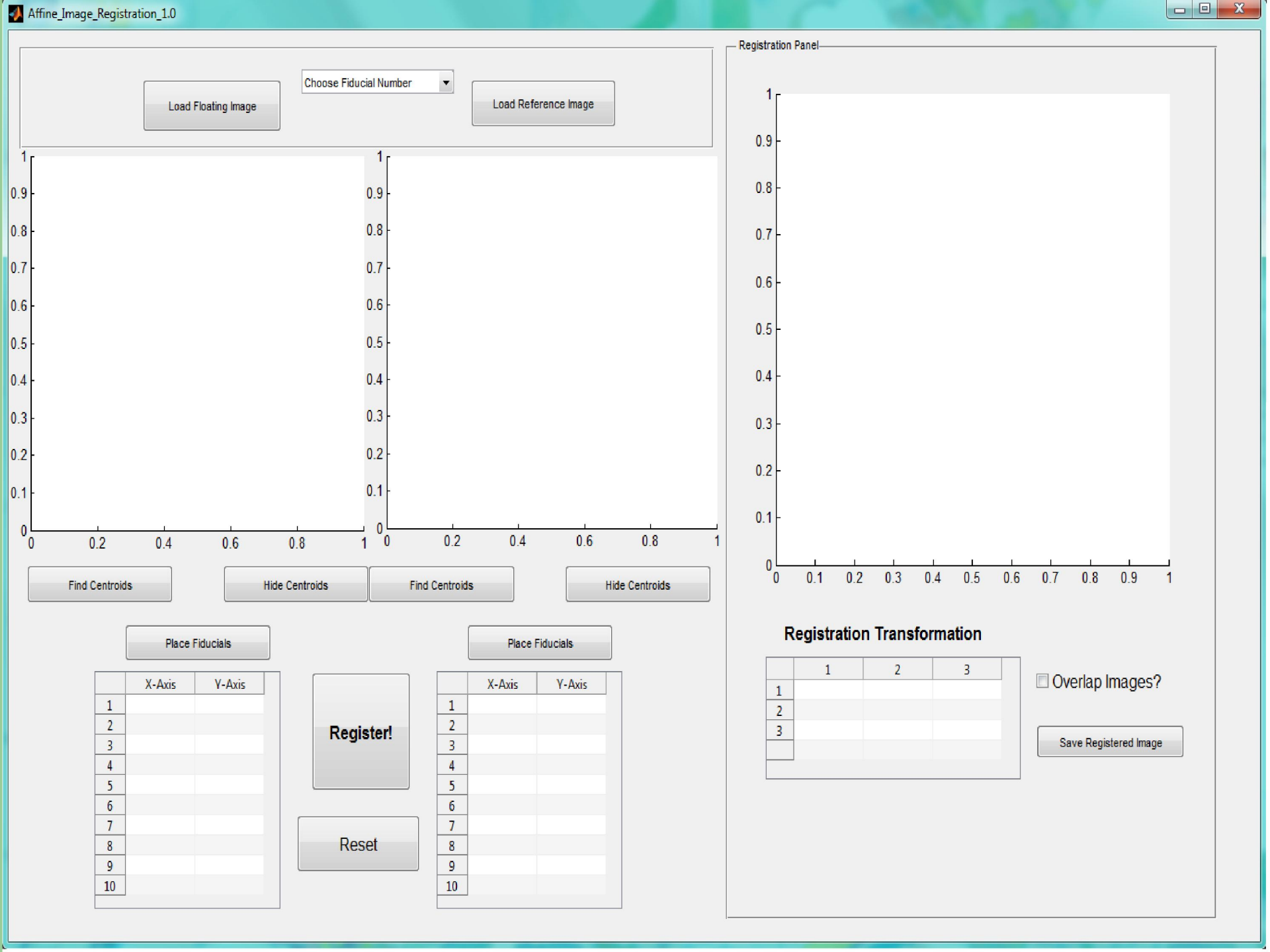
$$Sk = \begin{pmatrix} 1 & Sk_{xy} & Sk_{xz} & 0 \\ Sk_{yx} & 1 & Sk_{yz} & 0 \\ Sk_{zx} & Sk_{zy} & 1 & 0 \\ 0 & 0 & 0 & 1 \end{pmatrix}$$

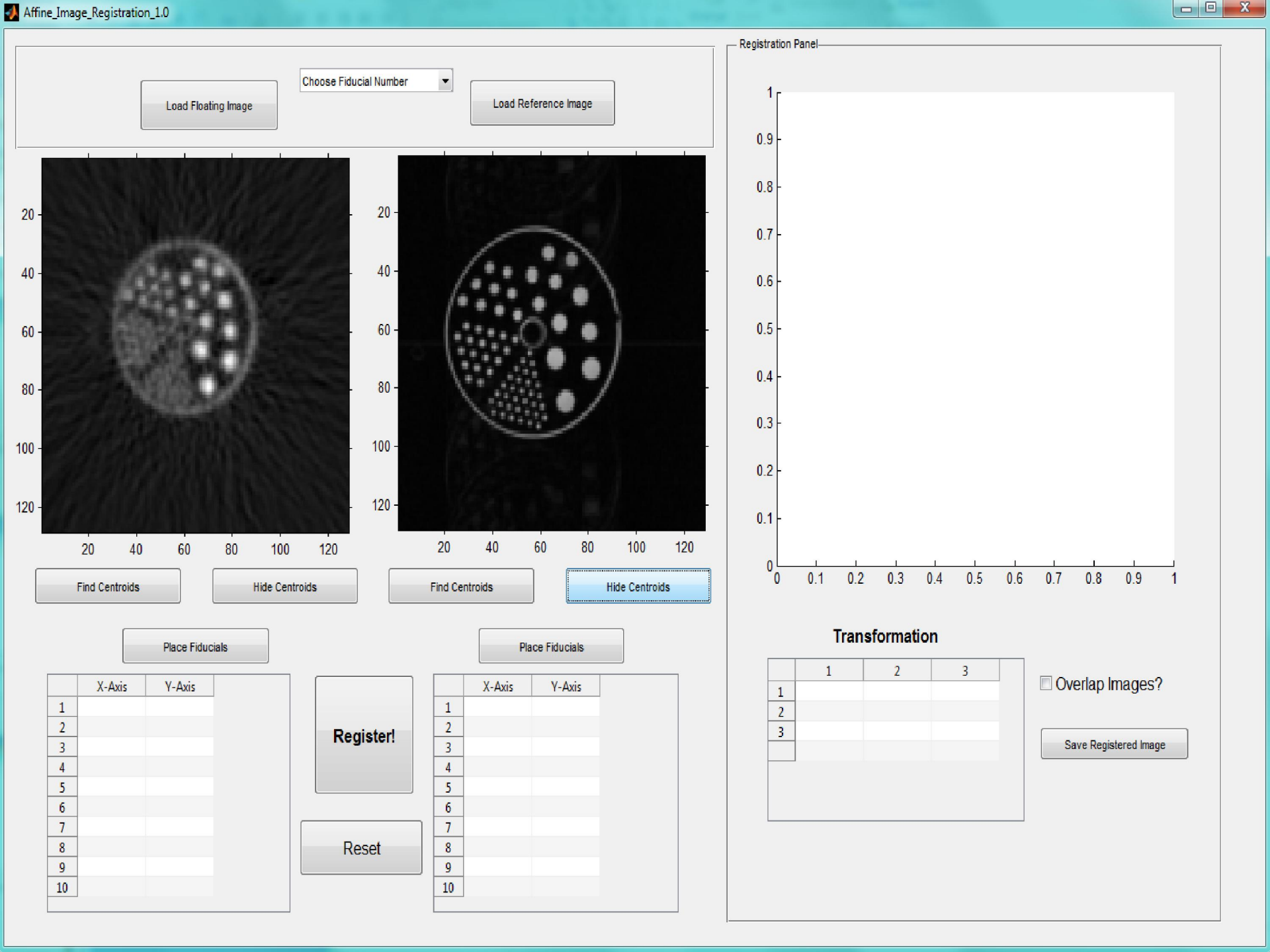
- Rotation Matrix about z-axis

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

- A simple affine transformation may be the solution
- Transformation is calculated using fixed points between the two images
  - Requires fiducial markers for accurate registration
    - Fiducial markers spheres filled with contrast agents visible in both imaging modalities
  - Can use anatomical landmarks, but not rigid enough for accurate registration

- Using Matlab software, a program was developed to perform affine image registration
  - The user loads in a floating image, and a reference image
    - Floating image is mapped to reference image
  - The user selects a number of fiducial markers, or landmarks
    - Must be # of Dimensions + 1 at minimum


Affine_Image_Registration_1.0
Load Floating Image
Choose Fiducial Number
Load Reference Image
Registration Panel
Find Centroids
Hide Centroids
Find Centroids
Hide Centroids
Place Fiducials
Place Fiducials
X-Axis
Y-Axis
Register!
Reset
Registration Transformation
Overlap Images?
Save Registered Image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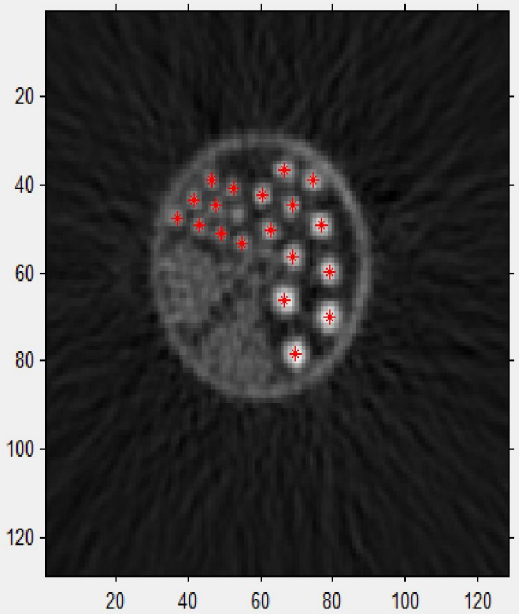
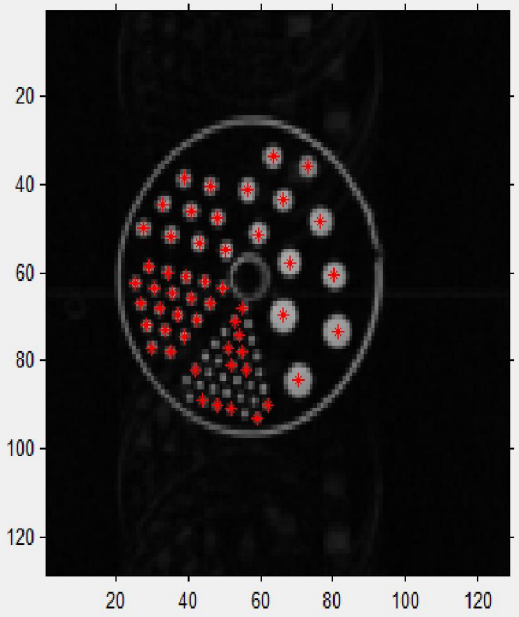
Load Floating Image

Choose Fiducial Number

Load Reference Image





Find Centroids

Hide Centroids

Find Centroids

Hide Centroids

Place Fiducials

	X-Axis	Y-Axis
1		
2		
3		
4		
5		
6		
7		
8		
9		
10		

Register!

Reset

Place Fiducials

	X-Axis	Y-Axis
1		
2		
3		
4		
5		
6		
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8		
9		
10		

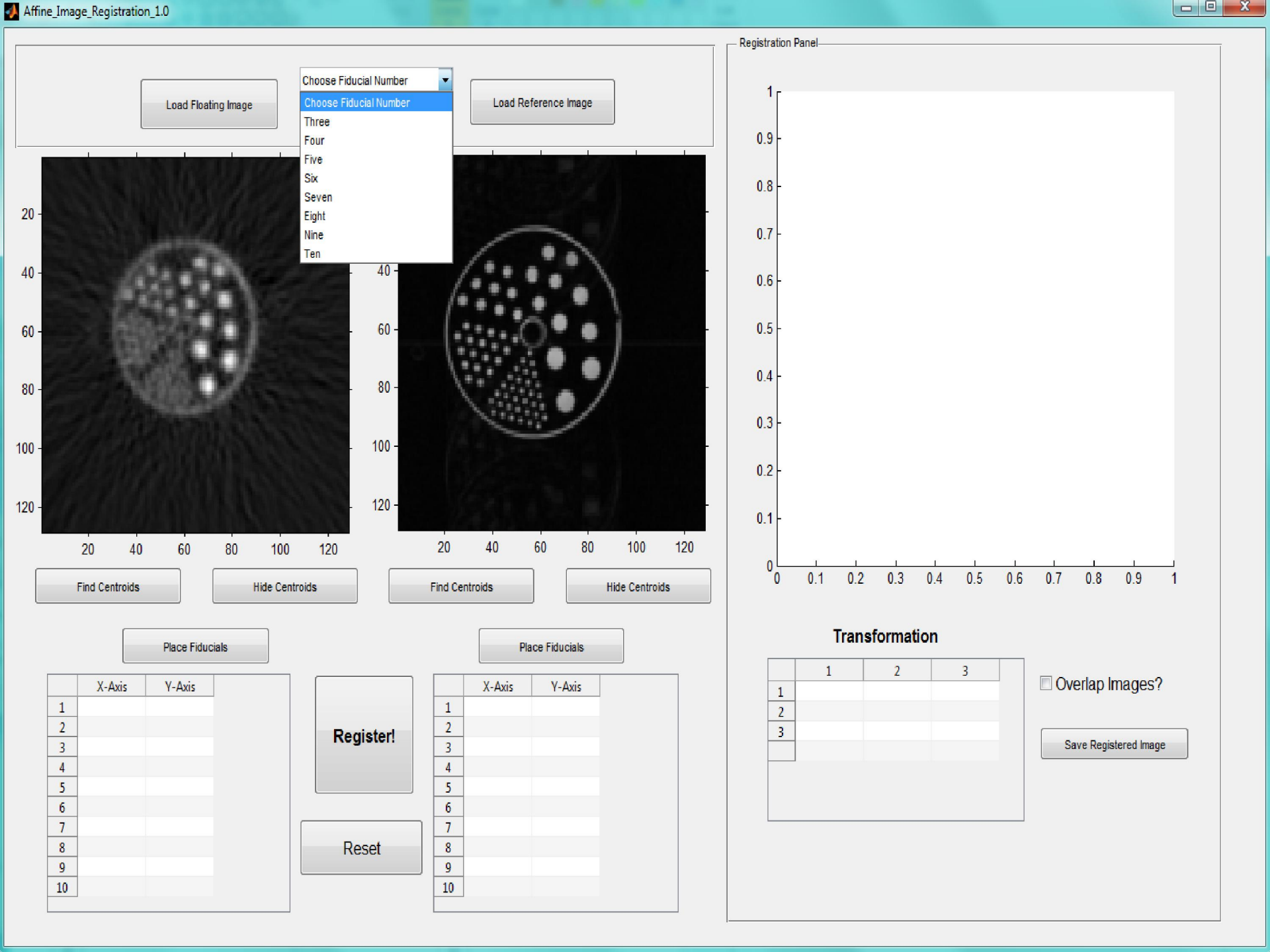
Registration Panel

Transformation

	1	2	3
1			
2			
3			

Overlap Images?

Save Registered Image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Load Floating Image
Choose Fiducial Number
Choose Fiducial Number
Three
Four
Five
Six
Seven
Eight
Nine
Ten
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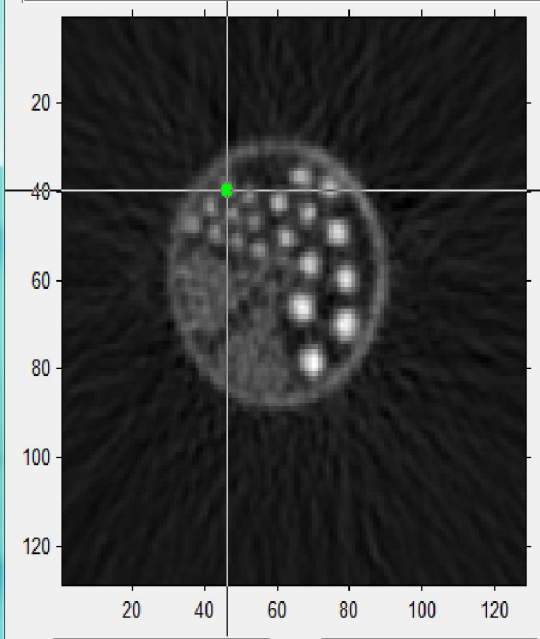
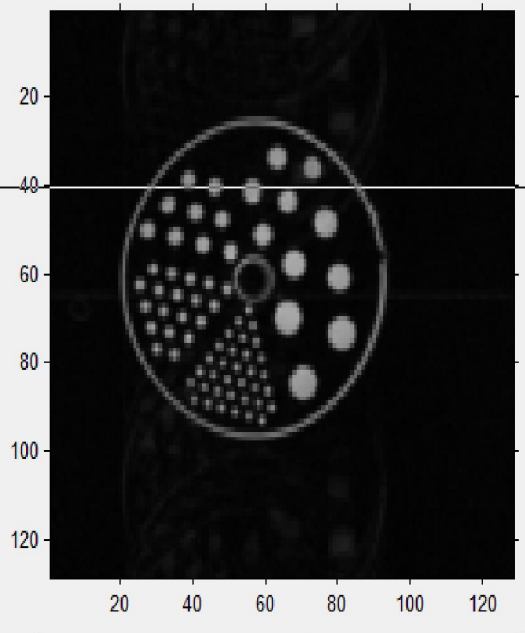
Affine_Image_Registration_1.0

Load Floating Image

Five

Load Reference Image





Find Centroids

Hide Centroids

Find Centroids

Hide Centroids

Place Fiducials

	X-Axis	Y-Axis
1	46.1331	39.6953
2	0	0
3	0	0
4	0	0
5	0	0
6	0	0
7	0	0
8	0	0
9	0	0
10	0	0

Register!

Reset

Place Fiducials

	X-Axis	Y-Axis
1		
2		
3		
4		
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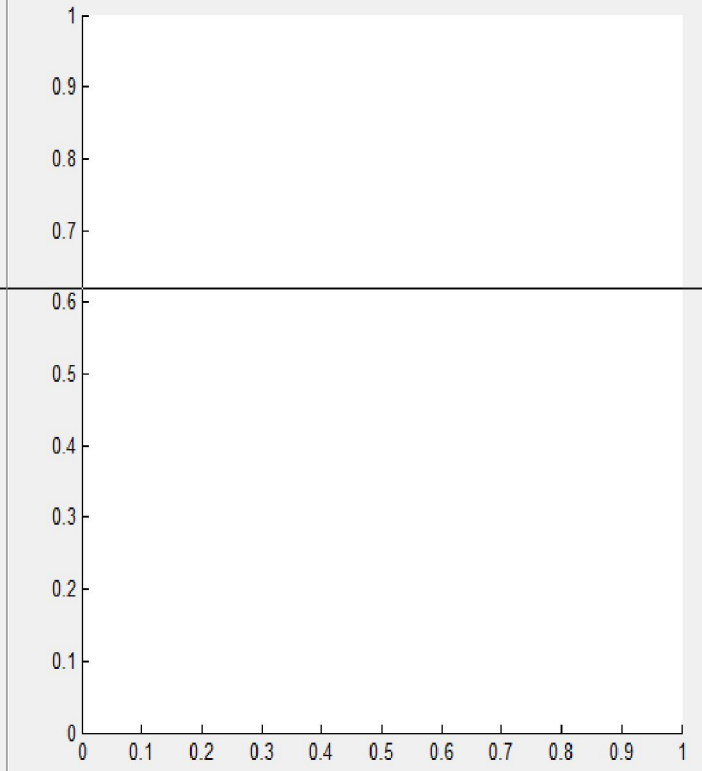
8		
9		
10		

Registration Panel



Transformation

	1	2	3
1			
2			
3			

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Affine_Image_Registration_1.0

Load Floating Image

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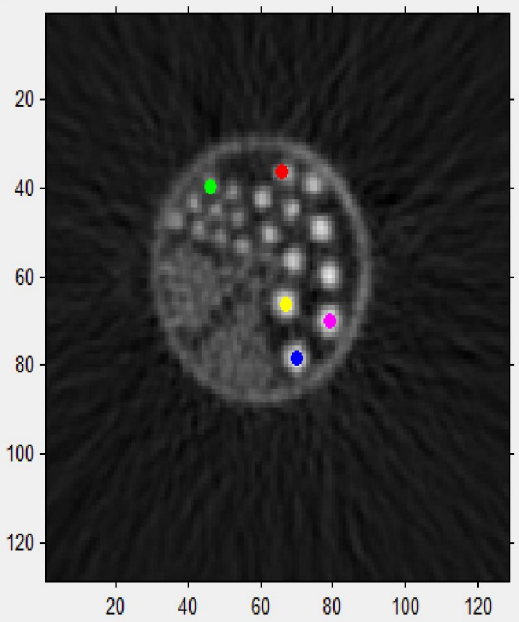
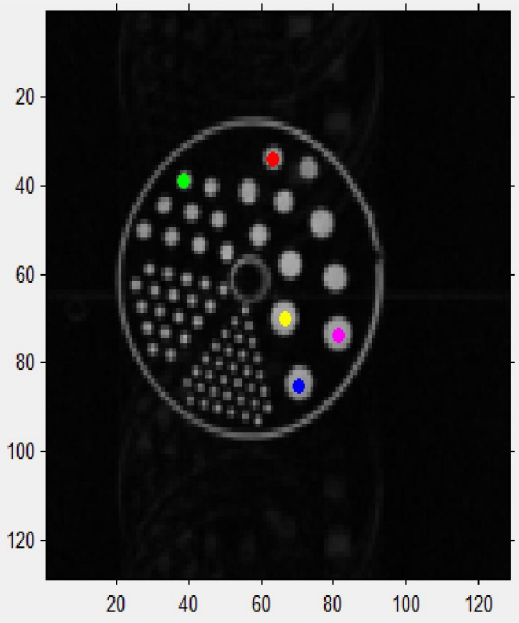




Find Centroids

Hide Centroids

Find Centroids

Hide Centroids

Place Fiducials

	X-Axis	Y-Axis
1	46.1331	39.6953
2	65.8254	36.2870
3	69.9911	78.3225
4	79.0799	69.9911
5	66.9615	66.2041
6	0	0
7	0	0
8	0	0
9	0	0
10	0	0

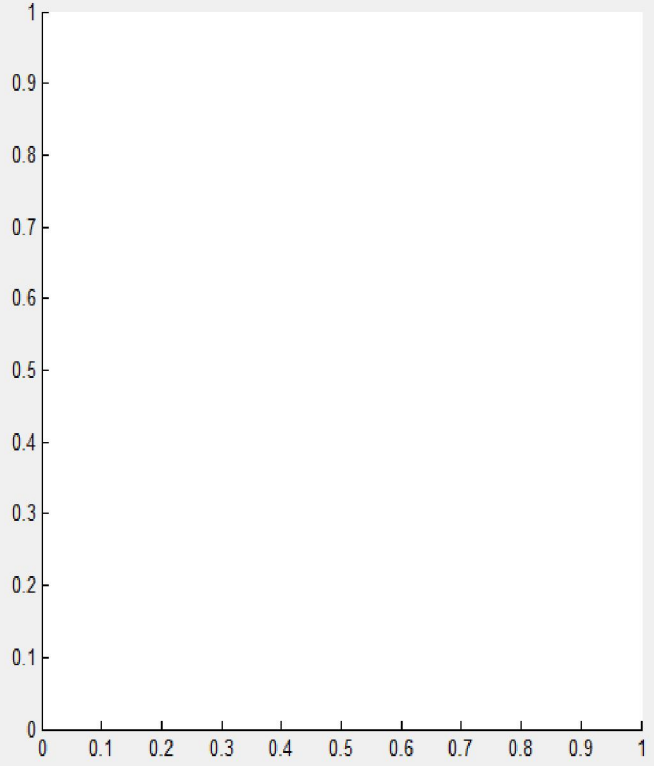
Register!

Reset

Place Fiducials

	X-Axis	Y-Axis
1	38.5592	38.9379
2	63.1746	34.0148
3	70.3698	85.1391
4	81.3521	73.7781
5	66.5828	69.9911
6	0	0
7	0	0
8	0	0
9	0	0
10	0	0

Registration Panel



Transformation

	1	2	3
1			
2			
3			

Overlap Images?

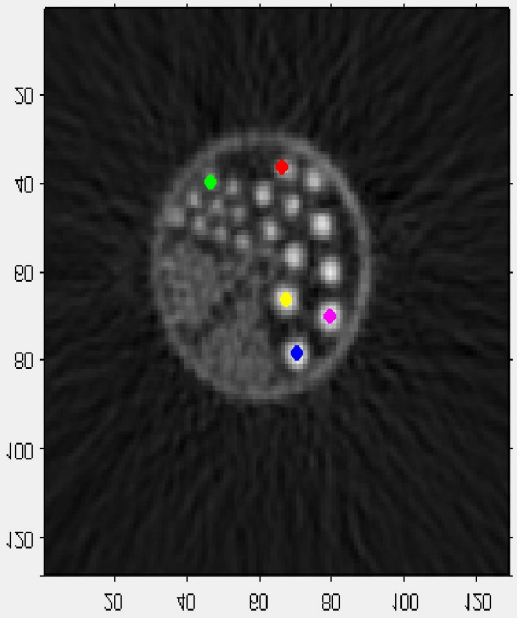
Save Registered Image

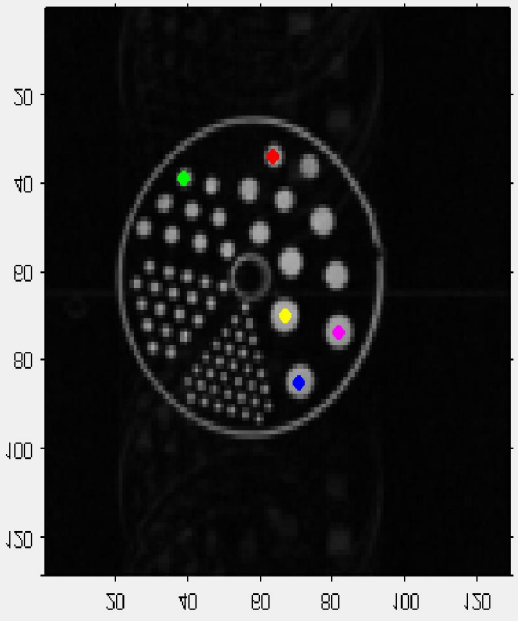
Affine_Image_Registration_1.0

Load Floating Image

Five

Load Reference Image





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5	66.9615	66.2041
6	0	0
7	0	0
8	0	0
9	0	0
10	0	0

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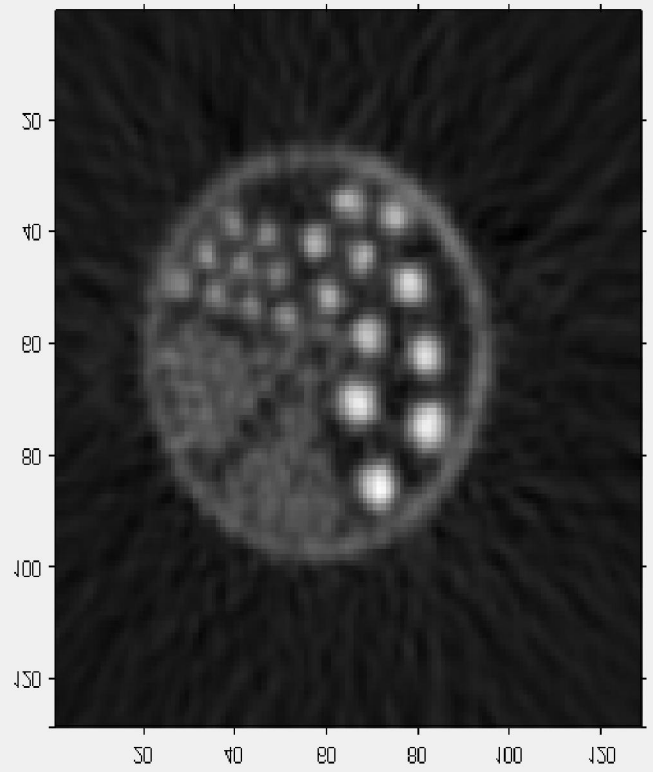
10	0	0

Registration Panel



Transformation

	1	2	3
1	1.2528	-0.0515	0
2	0.0581	1.2187	0
3	-21.1692	-6.6212	1

Overlap Images?

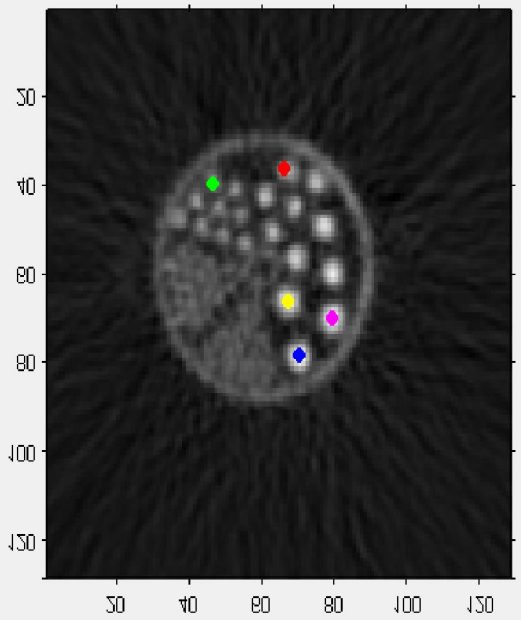
Save Registered Image

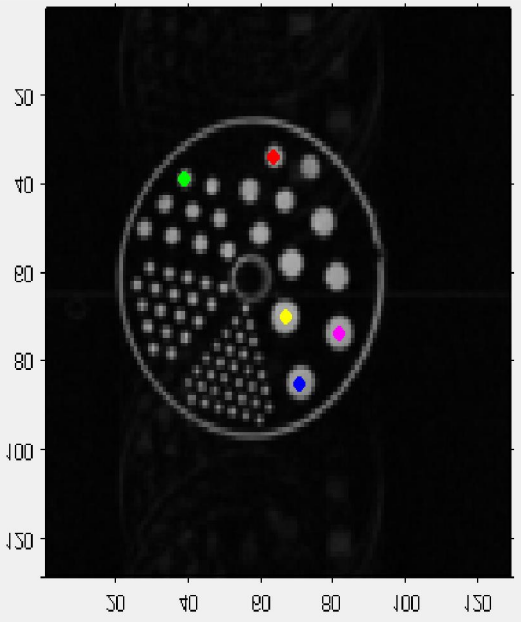
Affine_Image_Registration_1.0

Load Floating Image

Five

Load Reference Image





Find Centroids

Hide Centroids

Find Centroids

Hide Centroids

Place Fiducials

	X-Axis	Y-Axis
1	46.1331	39.6953
2	65.8254	36.2870
3	69.9911	78.3225
4	79.0799	69.9911
5	66.9615	66.2041
6	0	0
7	0	0
8	0	0
9	0	0
10	0	0

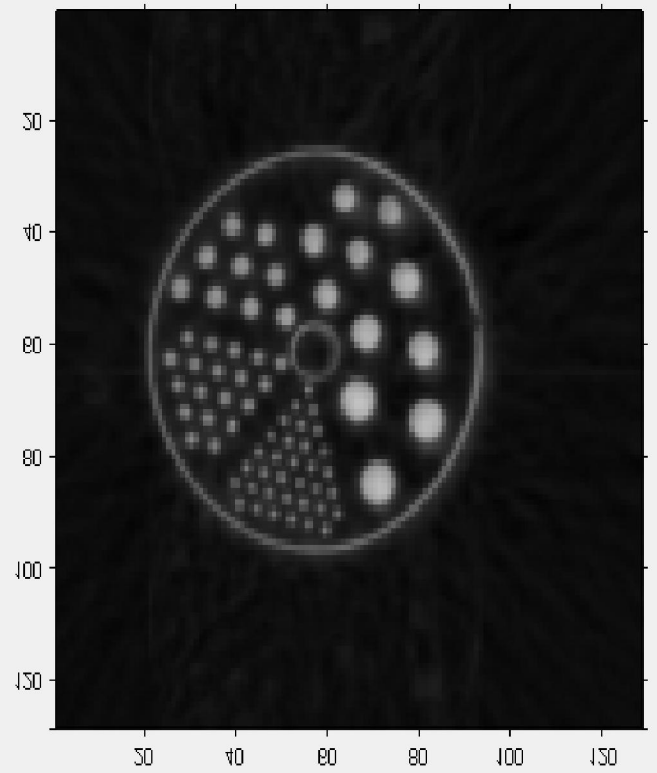
Register!

Reset

Place Fiducials

	X-Axis	Y-Axis
1	38.5592	38.9379
2	63.1746	34.0148
3	70.3698	85.1391
4	81.3521	73.7781
5	66.5828	69.9911
6	0	0
7	0	0
8	0	0
9	0	0
10	0	0

Registration Panel



Transformation

	1	2	3
1	1.2528	-0.0515	0
2	0.0581	1.2187	0
3	-21.1692	-6.6212	1

Overlap Images?

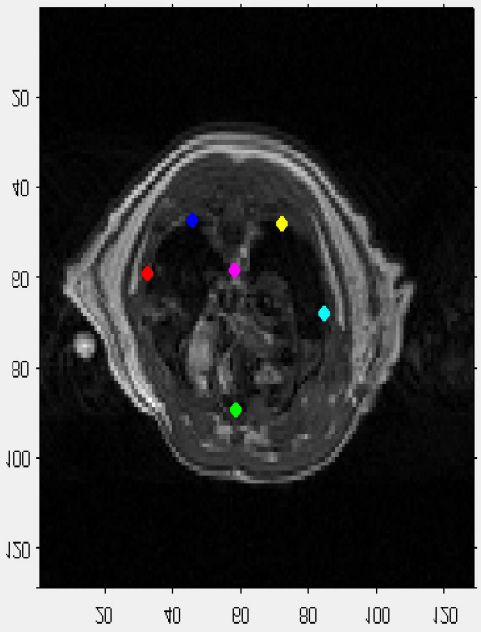
Save Registered Image

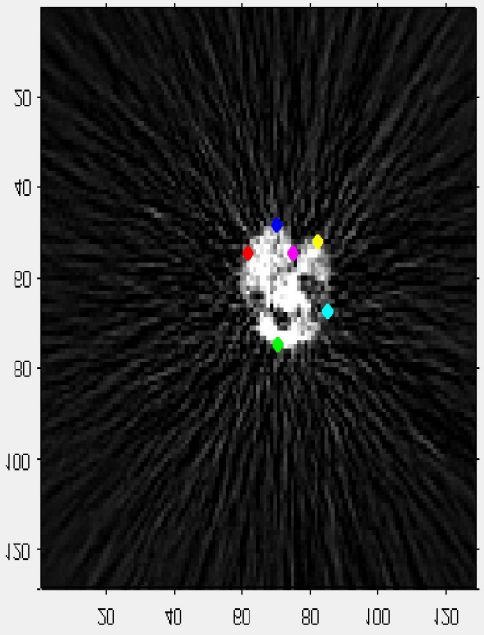
Affine_Image_Registration_1.0

Load Floating Image

Six

Load Reference Image





Find Centroids

Hide Centroids

Find Centroids

Hide Centroids

Place Fiducials

	X-Axis	Y-Axis
1	58.2471	89.3276
2	32.1322	59.1667
3	45.3736	47.3966
4	57.8793	58.4310
5	71.8563	48.1322
6	84.3621	67.9943
7	0	0
8	0	0
9	0	0
10	0	0

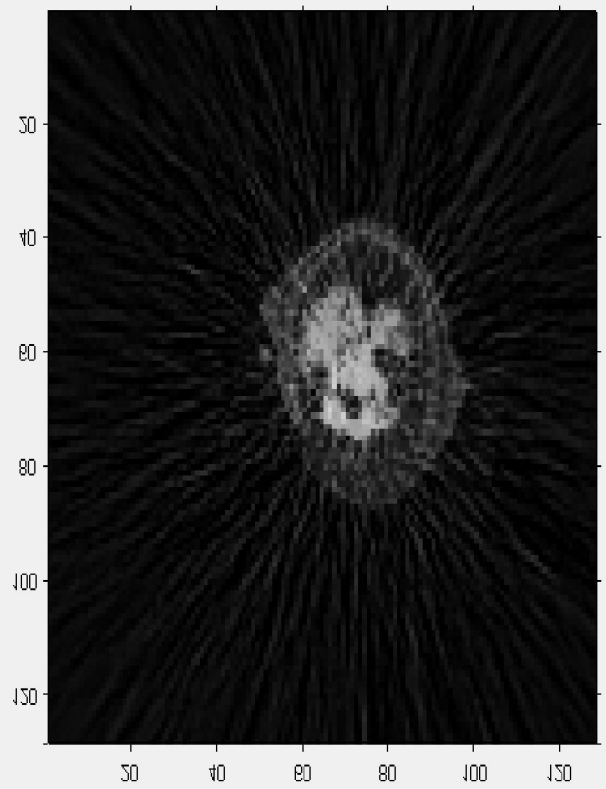
Register!

Reset

Place Fiducials

	X-Axis	Y-Axis
1	70.1848	74.7693
2	61.3825	54.5974
3	69.8181	48.3625
4	74.5860	54.5974
5	81.9212	52.0301
6	84.8553	67.4341
7	0	0
8	0	0
9	0	0
10	0	0

Registration Panel



Transformation

	1	2	3
1	0.4701	0.1366	0
2	-0.1388	0.6085	0
3	54.8140	12.9741	1

Overlap Images?

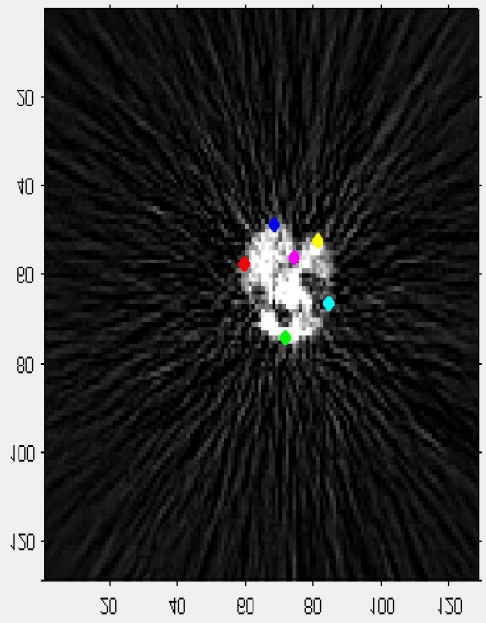
Save Registered Image

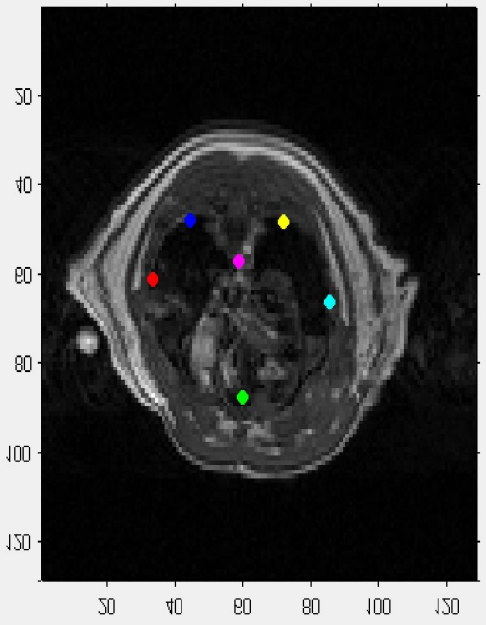
Affine_Image_Registration_1.0

Load Floating Image

Six

Load Reference Image





Find Centroids

Hide Centroids

Find Centroids

Hide Centroids

Place Fiducials

	X-Axis	Y-Axis
1	71.4885	74.2471
2	59.3506	57.6954
3	68.1782	48.8678
4	74.0632	56.2241
5	81.0517	52.5460
6	84.3621	66.5230
7	0	0
8	0	0
9	0	0
10	0	0

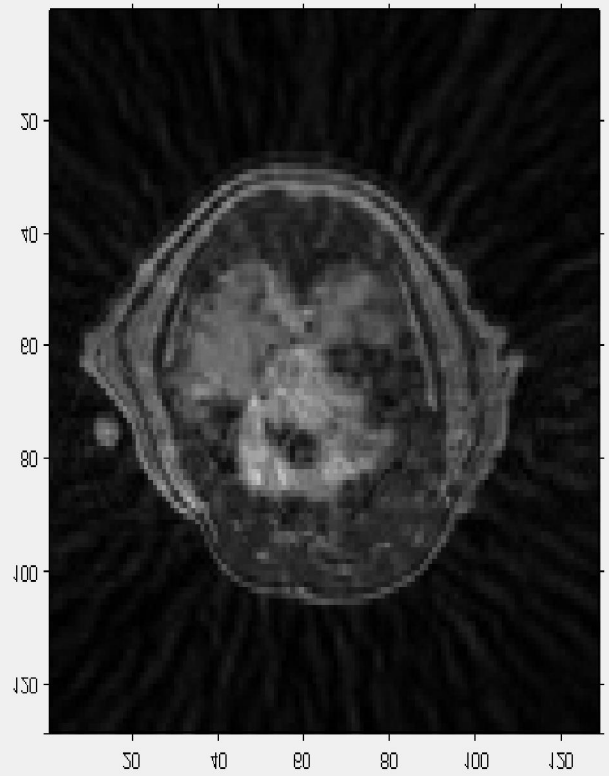
Register!

Reset

Place Fiducials

	X-Axis	Y-Axis
1	59.5487	87.6060
2	33.1418	61.1991
3	44.1447	47.9957
4	58.4484	57.1648
5	71.6519	48.3625
6	85.2221	66.3338
7	0	0
8	0	0
9	0	0
10	0	0

Registration Panel



Transformation

	1	2	3
1	1.9660	-0.3642	0
2	0.3632	1.5849	0
3	-106.5991	-6.0769	1

Overlap Images?

Save Registered Image

Testing Automated Software

- We used small hollow spheres (31 μl) as fiducial markers
- Filled with FDG and $CuSO_4$ solution as PET and FDG contrasts and attached to phantoms or animal bed
- Imaged with PET and MR
- Image registration using above mentioned automated software
- Calculate fiducial registration error as a metric for image registration

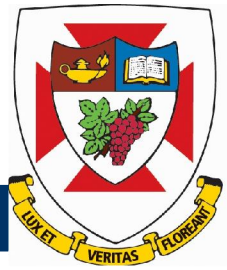
Fiducial Registration Error

Program	Method	Average X FRE	Average Y FRE	FRE Norm
MIPAV	CR	1.58	1.10	1.93
MIPAV	NCC	1.43	1.05	1.77
MIPAV	NMI	2.19	0.61	2.27
FLIRT	CR	1.70	0.94	1.94
FLIRT	NCC	1.11	0.93	1.45
FLIRT	MI	1.69	1.09	2.01
FLIRT	NMI	2.02	1.30	2.40
AIR	Woods	10.75	1.10	10.81
MAR	GUI	1.13	0.76	1.36

Fiducial registration error (FRE) results in units of mm. The methods of registration are as follows: correlation ratio (CR), normalized cross correlation (NCC), mutual information (MI), normalized mutual information (NMI), and the Woods algorithm (Woods). The FRE is calculated for each ducial and averaged for each axis. The nal column is the Euclidean norm of the average x and y FRE.

Summary

- Landmark registration is a simple and effective way to register images, that more sophisticated methods cannot
- Further work required
  - Add optimization routine
  - Read 3D formats (DICOM, NifTi, Analyze...)
- More image editing features, relevant to stem cell quantification



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