Effectiveness of Intensity Normalization on MRIs of Human Brains with Multiple Sclerosis

Mohak Shah[1,3], Yiming Xiao[1], Simon Francis[2,3], Douglas Arnold[2,3], D. Louis Collins[2], Tal Arbel[1]

[1]Centre for Intelligent Machines, McGill University
[2]Montreal Neurological Institute, McGill University
[3]NeuroRx Research, Montreal

Workshop on Medical Image Analysis on Multiple Sclerosis
MIAMS-2009

September 20, 2009

Mohak Shah

Outline

- Introduction
- Nyul Intensity Normalization
- Evaluation of Nyul approach
- Qualitative and Quantitative evaluation
- Conclusion and Future work

The Need for Intensity Normalization

- Variations in MRIs
  - Acquisition protocols;
  - Multi-site scans; scanner manufacturers; models from same manufacturer;
  - Effect of pathology; Varying stages of disease
- Lack of standard scale makes the generalization of intensity behavior difficult
- Reliance on assumptions over distribution of tissue intensities
  - large variations in intensity ranges can violate these

The Need for Intensity Normalization

- These variations are accounted for by
  - Standard acquisition protocols
  - Intensity in-homogeneity correction
  - Intensity Normalization (Standardization)

The Need for Intensity Normalization

- These variations are accounted for by
  - Standard acquisition protocols
  - Intensity in-homogeneity correction
  - **Intensity Normalization (Standardization)**

Approaches to Intensity Normalizations

- Various Approaches
  - (Christensen, 1996); (Weisenfeld and Warfield, 2004); (Hellier, 2003); (Jäger *et al*, 2006)
- Main drawback
  - Accuracy vs. Speed vs. Adaptability
- Nyul Approach (Nyul et. al., 1999, 2000)
  - Best of both worlds
  - One of the most widely approaches

Nyul Intensity Normalization (Nyul *et al.* 1999, 2000)

- Extensive Evaluation
  - available on inter- and intra-patient variations
  - But not on multi-site multi-scanner multi-spectral data
  - Neither in the presence of pathology

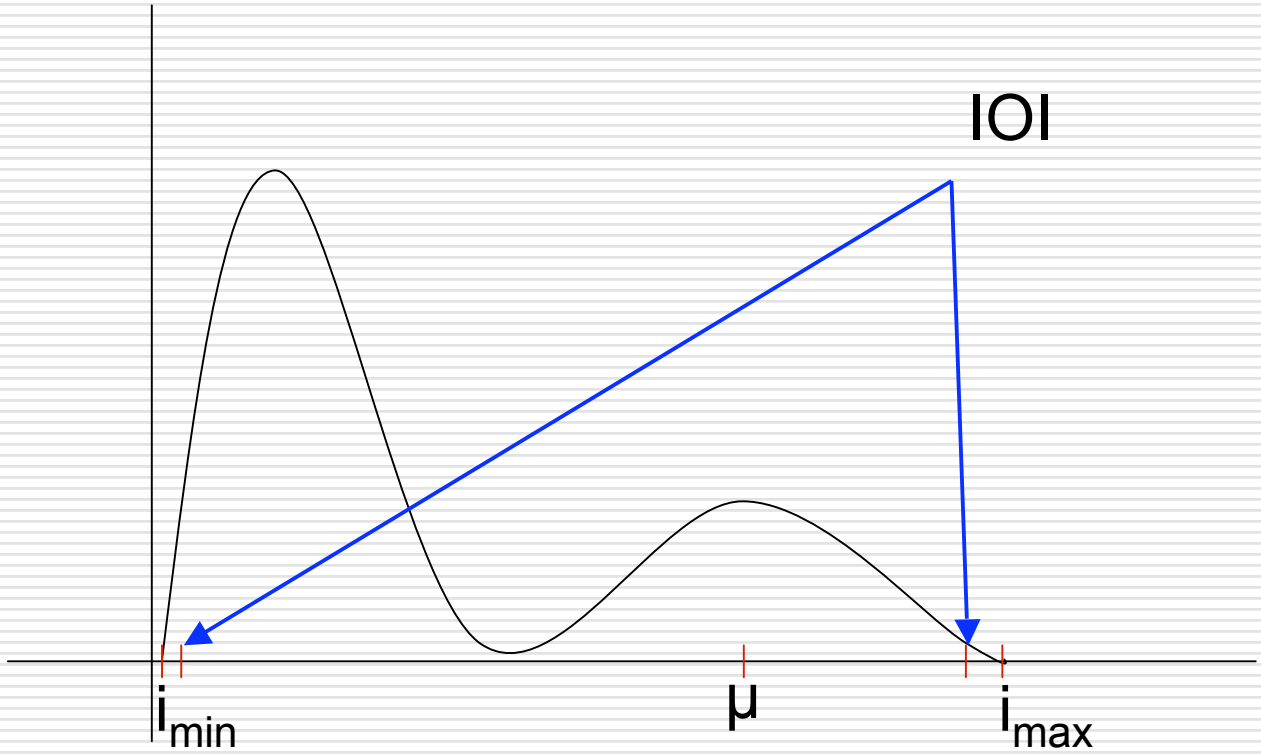
Nyul Intensity Normalization (Nyul *et al.* 1999, 2000)

- Extensive Evaluation
  - available on inter- and intra-patient variations
  - But not on multi-site multi-scanner multi-spectral data
  - Neither in the presence of pathology

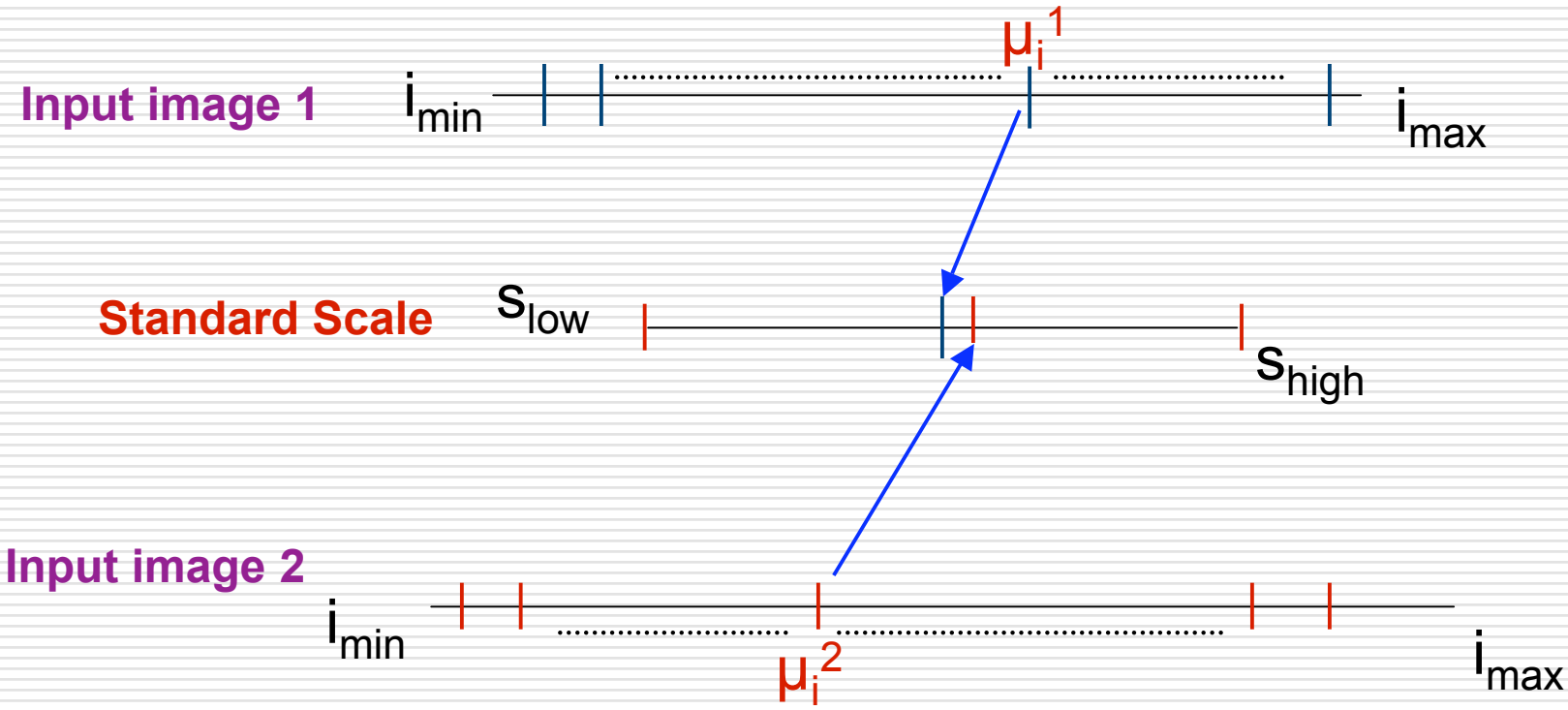
Nyul Approach in a nutshell

- Decile Formulation (Nyul *et al.* 2000)
- Two stage approach
- Training
  - Input a value range for forming a standard scale
  - Determine standard scale landmarks (mapping points) from the training data
- Transformation
  - Use standard scale for a piece-wise linear mapping of input image to standard scale

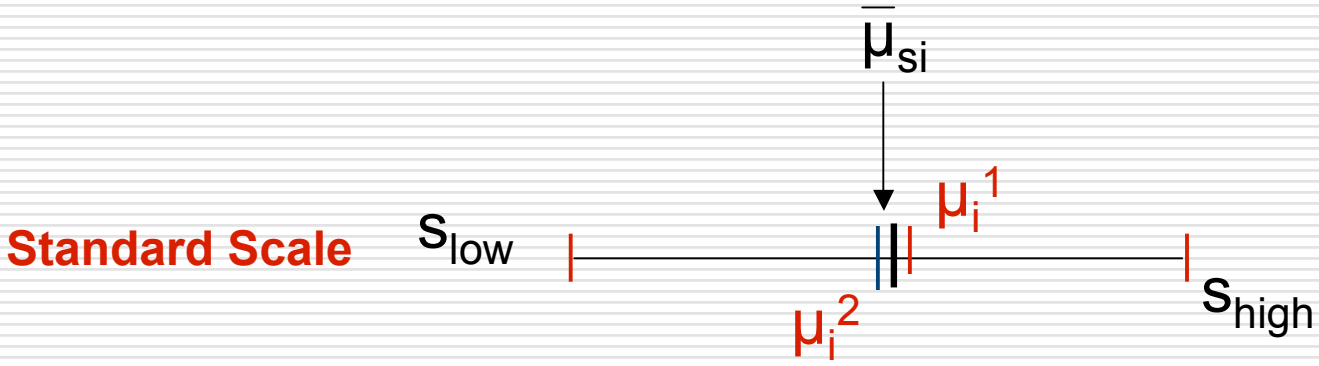
The Intensity Normalization (Training):
Intensity of Interest (IOI)



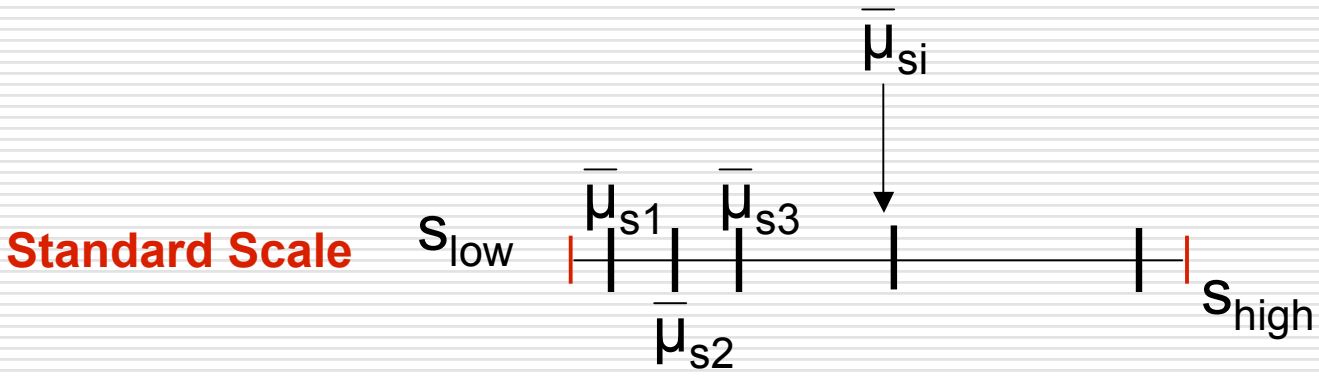
The Intensity Normalization (Training):
mapping to Standard scale



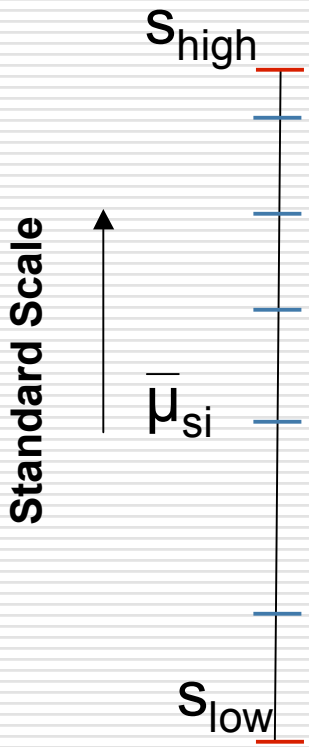
The Intensity Normalization (Training):
mapping to Standard scale



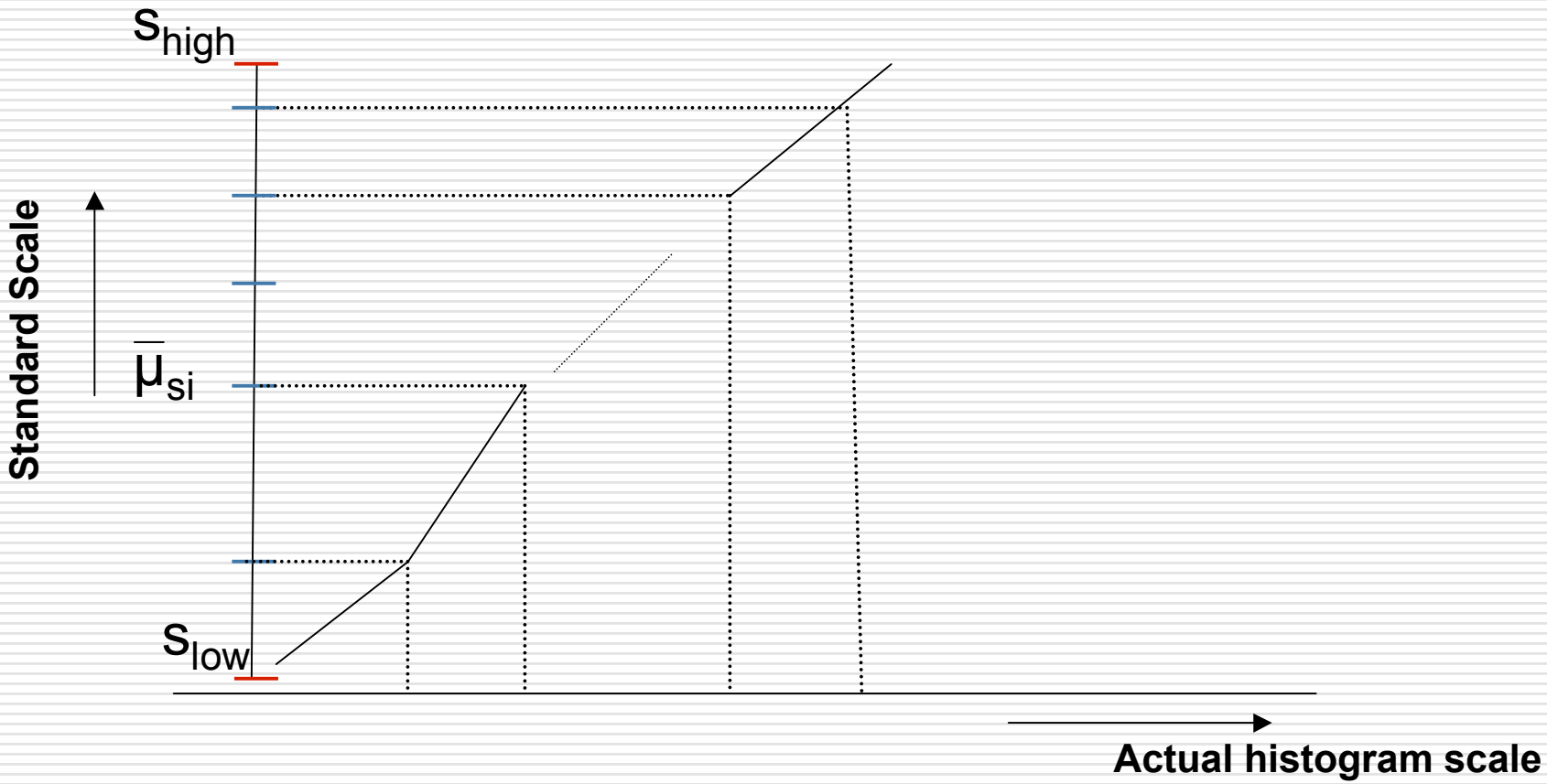
The Intensity Normalization (Training):
Standard scale



The Intensity Normalization:
Standard Scale



The Intensity Normalization:
Transformation



Evaluation of Nyul approach

Data Acquisition (data courtesy NeuroRx Research, Montreal)

- 21 multi-spectral (T1w, T2w and PDw) MRI scans
  - 7 subjects each from GE, Philips and Siemens
- Within each sub-group, patients with
  - Varying ventricle sizes
  - Varying MS lesion loads
- Protocols standardized to obtain similar contrasts
- Each MRI volume with
  - 1x1x3 mm resolution
  - 50 slices (vertex to the foramen magnum)

Pre-processing

- Image Modalities' Alignment
  - Image modalities aligned to a common stereotaxic space for deterministic spatial voxel mapping
- Intensity in-homogeneity correction
  - To account for scanner-specific variations

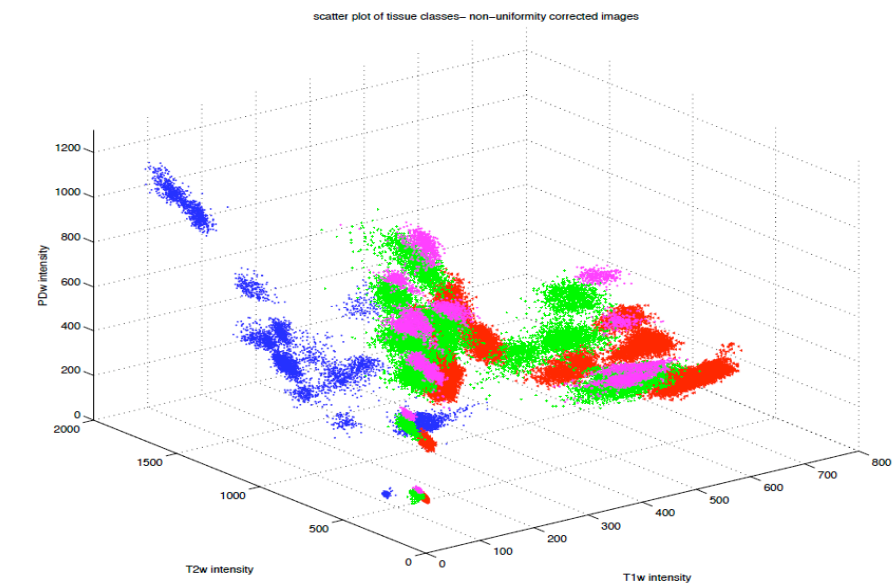
Tissue Sampling

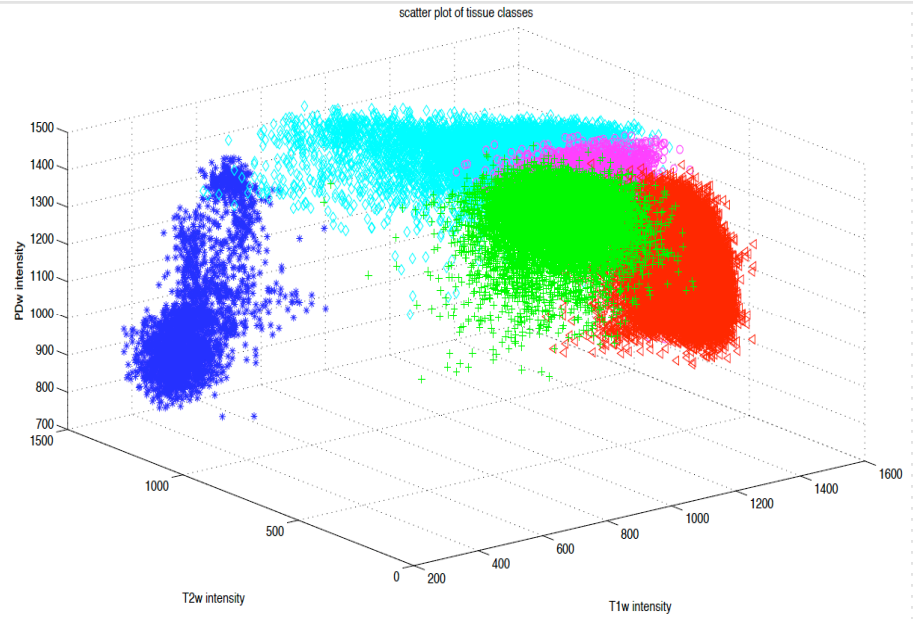
- "Pure" tissue samples
- Tissue types
  - Cortical Gray Matter (CGM), Deep Gray Matter (DGM), White Matter (WM), and Cerebrospinal Fluid (CSF)
- 1000 manual samples for each tissue per MRI
  - about 20 slices (alternate) per brain volume
- Samples obtained both before and after normalization
- Lesions identified automatically followed by expert validations by 5 expert radiologists (consensus)

Evaluation

- Training
  - 100 volumes with varying lesion loads and MS pathology
  - Standard scale histogram parameters obtained
    - Same for all modalities
- Standard scale then used in the Transformation stage
- Evaluation Criteria
  - Effect of normalization on heterogenous MRIs
    - Multi-site, Multi-scanner (different manufacturers/brands)
  - Distributional assumption
  - Role of normalization in tissue separation
  - Effect of pathology

Qualitative Evaluation





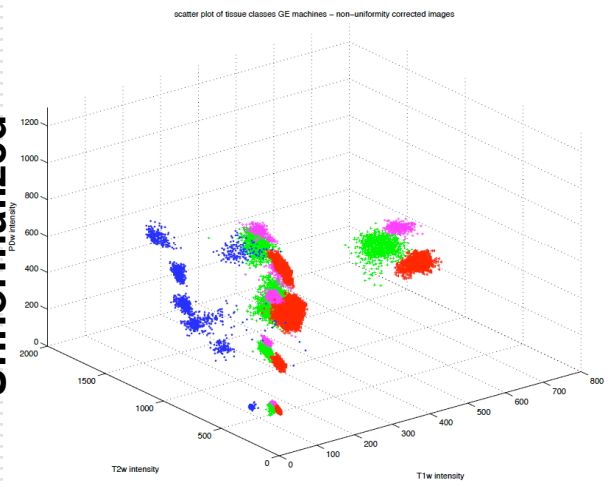
Un-normalized

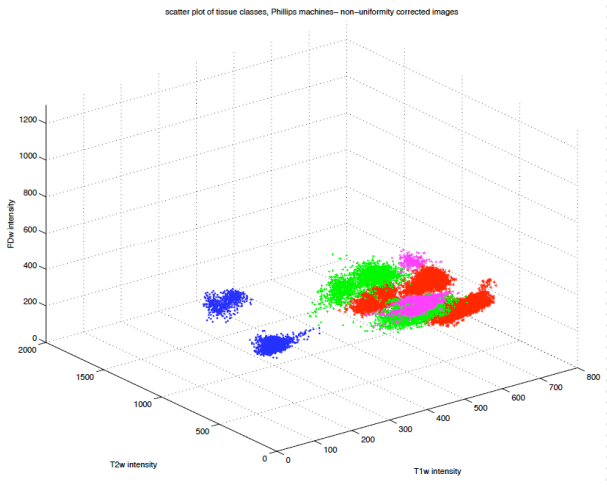
Normalized

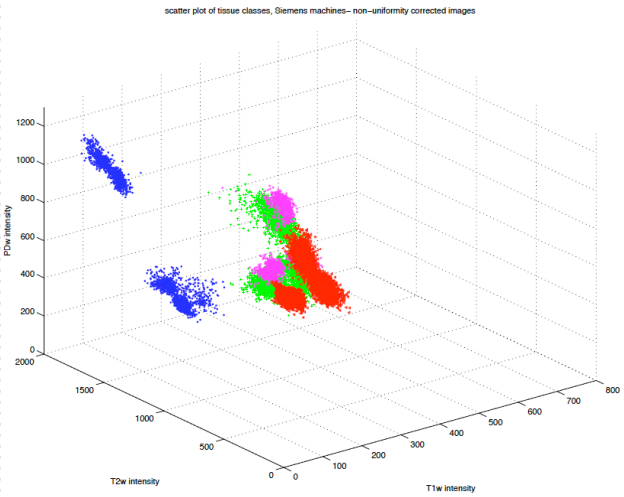
Red: WM, Green: CGM, Magenta: DGM, Blue: CSF, Cyan:Lesions

Qualitative Evaluation: by manufacturers

Unnormalized





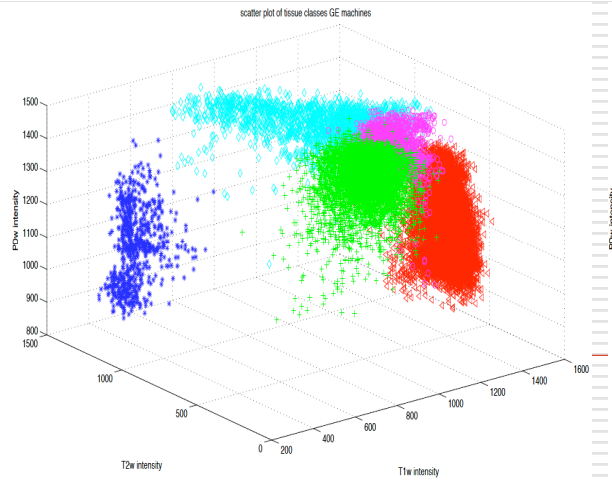


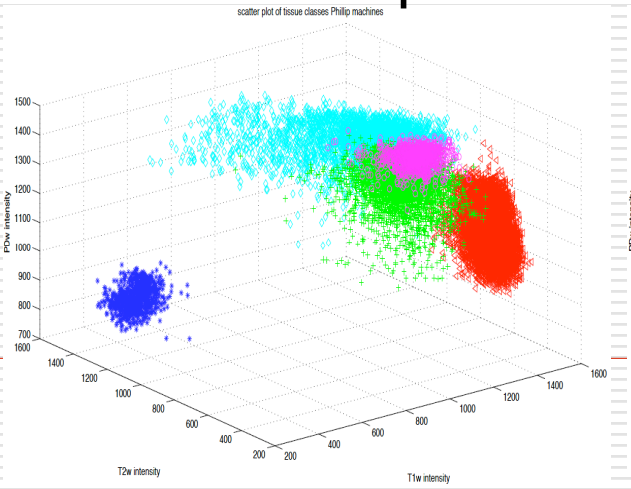
GE

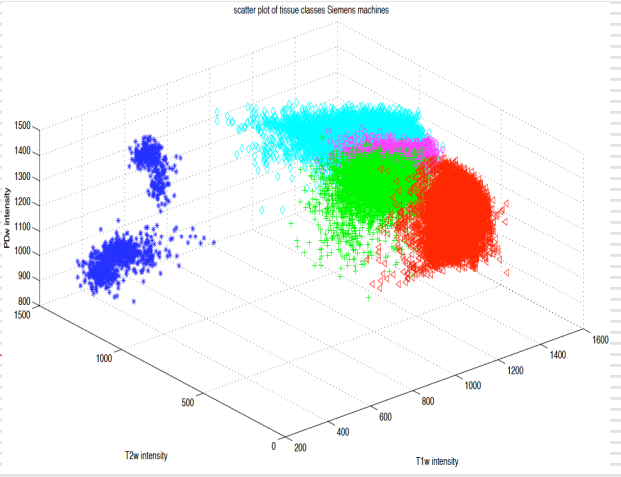
Philips

Siemens

Normalized







Quantitative Evaluation

- Tissue behavior in individual modalities
- Effect on Gaussian distribution assumption
- Jeffrey Divergence criterion

$$JD(p,q) = \int_{-\infty}^{\infty} p(x) \log \frac{p(x)}{q(x)} dx + \int_{-\infty}^{\infty} q(x) \log \frac{q(x)}{p(x)} dx$$

Verifying Gaussian assumptions

- For un-normalized images:
  - Calculate intensity histogram for each tissue type from the input image (bin size 100). Call it **D1-u**
  - Calculate data mean m and covariance c
  - Generate a Gaussian at (m, c). Call it **D2-u**
  - Calculate the Jeffrey Divergence between D1-u and D2-u: **JD-u**
- For normalized images
  - Do as above and calculate **JD-n**
- Compare JD-u and JD-n

Hypothesis for Evaluation

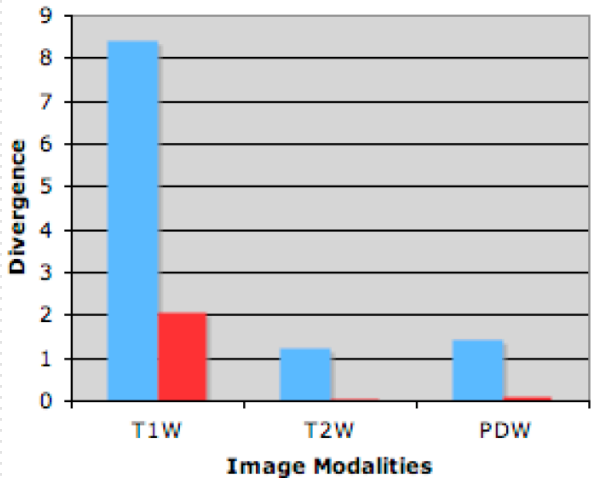
- If the data comes from a Gaussian distribution then JD-u shouldn't be large

- Further if normalization doesn't have any effect on data distribution then the difference in JD-u and JD-n should be insignificant

Results

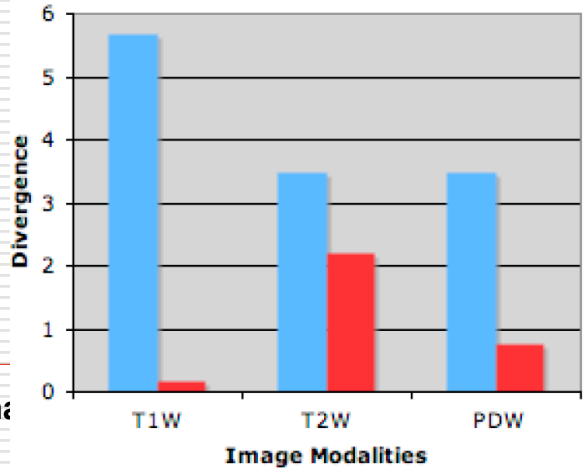
Jeffrey Divergences: All machines

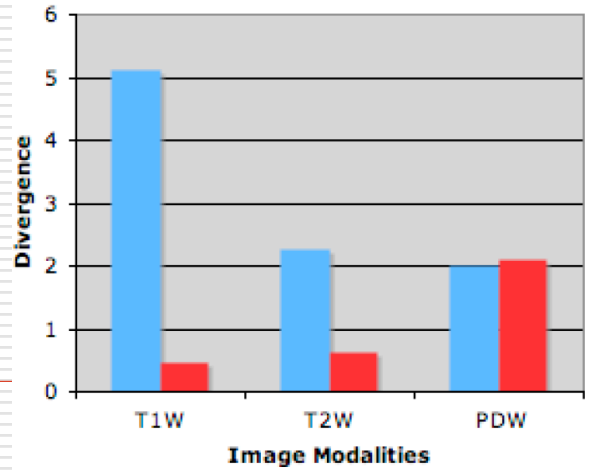
WM



GM

CSF



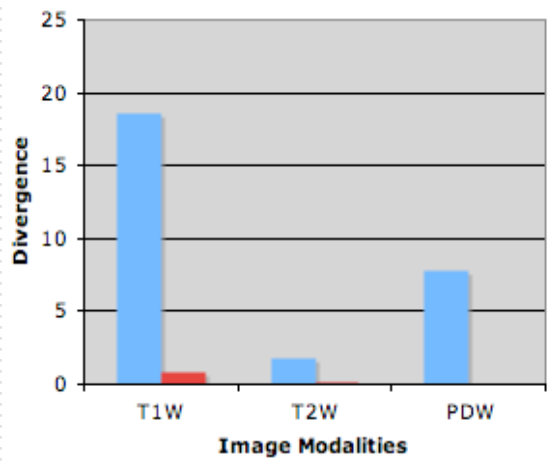


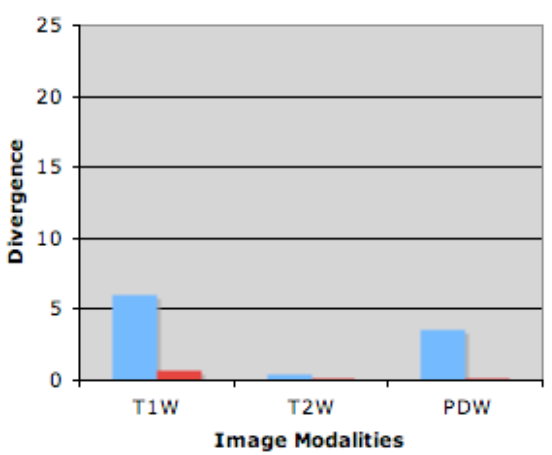
Lesions

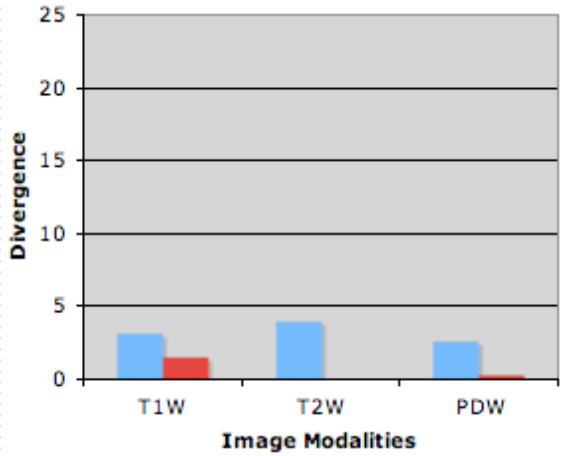
Results

WM and GM : Jeffrey Divergences, by Manufacturers

WM





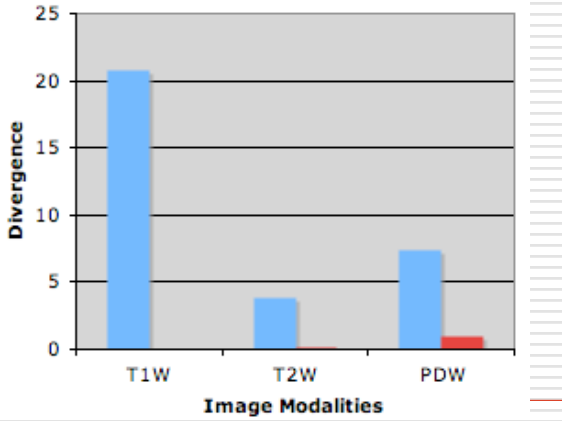


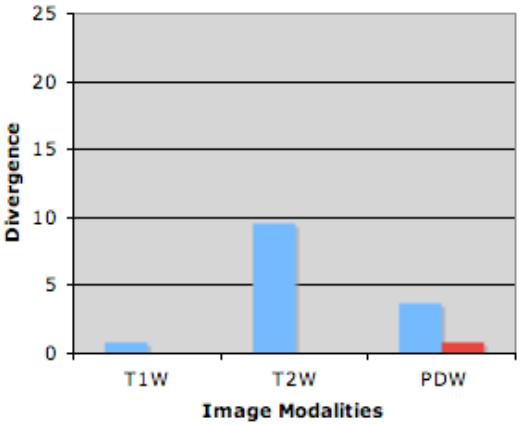
GE

Philips

Siemens

GM

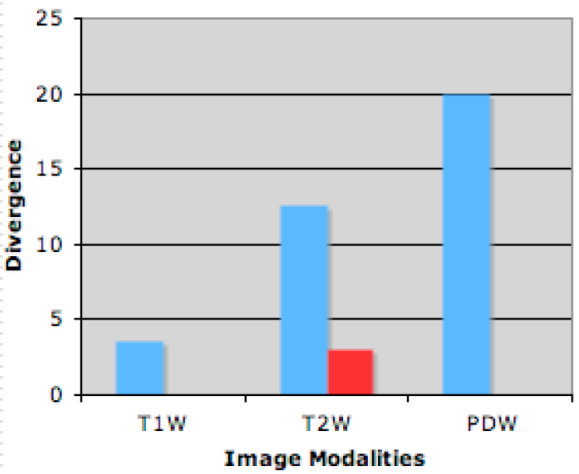




Results

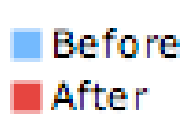
CSF : Jeffrey Divergences, by Manufacturers

GE



Philips

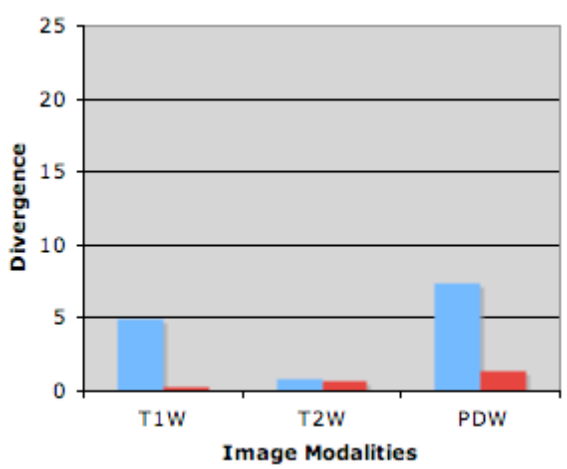
Siemens



Results

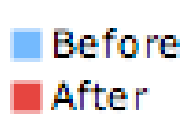
Lesions : Jeffrey Divergences, by Manufacturers

GE

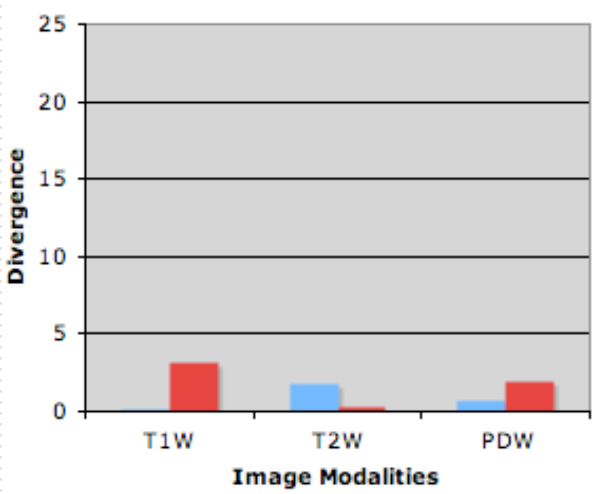


Philips

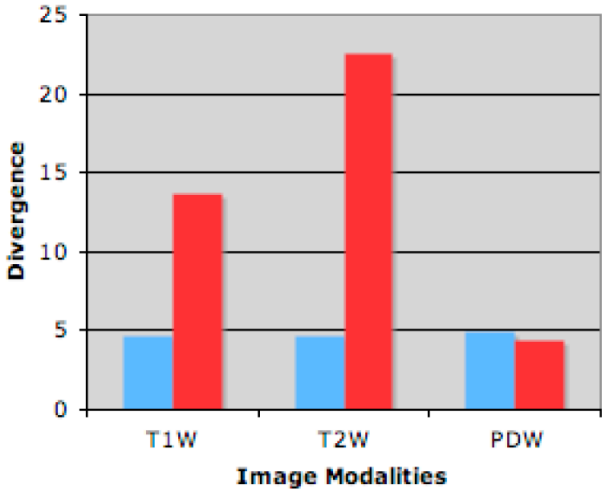
Siemens



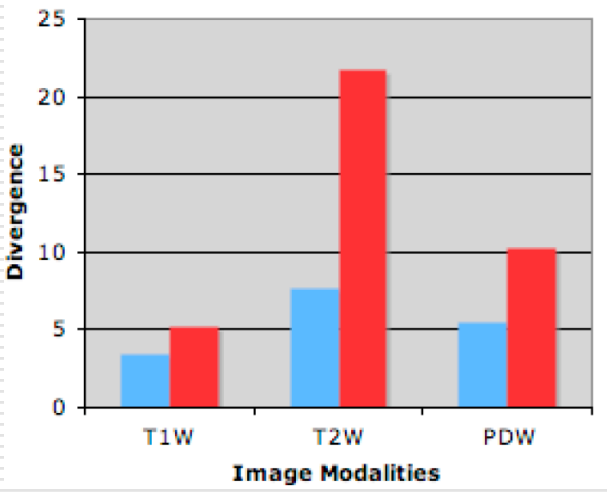
Tissue Contrast



WM:GM



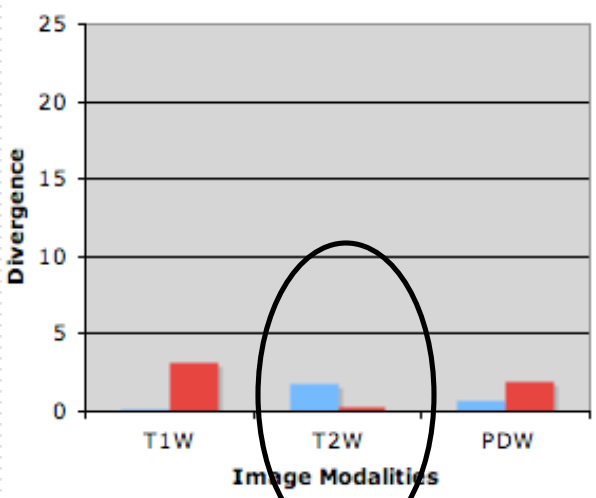
WM:CSF



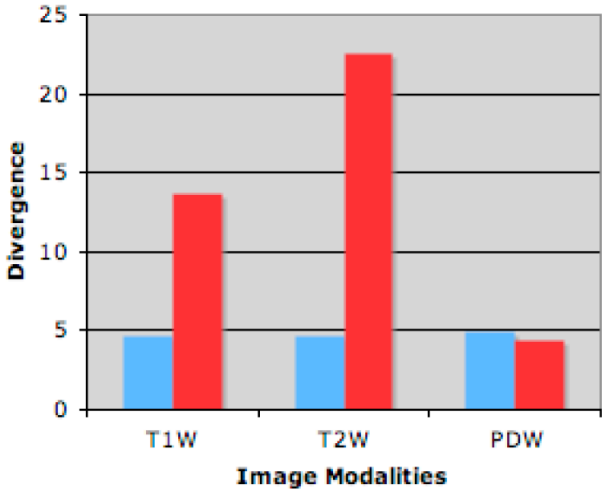
GM:CSF

Before
After

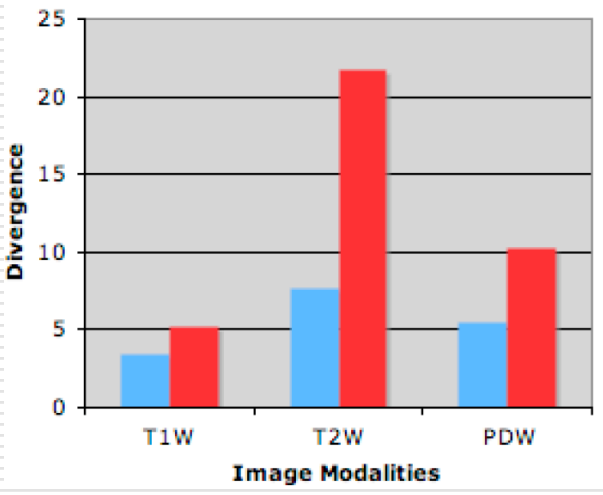
Tissue Contrast



WM:GM



WM:CSF



GM:CSF

Conclusion and Future Work

- Nyul approach affects the tissue intensity distribution
  - Homogenizing same tissues
  - Better separation between different tissues
- Makes the distribution amenable to application of segmentation algorithms
- Robust in the presence of pathology
- **To Do:**
  - Effect on segmentation results
  - Lesion load dependent analysis
  - Incorporating this knowledge into automatic approaches

Thank You