Medical Image Synthesis Methods and Applications

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with
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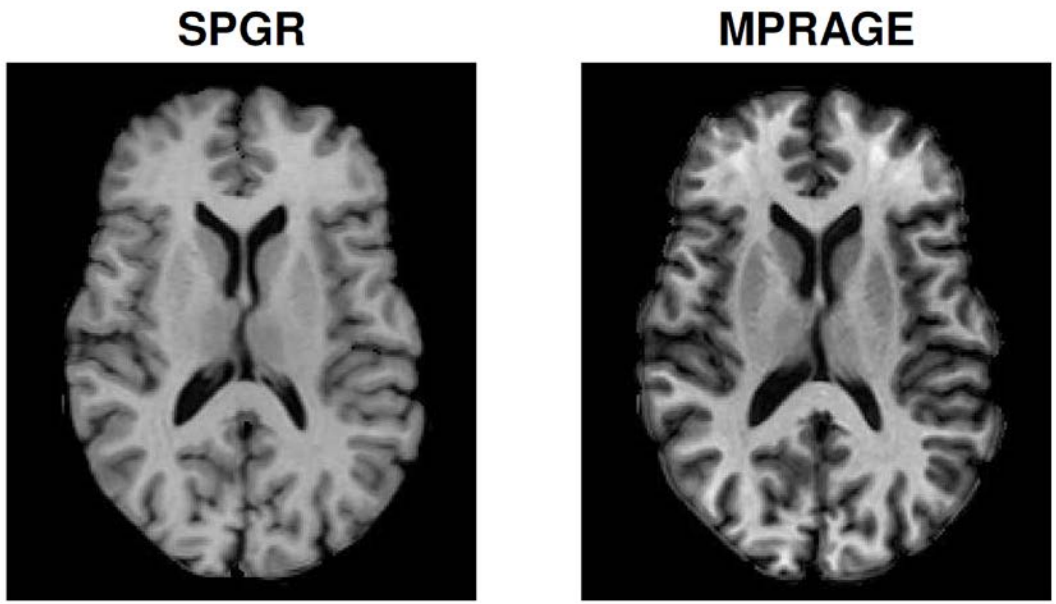
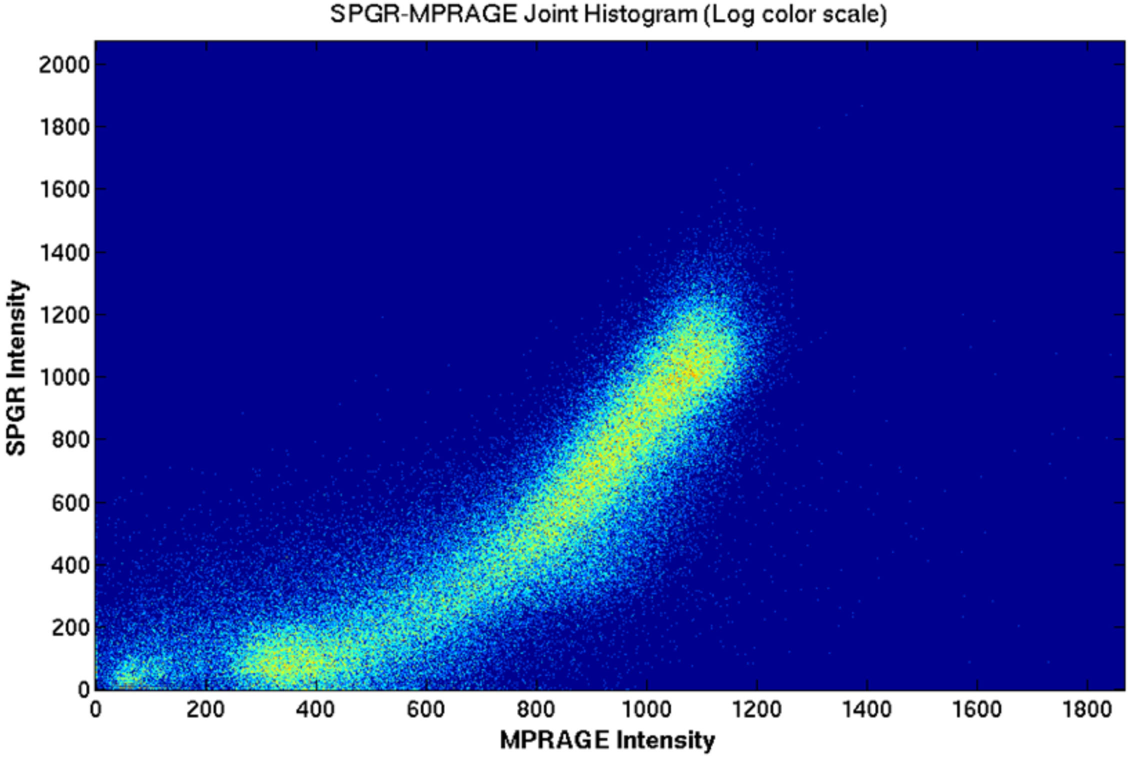
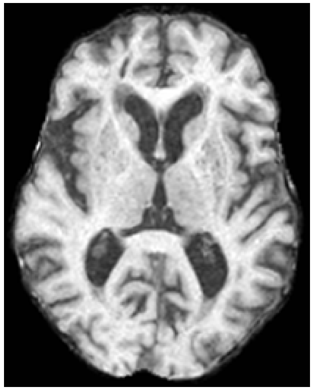
MR Intensity Scale is Arbitrary



- This causes problems in most postprocessing methods
  - Inconsistency or algorithm failure

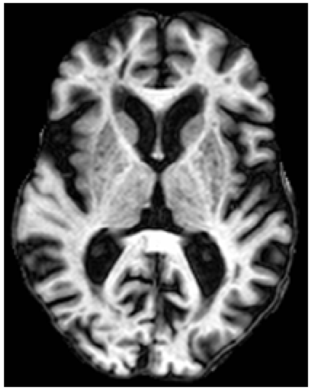
Joint Histogram





1.5 T GE SPGR

3 T Philips MPRAGE

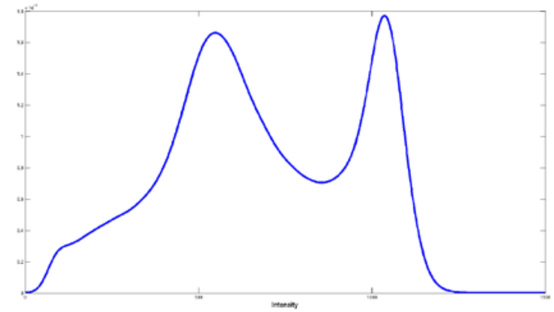


Problem With Histogram Matching

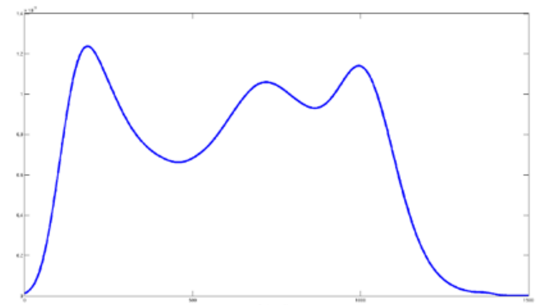
Image

Histogram

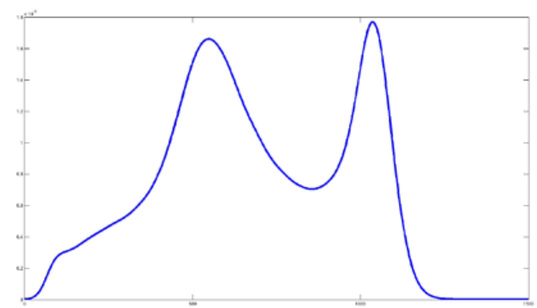
Target



Subject



Histogram Matched Subject

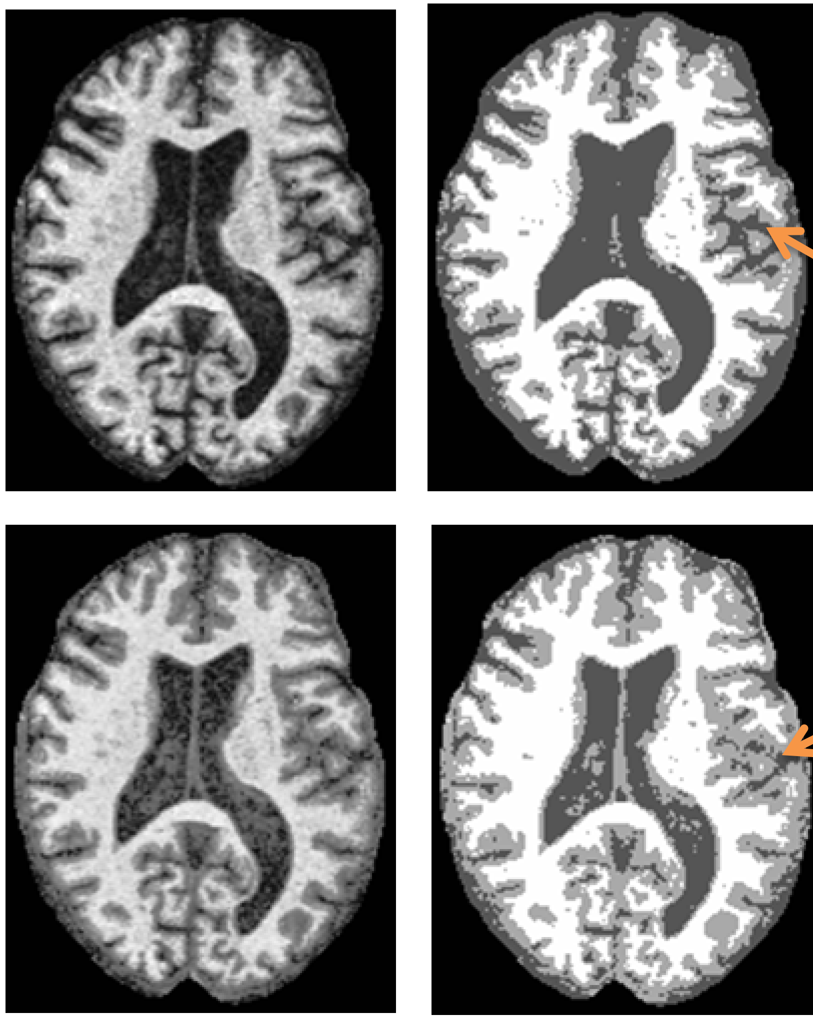


Tissue Classification Result

Image — Tissue Classified

Original

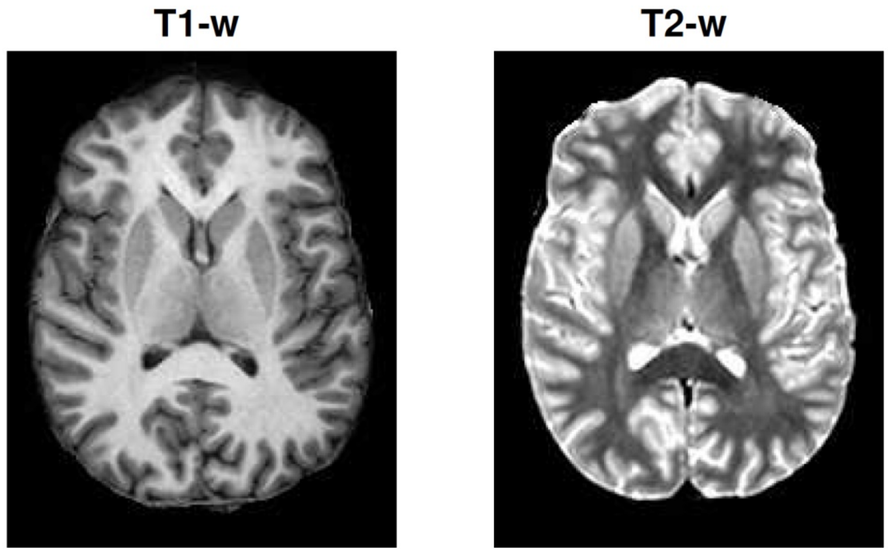
Histogram Matched



Correct classification

This result yields an underestimation of CSF

MRI Has Multiple Tissue Contrasts



- Uses:
  - Ideal for visualization of certain anomalies
  - Helps in intersubject registration
- Problems:
  - A pulse sequence/image contrast can be missing
  - Desired image can be corrupted or have low resolution

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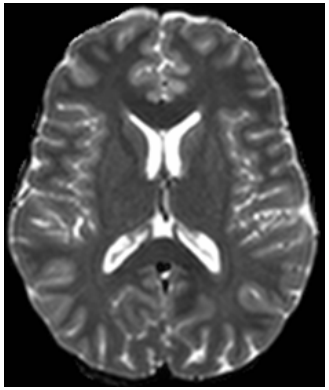
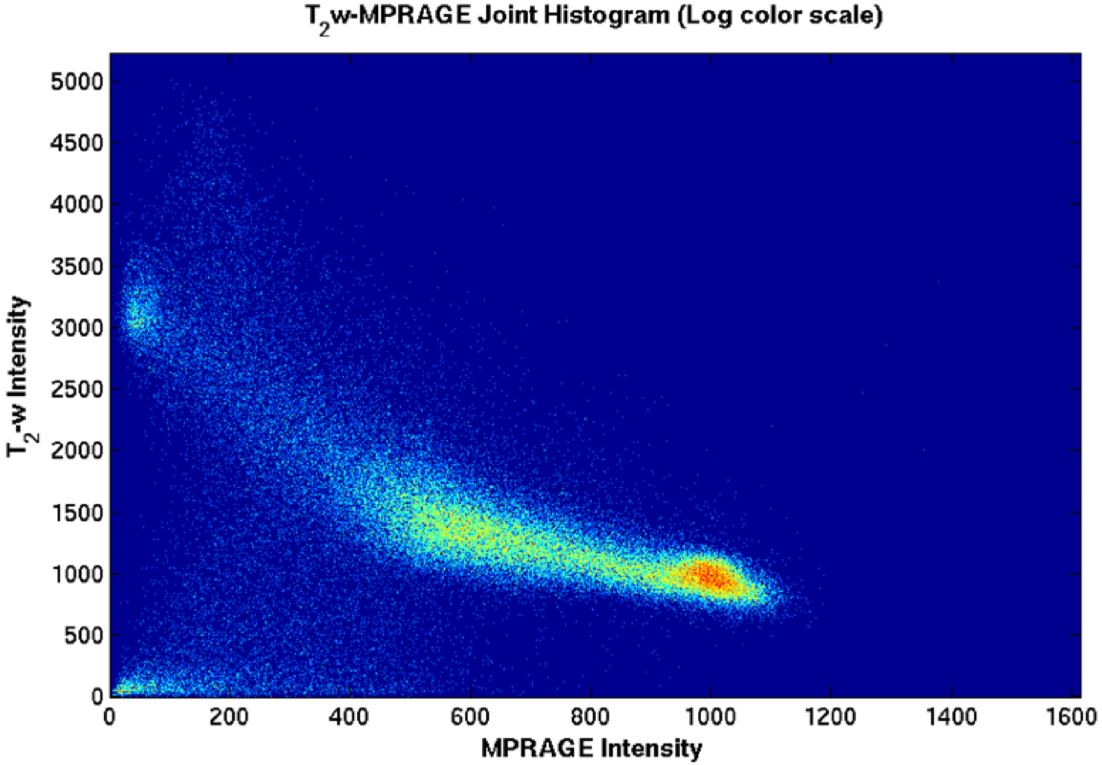
Joint Histogram



3 T T2w



3 T MPRAGE

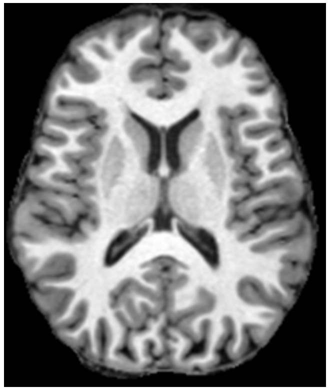


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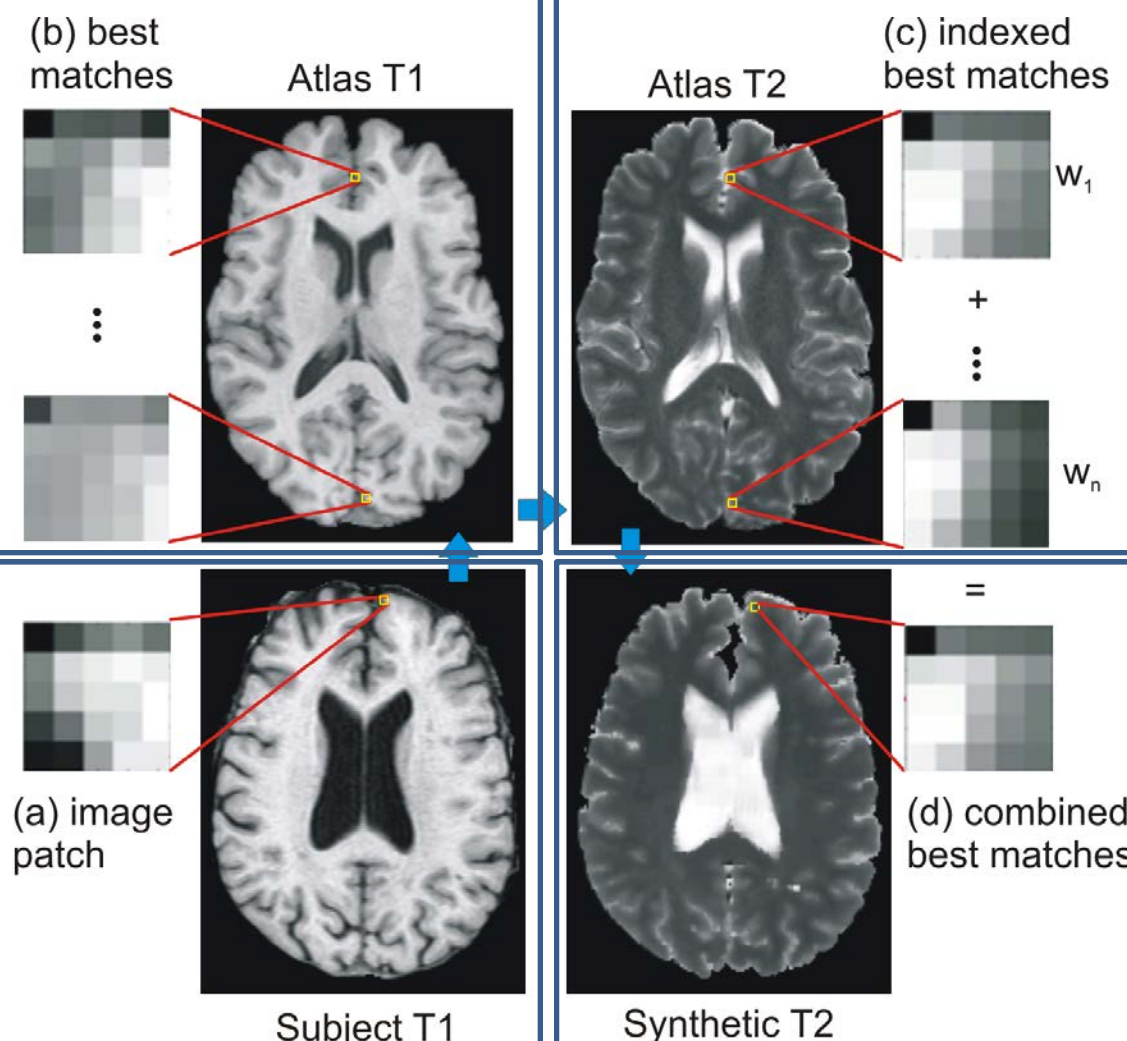
Image Synthesis Framework

Find patches in the atlas image that match that patch

Find the patches in the same positions as the best matches



Consider an image patch in the source image

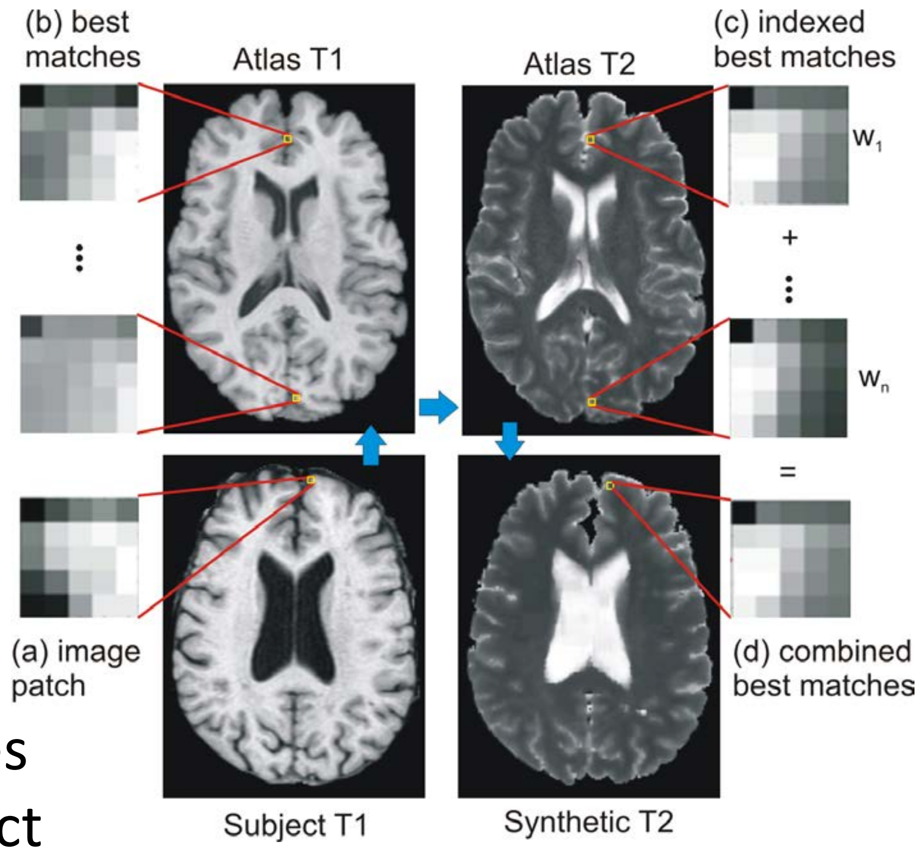
Combine these patches and retain the central pixel

MIMECS SYNTHESIS METHOD

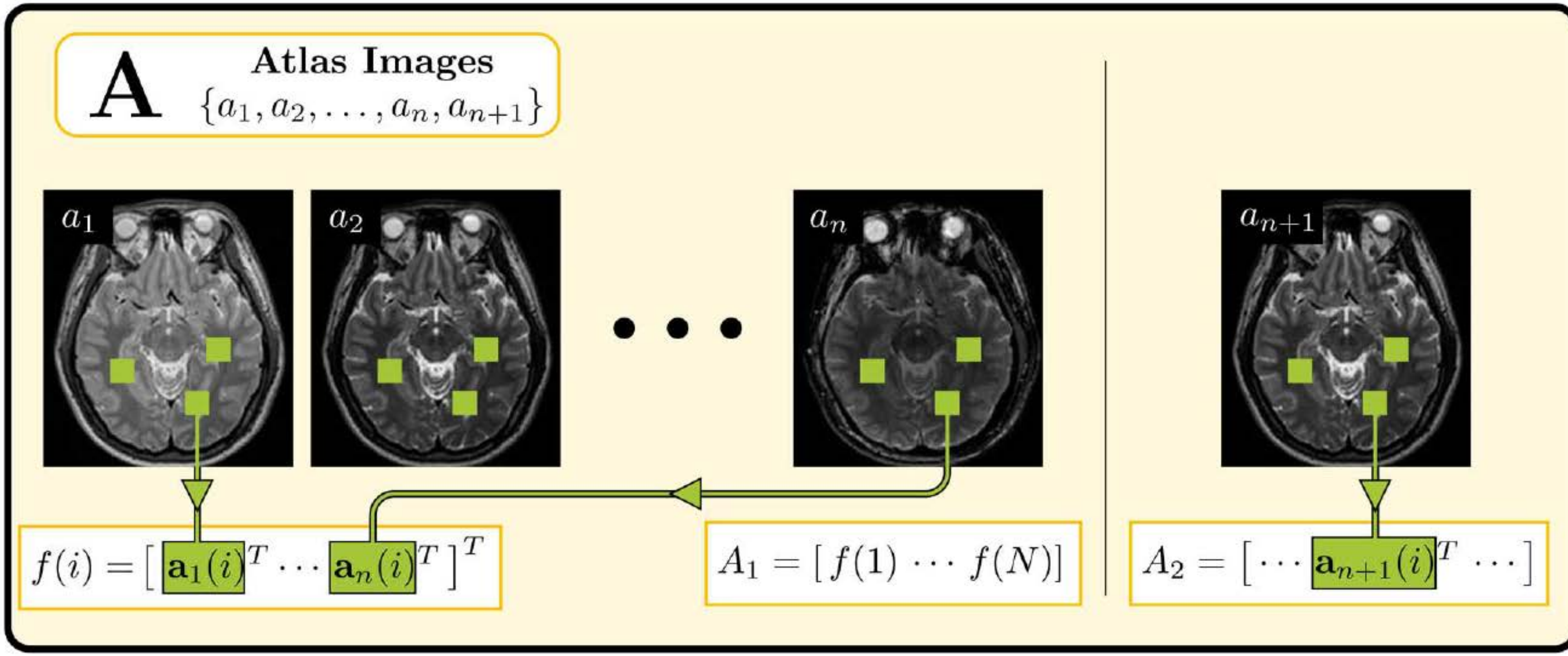
MR IMage Examplar-based Contrast Synthesis

MIMECS and Sparsity

- Choose one patch?
  - Probably not quite a good match to the subject
- Combine many patches?
  - Any one (bad) patch can spoil the combination
- It is best to use sparsity:
  - Find a small number of patches that will reconstruct the subject patch
  - Use the same coefficients to reconstruct the synthetic patch



The MIMECS Atlas

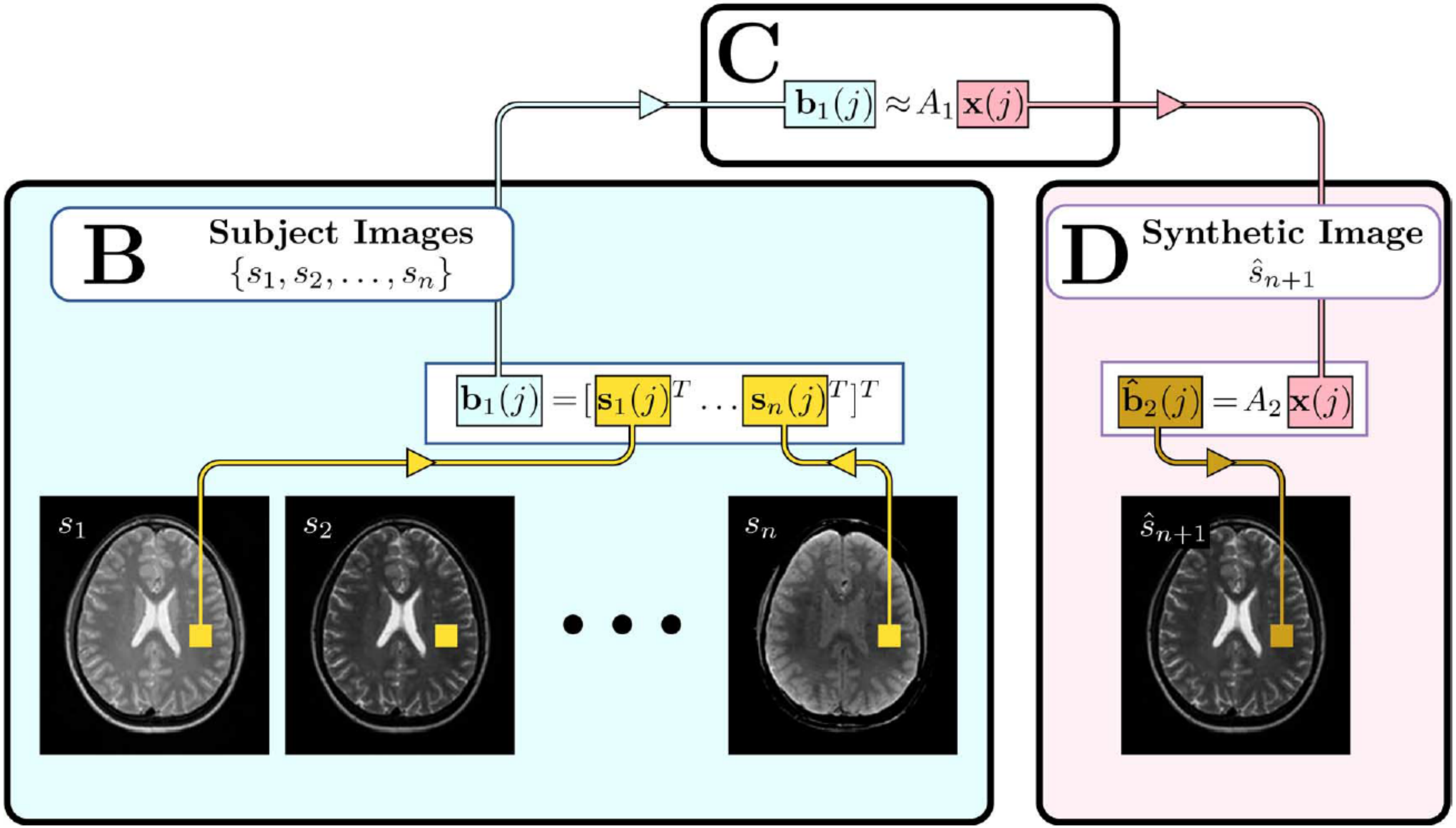


Subject

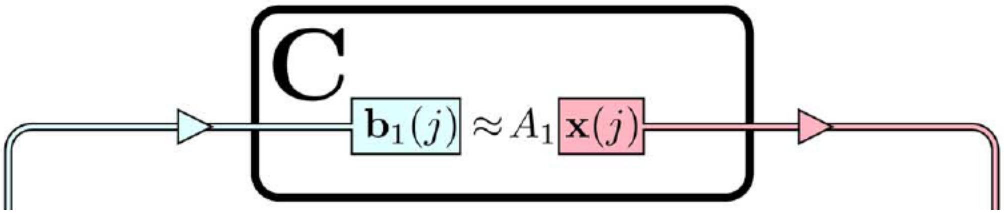
Target

An overcomplete patch dictionary

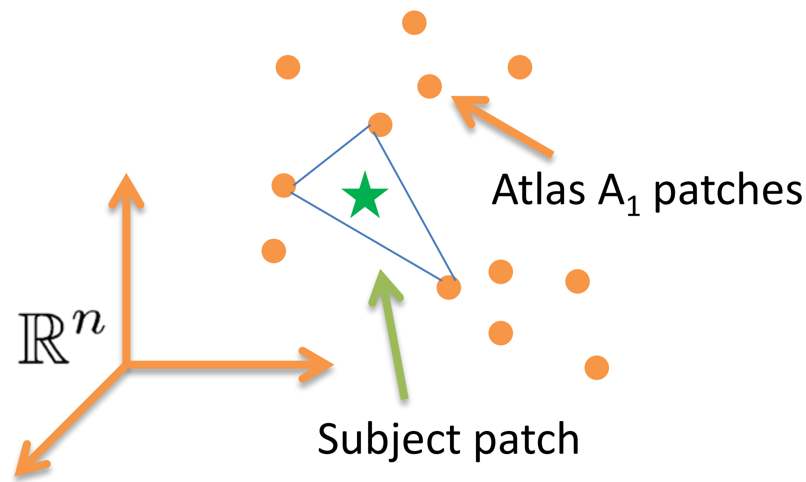
The MIMECS Algorithm



Sparse Reconstruction



- The reconstruction should closely match the subject patch $\mathbf{b}_1(j)$
- The coefficients in $\mathbf{x}(j)$ should be sparse
- L2-L1 reconstruction:

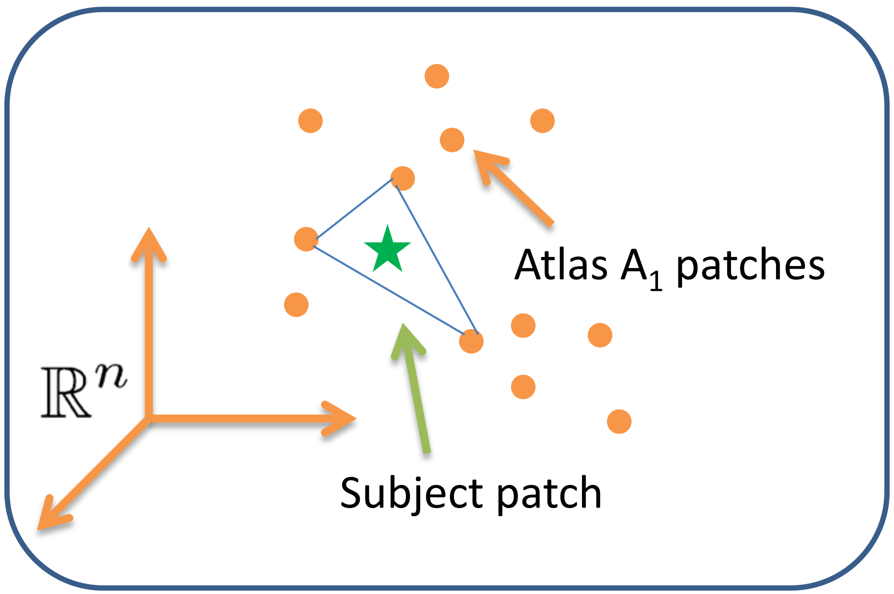


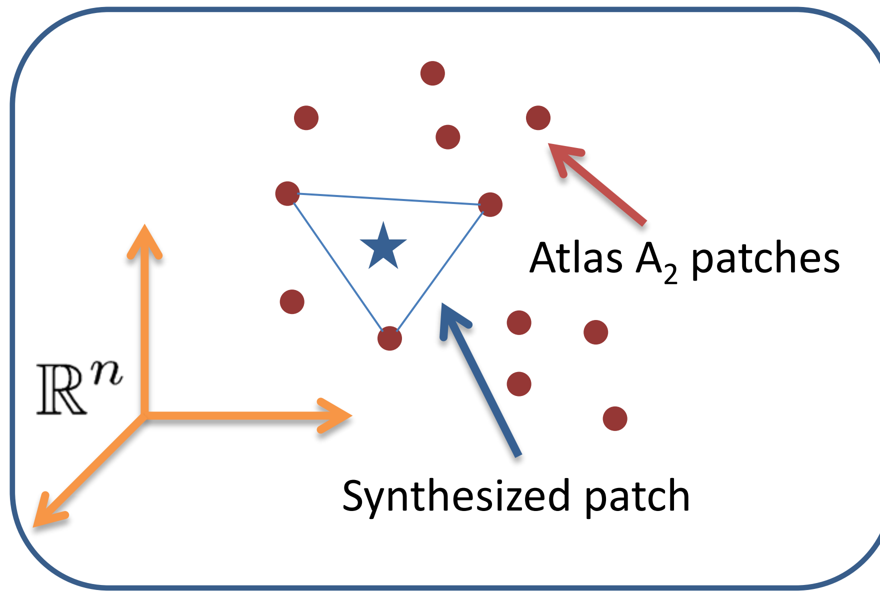
$$\hat{\mathbf{x}}(j) = \arg\min_{\mathbf{x}} \{ \|\mathbf{b}_1(j) - A_1 \mathbf{x}\|_2^2 + \lambda \|\mathbf{x}\|_1 \}$$

Reconstruct the Patch in A_2

- Reconstruct A_2 patch using corresponding patches and the same sparse coefficients

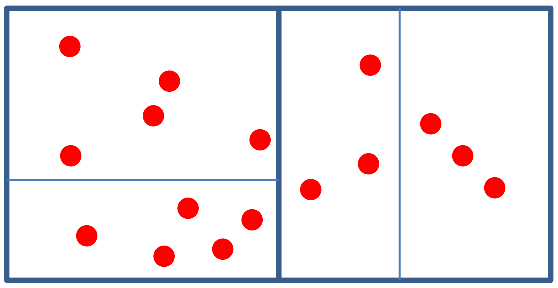
$$\hat{\mathbf{b}}_2 = A_2\mathbf{x}$$

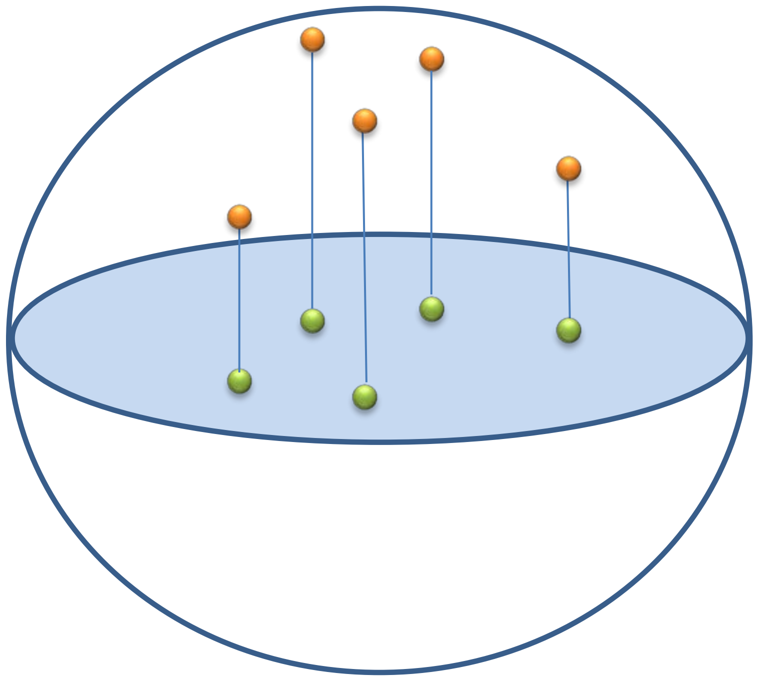




A Few "Tricks"

- Use kd-tree to reduce the size of A_1
  - Use L_2 similarity
  - Rapidly finds roughly 100 patches
- We have also explored dictionary learning
- Use +1 higher dimension to normalize patches
  - Dictionary elements should have unit norm
  - If patch dimension = n-1
  - Project to sphere in R^n



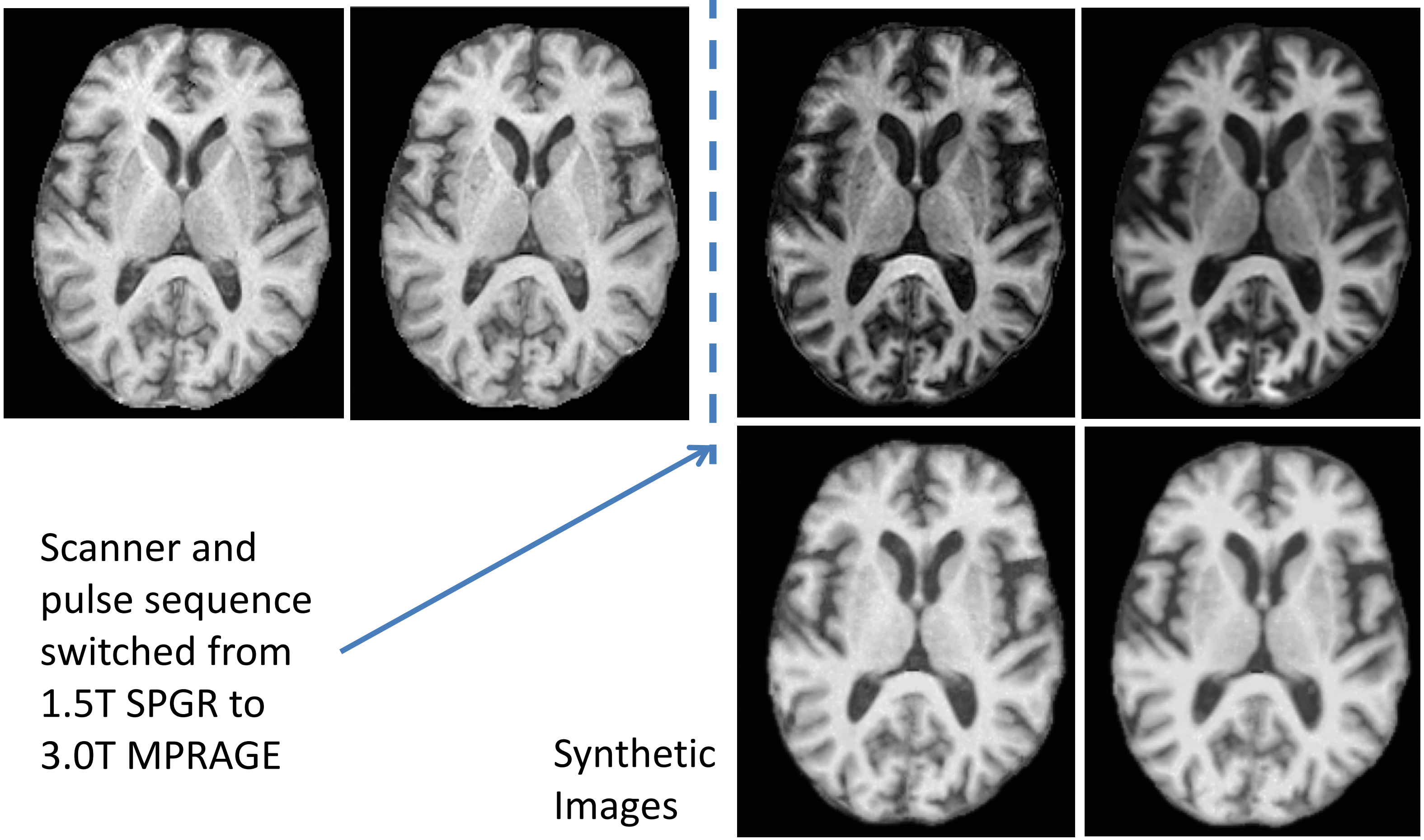


Example 1: Longitudinal Analysis

Year 1 Year 4 Year 12 Year 13

Single Subject

Original Images



Scanner and pulse sequence switched from 1.5T SPGR to 3.0T MPRAGE

Synthetic Images

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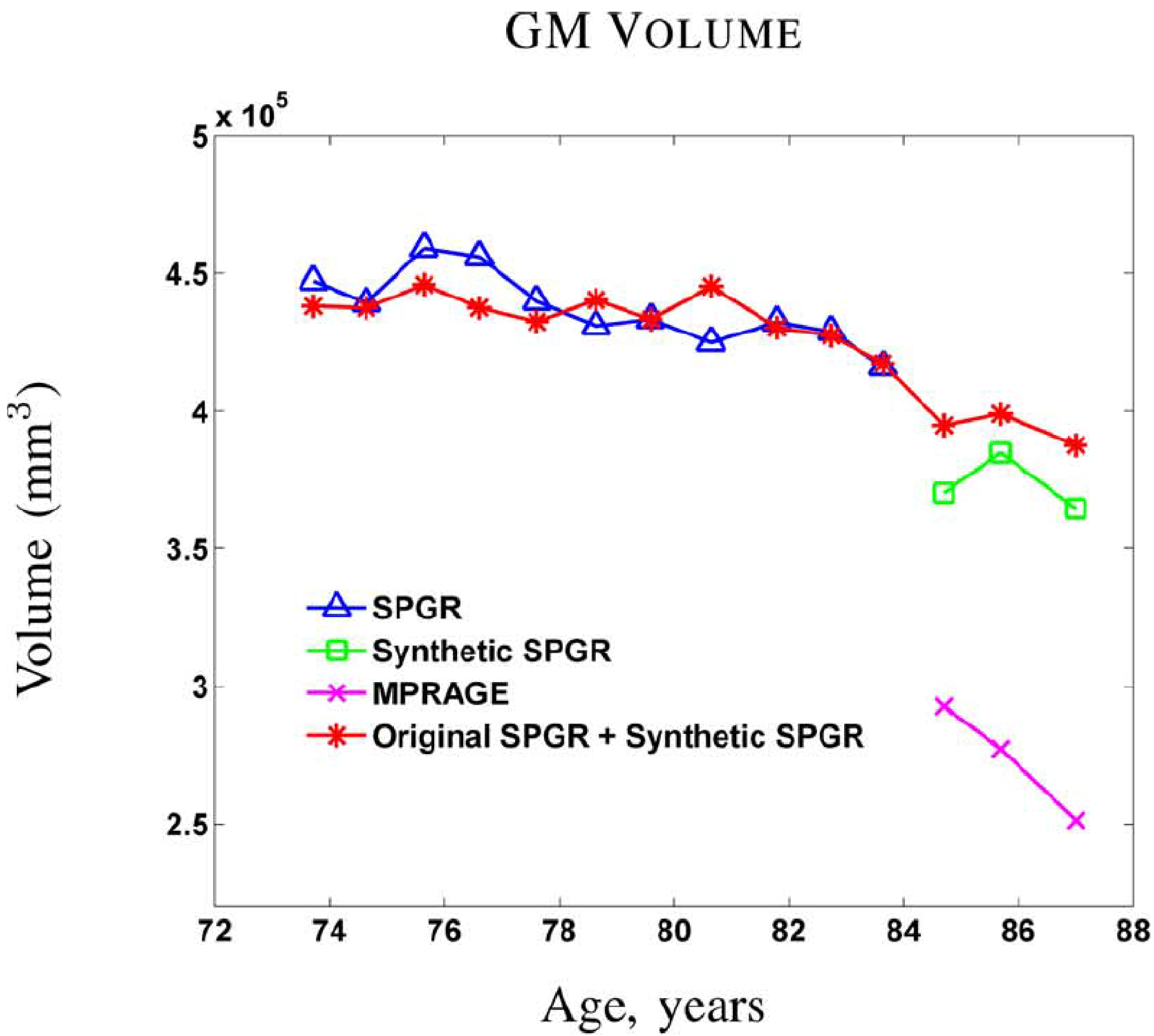
Example 1: Longitudinal Analysis



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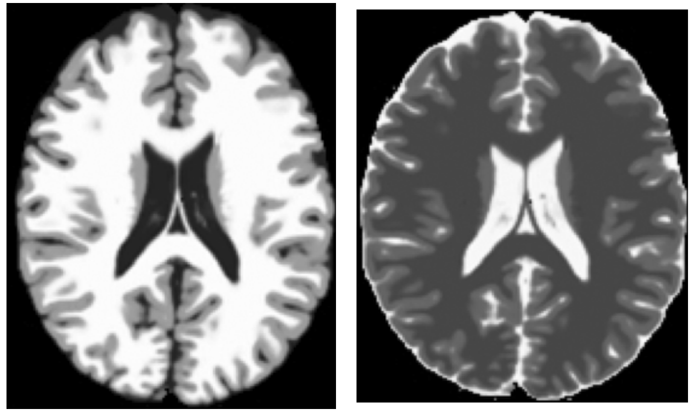
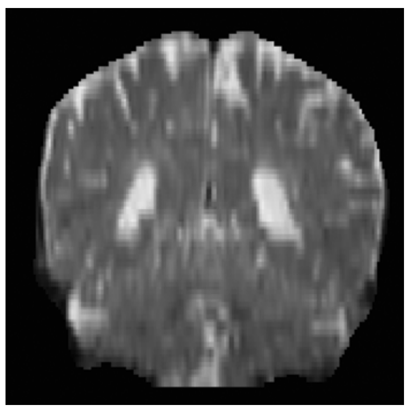
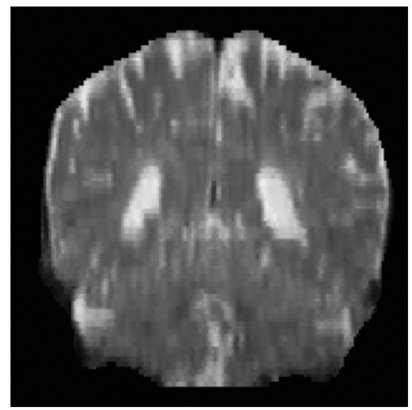
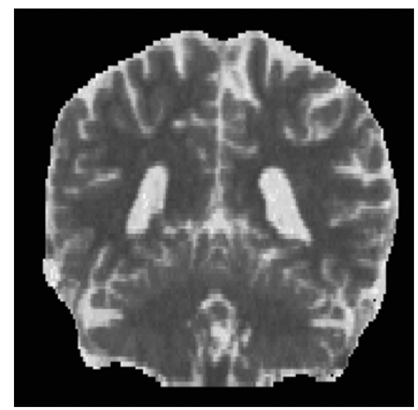
Example 2: High Res T2 Synthesis

Brainweb atlas.
Both images are high-resolution









Subject SPGR

Subject T2

Nonlocal means superresolution reconstruction

MIMECS synthesized superresolution image

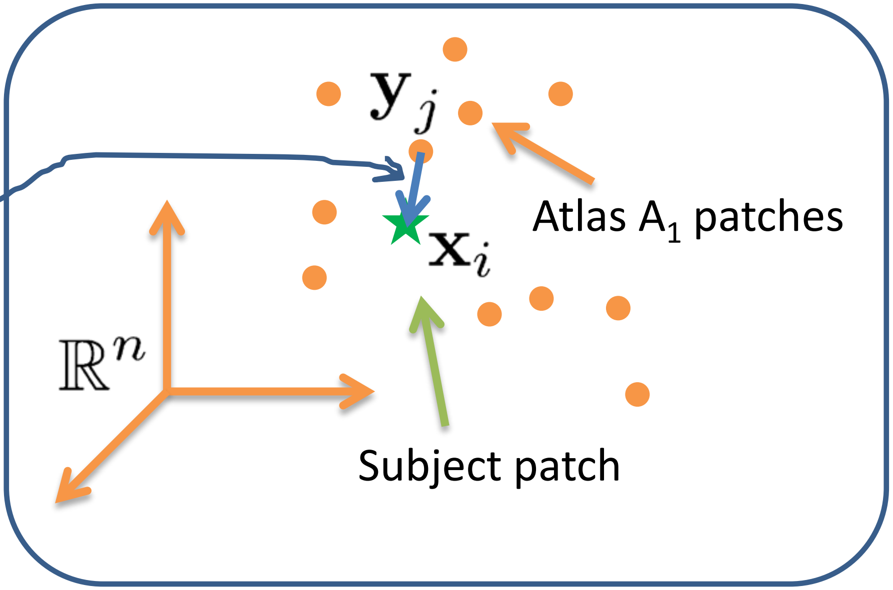
GENESIS SYNTHESIS METHOD

Generative Sub-Image Synthesis

Gaussian Observation Model

- Suppose each subject patch $\mathbf{x}_i$ originates from a single atlas patch $\mathbf{y}_j$ as a Gaussian random vector
- Let

$$\mathbf{f}_{ij} = \mathbf{x}_i - \mathbf{y}_j$$

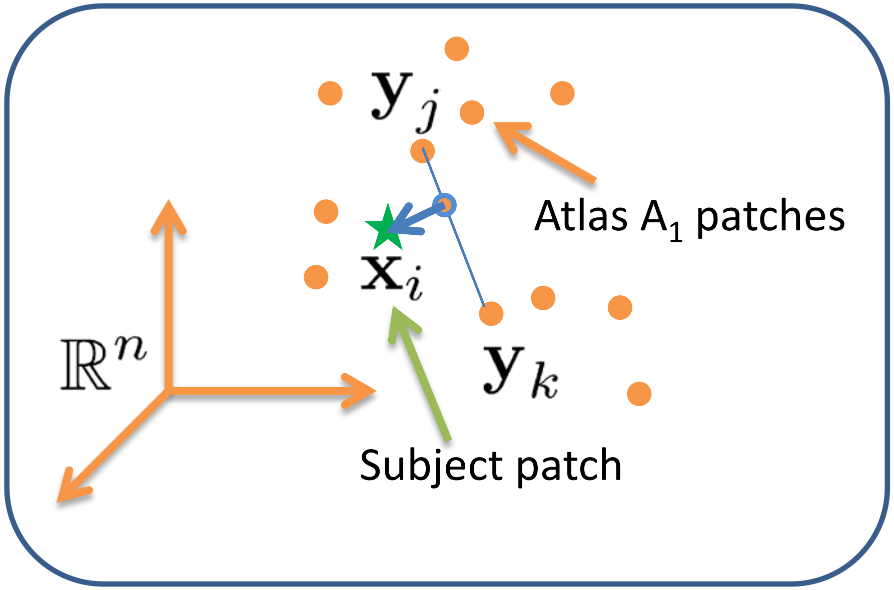


- Then

$$p(\mathbf{x}_i; \mathbf{y}_j, \Sigma_j) = \frac{1}{\sqrt{(2\pi)^n |\Sigma_j|}} \exp\left\{ -\frac{1}{2} \mathbf{f}_{ij}^T \Sigma_j^{-1} \mathbf{f}_{ij} \right\}$$

Sparsity-2 Model Is Better

- Suppose each subject patch $\mathbf{x}_i$ originates from two atlas patches $\mathbf{y}_j$ and $\mathbf{y}_k$ as a Gaussian random vector



- Let $t = \{j, k\}$ and

$$\mathbf{f}_{it} = \mathbf{x}_i - (\alpha_{it}\mathbf{y}_j + (1 - \alpha_{it})\mathbf{y}_k)$$

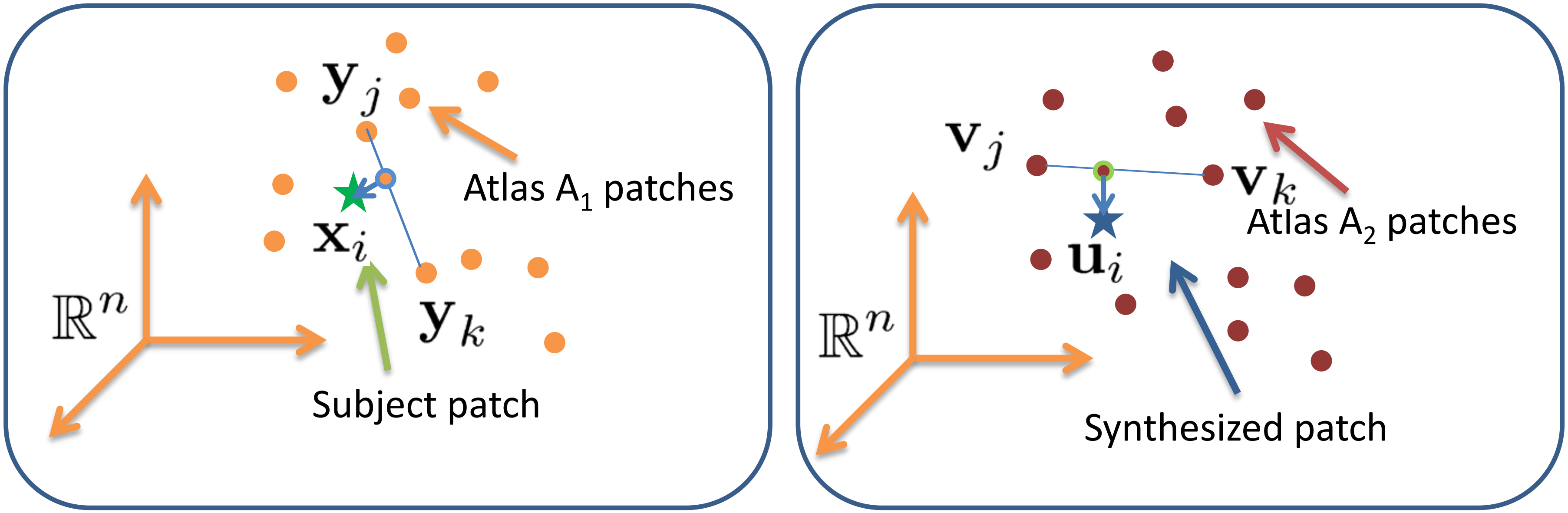
- Then

$$p(\mathbf{x}_i; \mathbf{y}_j, \mathbf{y}_k, \Sigma_t, \alpha_{it}) = \frac{1}{\sqrt{(2\pi)^n |\Sigma_t|}} \exp\left\{-\frac{1}{2}\mathbf{f}_{it}^T \Sigma_t^{-1} \mathbf{f}_{it}\right\}$$

What about the Second Modality?

- Assume the same convex combination $$\mathbf{g}_{it} = \mathbf{u}_i - (\alpha_{it}\mathbf{v}_j + (1-\alpha_{it})\mathbf{v}_k)$$
- Assume independence

$$p(\mathbf{f}, \mathbf{g}, \mathbf{z}|\mathbf{\Theta}) = K \prod_{t \in \Psi} \prod_{i=1}^{N} \left[\frac{1}{\sigma_{1t}\sigma_{2t}} \exp\left\{ -\frac{\|\mathbf{f}_{it}\|^2}{2\sigma_{1t}^2} \right\} \exp\left\{ -\frac{\|\mathbf{g}_{it}\|^2}{2\sigma_{2t}^2} \right\} \right]^{z_{it}}$$



ML Estimation using EM Algorithm

- EM algorithm iteratively estimates

$$\boldsymbol{\Theta}^{(m)} = \{\sigma_{1t}^{(m)}, \sigma_{2t}^{(m)}, \alpha_{it}^{(m)}; i = 1, \ldots, N, \forall t\}$$

- The E-step computes

$$w_{it} = E[z_{it} | \mathbf{f}, \mathbf{g}, \boldsymbol{\Theta}^{m}]$$

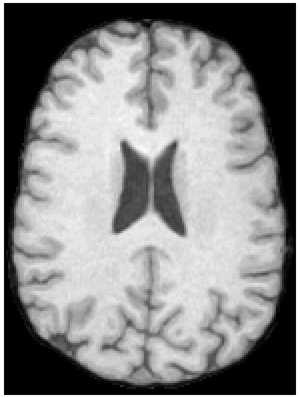
- The M-step maximizes likelihood w.r.t. $\boldsymbol{\Theta}$
- Patches are synthesized using

$$\hat{\mathbf{u}}_i = E[\mathbf{u}_i | \boldsymbol{\Theta}^{(m)}] = \sum_{t \in \Psi} w_{it}^{(m)} \left(\alpha_{it}^{(m)} \mathbf{v}_j + (1 - \alpha_{it}^{(m)}) \mathbf{v}_k \right)$$

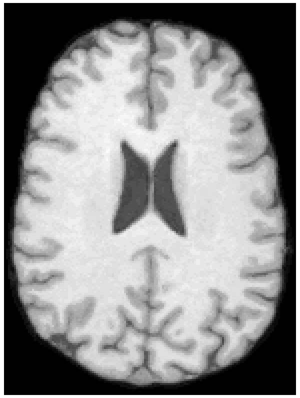
- They are linear combination of small number of atlas patches

Experiment 3: Intensity Normalization

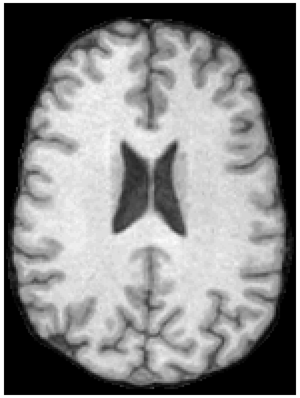
Subject (α = 20°)



Normalized to α = 30°

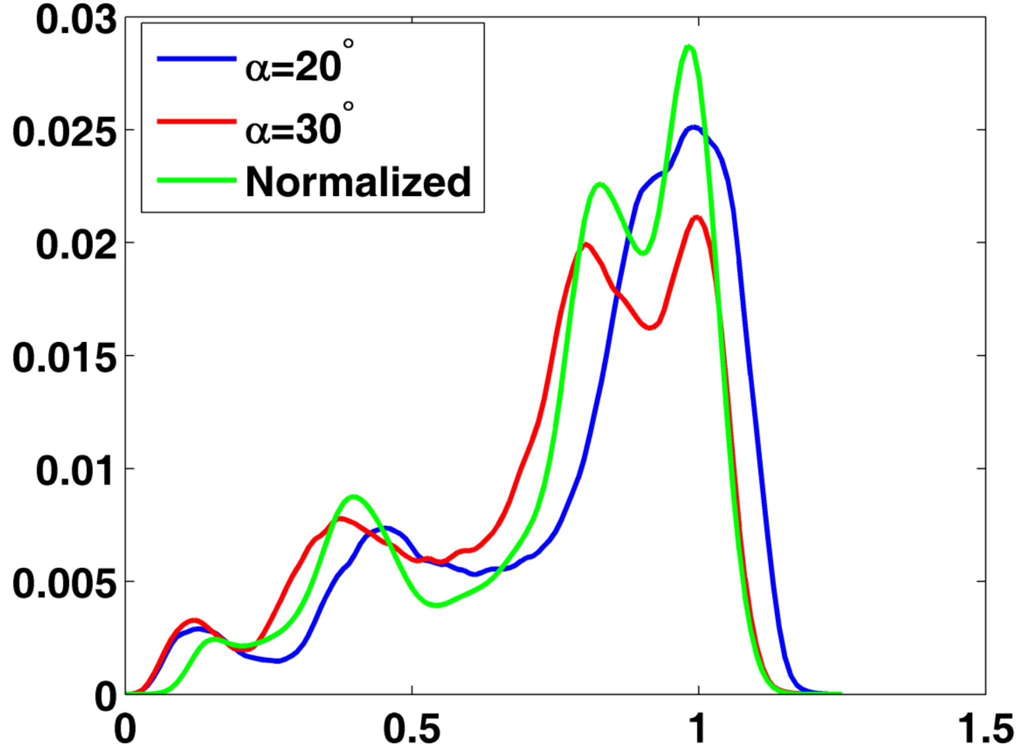


Subject (α = 30°)



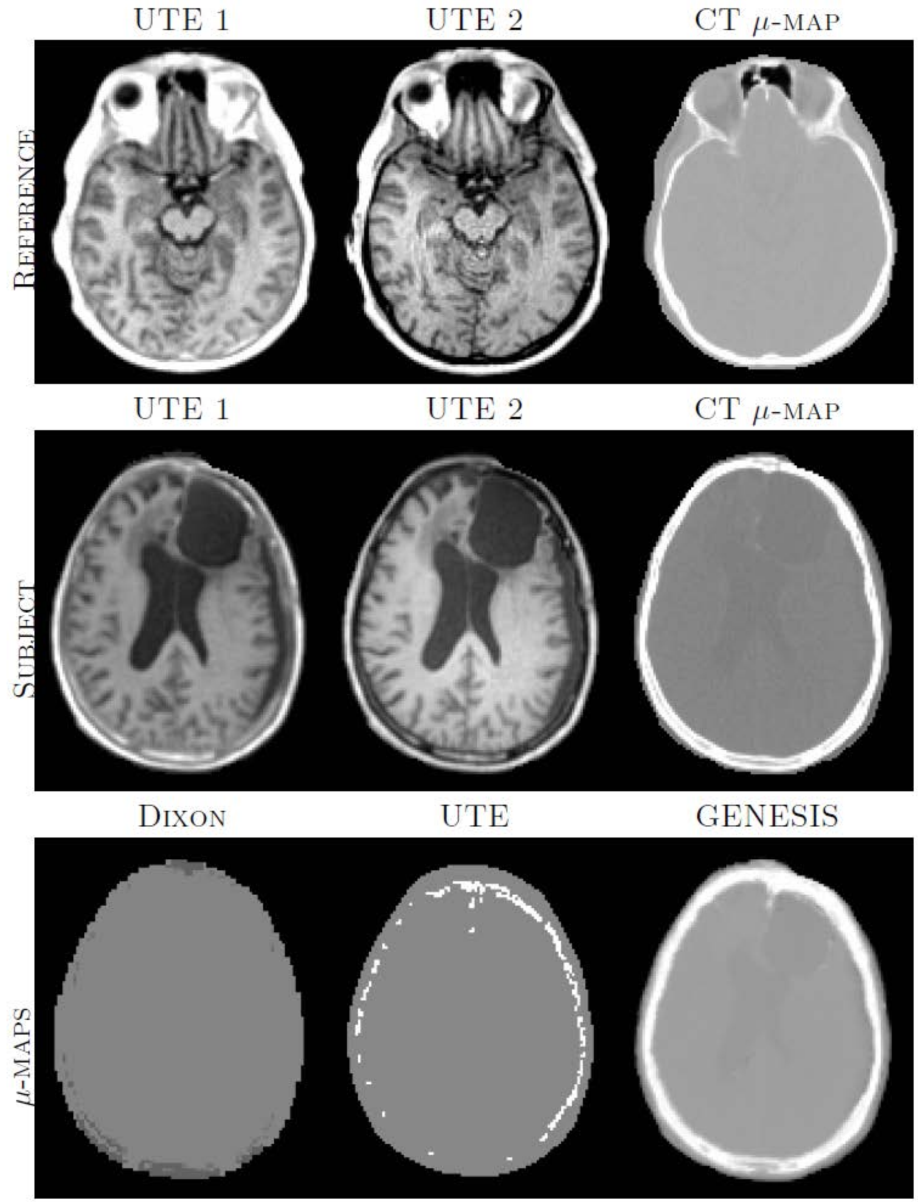
SPGR images with different tip angles

Histograms



Experiment 4: MR to CT Image Synthesis

- CT is needed for
  - Surgical planning
  - PET reconstruction
- Sometimes not acquired
  - Avoid dose
  - Not standard of care
  - PET/MR scanners
- Acquire two ultrashort TE MR (UTE) scans; atlas also has CT
- Compared to other methods, GENESIS is far superior



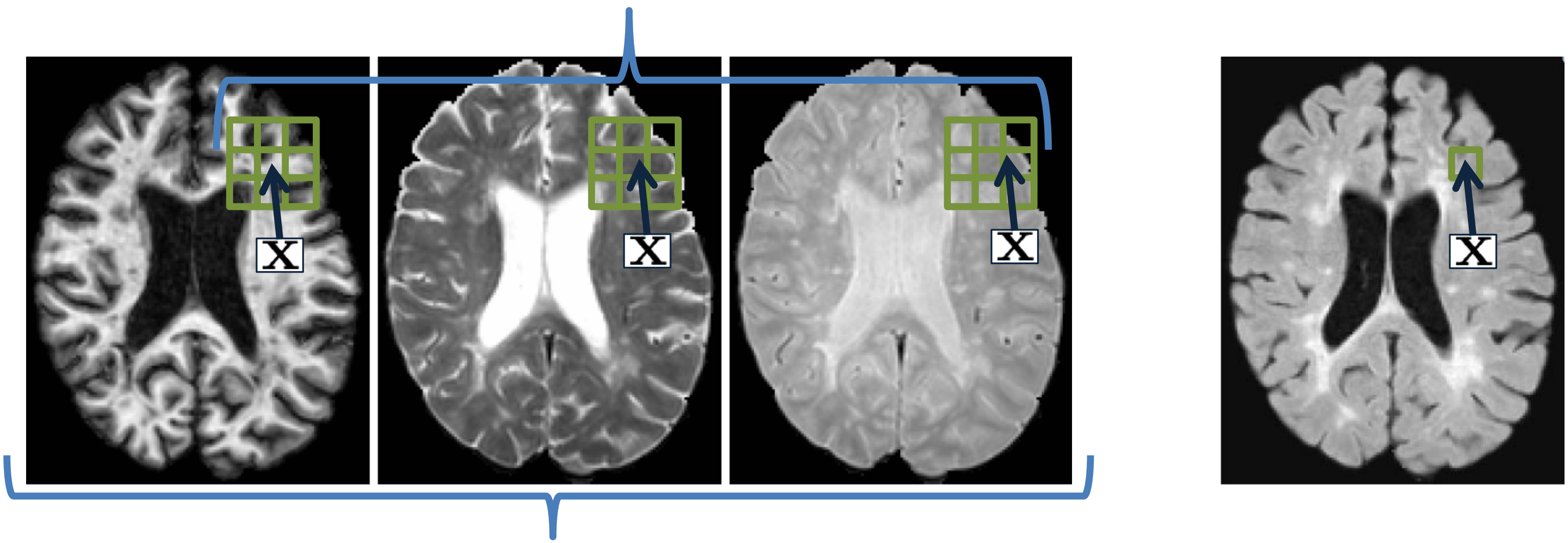
REPLICA SYNTHESIS METHOD

Regression Ensembles with Patch Learning for Image Contrast Agreement

Replica Uses a Regression Framework

Feature vector at $\mathbf{x}$: $\mathbf{f}(\mathbf{x})$

Image value at $\mathbf{x}$: $a(\mathbf{x})$



Source Images

Target Image

Given a training atlas learn $\mathcal{A}$ such that: $a(\mathbf{x}) \approx \mathcal{A}\{\mathbf{f}(\mathbf{x})\}$

Building a Single Regression Tree

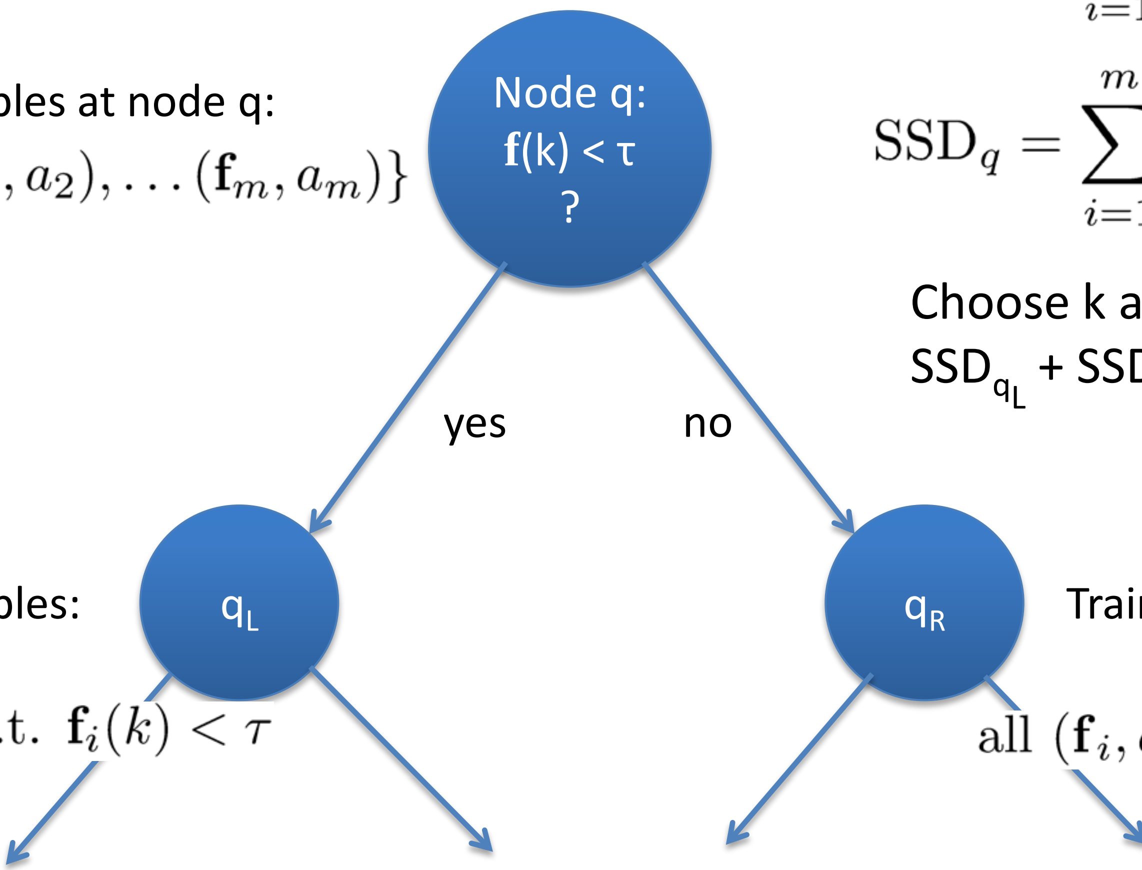
Let $\mathbf{f}_i = \mathbf{f}(\mathbf{x}_i) \quad a_i = a(\mathbf{x}_i)$

$$\bar{a}_q = \frac{1}{m}\sum_{i=1}^{m} a_i$$

Training samples at node q:

$$\{(\mathbf{f}_1, a_1), (\mathbf{f}_2, a_2), \ldots (\mathbf{f}_m, a_m)\}$$

$$\mathrm{SSD}_q = \sum_{i=1}^{m}(a_i - \bar{a}_q)^2$$



Choose k and τ to minimize $\mathrm{SSD}_{q_L} + \mathrm{SSD}_{q_R}$

Training samples:

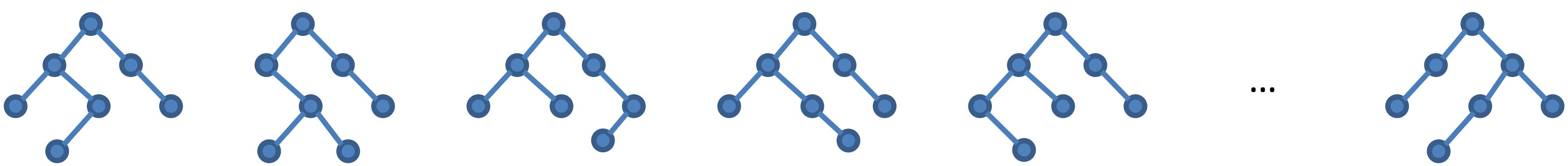
all $(\mathbf{f}_i, a_i)$ s.t. $\mathbf{f}_i(k) < \tau$

Training samples:

all $(\mathbf{f}_i, a_i)$ s.t. $\mathbf{f}_i(k) \geq \tau$

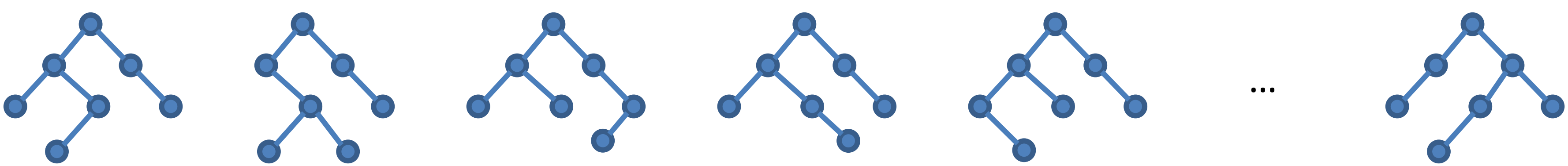
How to Create a Random Forest

- Train 60 regression trees:
  - At each nodal split, consider a random one third of the feature elements
  - Minimize the least squares criterion for these features
  - Recursively partition until there are no fewer than 5 training samples remaining in each leaf node
  - Average each leaf node
- To start, each tree uses bootstrapped training data (patches):
  - Training data are ~10^5 patches from 5 subjects
  - Sampled from all patches (with replacement)
- Training time is approximately 20 minutes

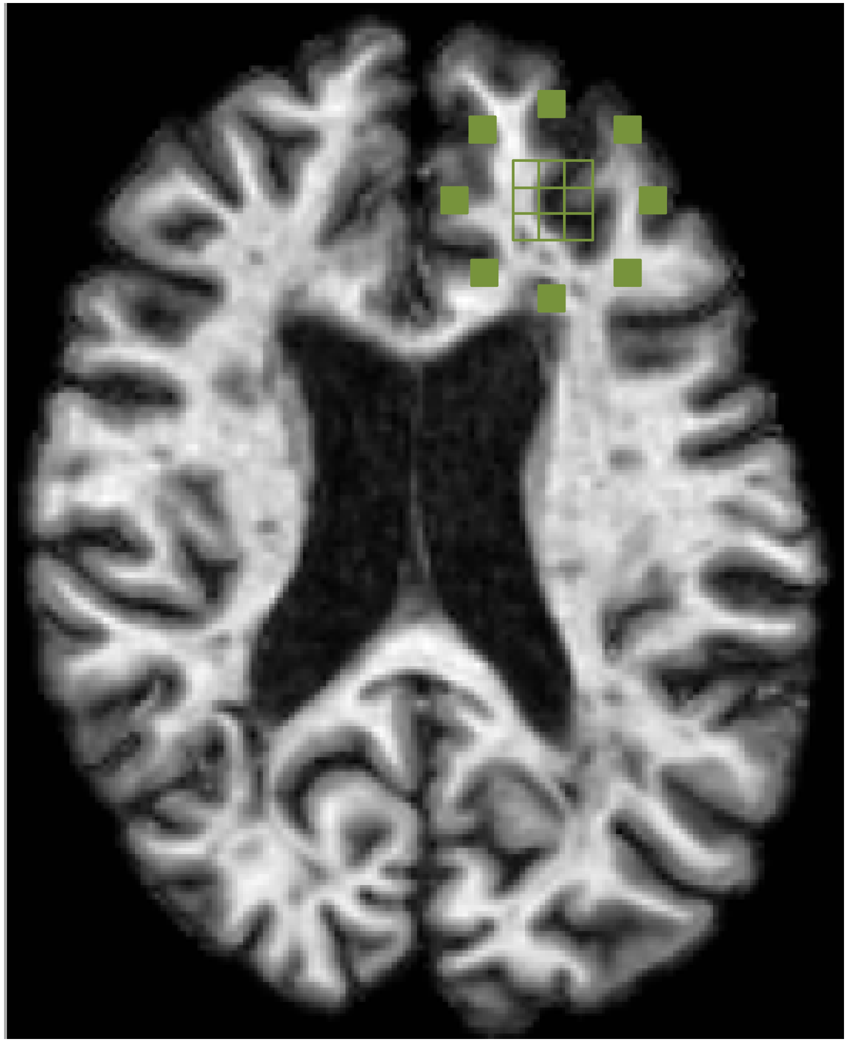


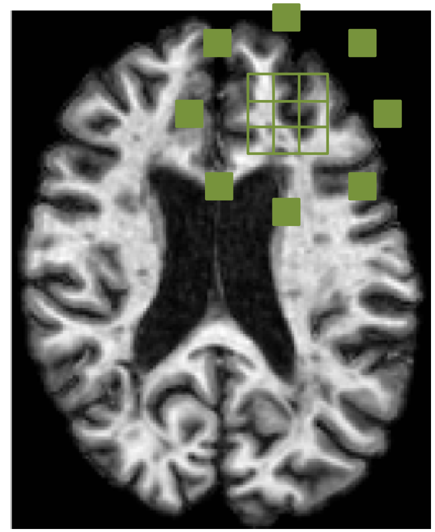
How to Use a Random Forest

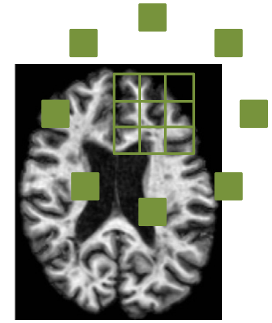
- Processing subject images
  - White matter peak normalize all images
  - Form patches and append into feature vectors
- Subject patches
  - Apply to each tree
  - Trace through each tree until hits leaf node
  - Average all leaf nodes to create synthetic image value
- Synthesis takes approximately 1 minute



Patch + Context + Multiscale Features

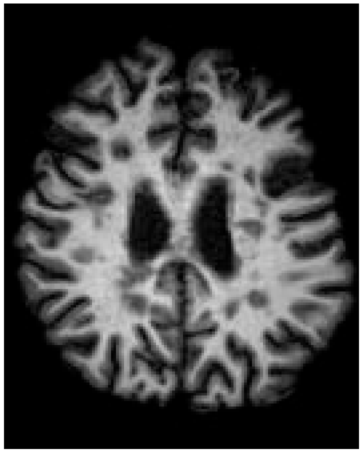






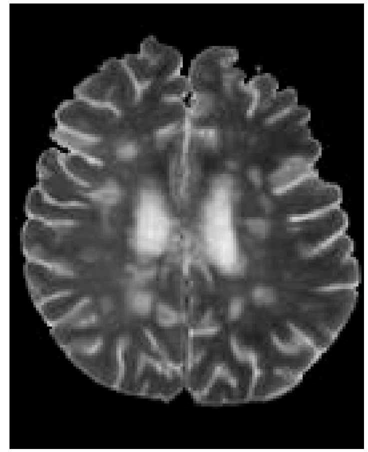
- Coarse-to-fine process:
  - Synthesize at coarsest level
  - Upsample
  - At next finer level, augment features with coarser synthetic value

Experiment 5: Synthetic FLAIR Images

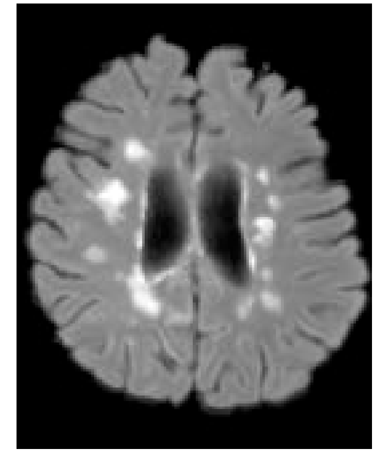


T1-w

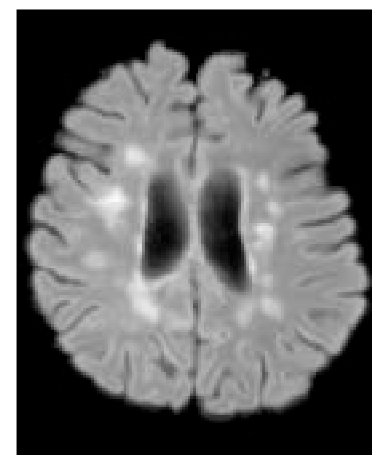
PD-w



T2-w



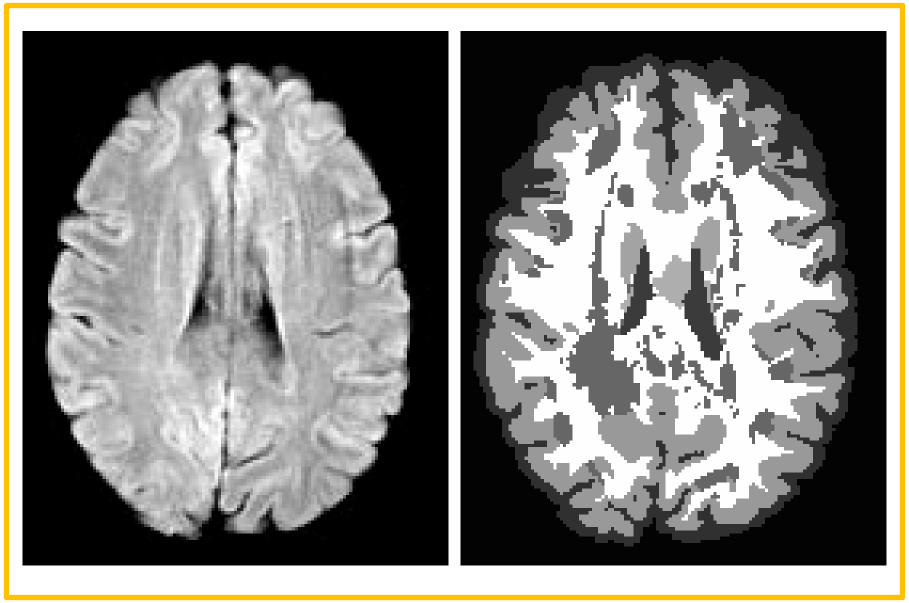
Synthetic FLAIR



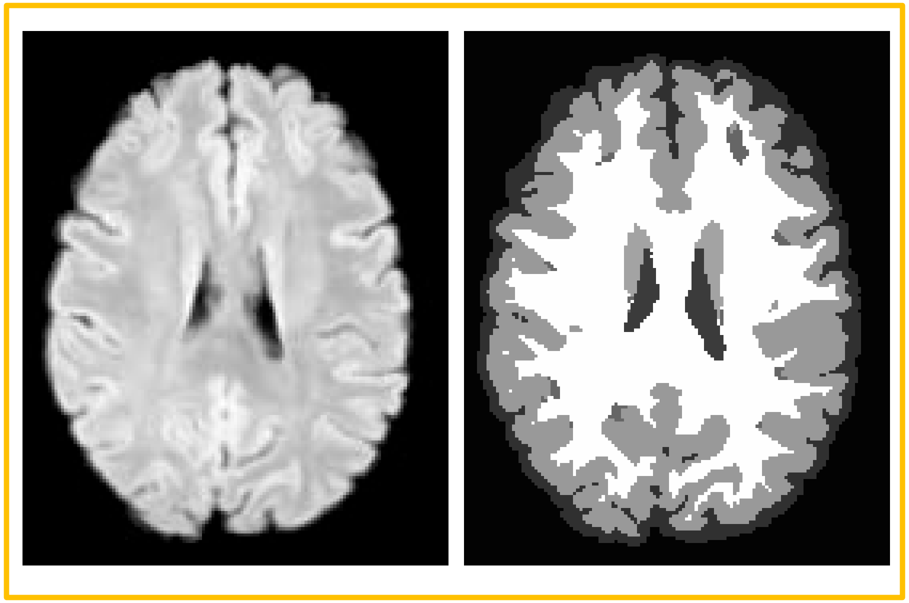
True FLAIR

- Subject images include T1w, T2w, PDw
- Atlas images include T1w, T2w, PDw

Synthetic FLAIR: Saving a “Bad” Dataset



True FLAIR + Lesion TOADs seg.



Synth. FLAIR + Lesion TOADs seg.

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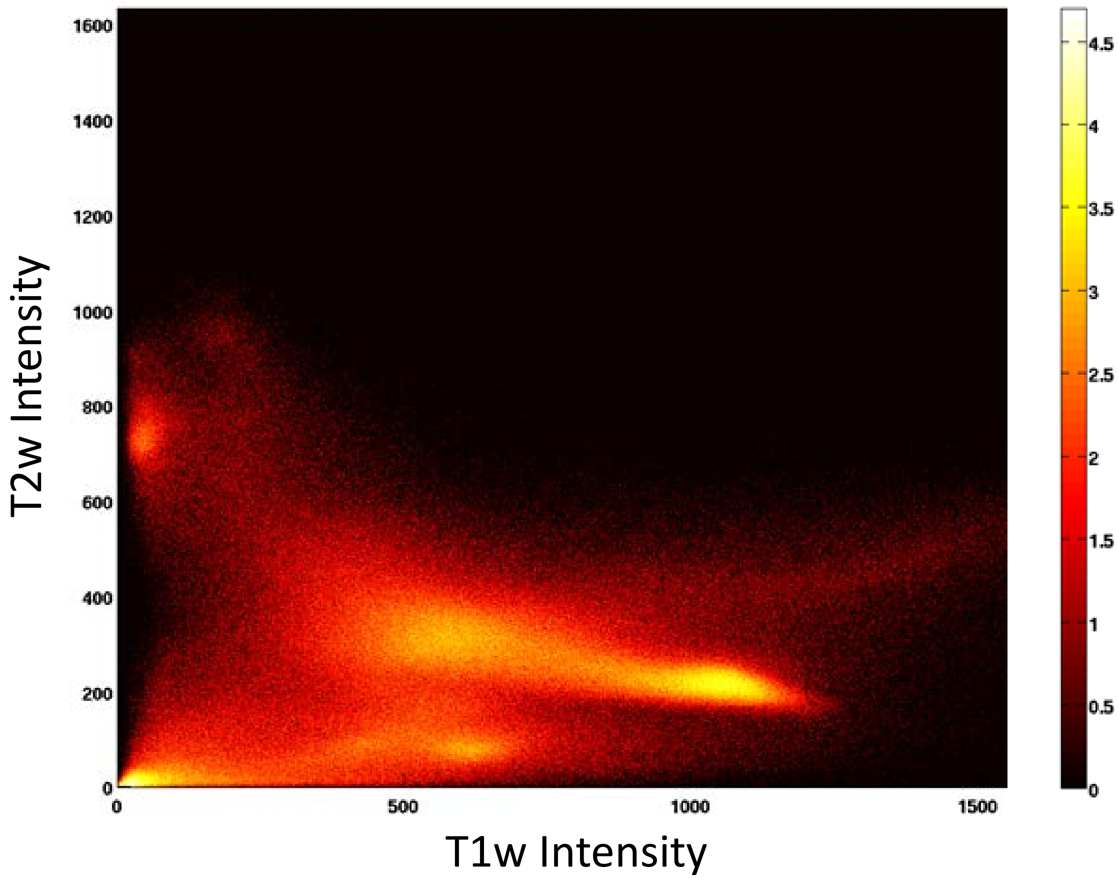
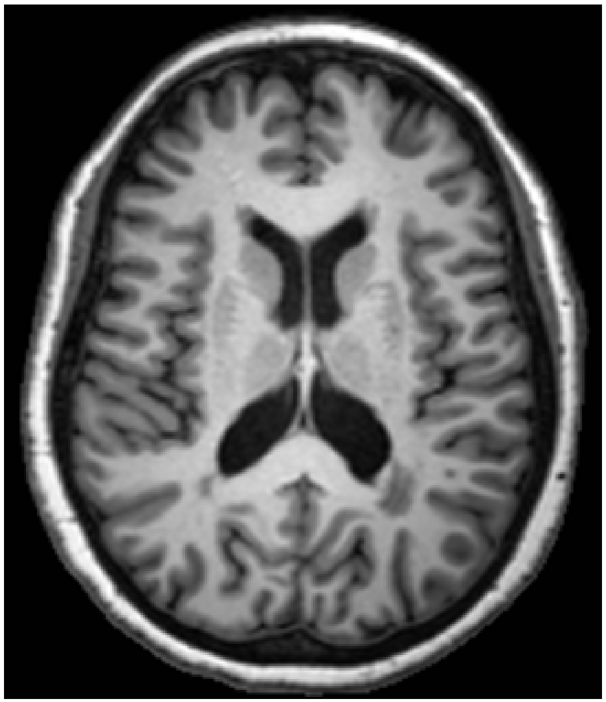
Experiment 6: Synthesis with Skull

- T1 → T2 problematic due to intensity ambiguity
- T1-T2 Histogram:

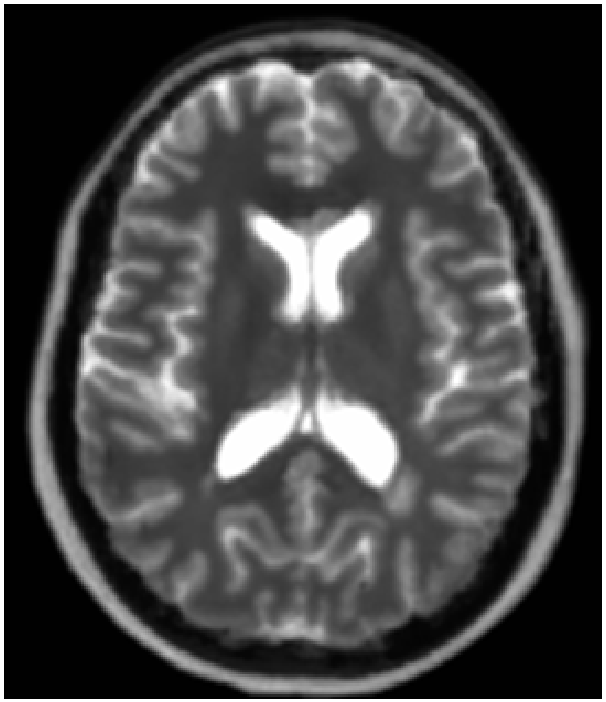


Experiment 6: T2 Synthesis with Skull

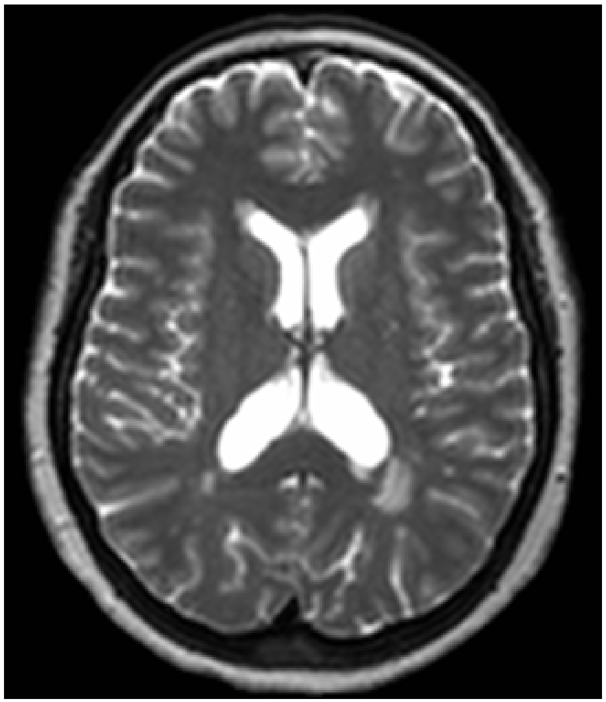
- Context features and multiscale are critical



MPRAGE (Subject)



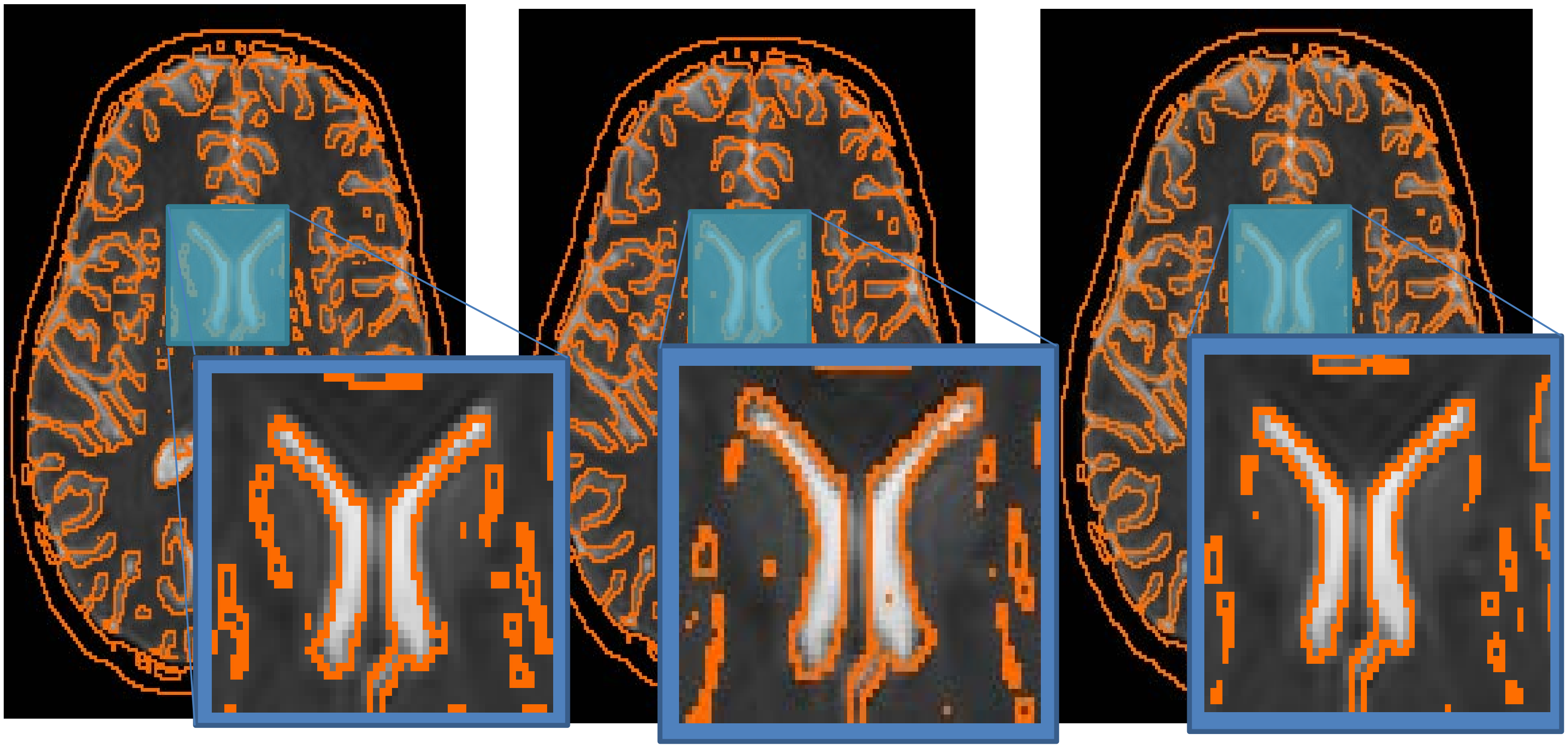
T2 (Synthetic)



T2 (Actual)

Experiment 7: Intrasubject Registration

Intrasubject T1w ➔ T2-w deformable registration



Rigid NMI

T1 $\longrightarrow$ T2
NMI

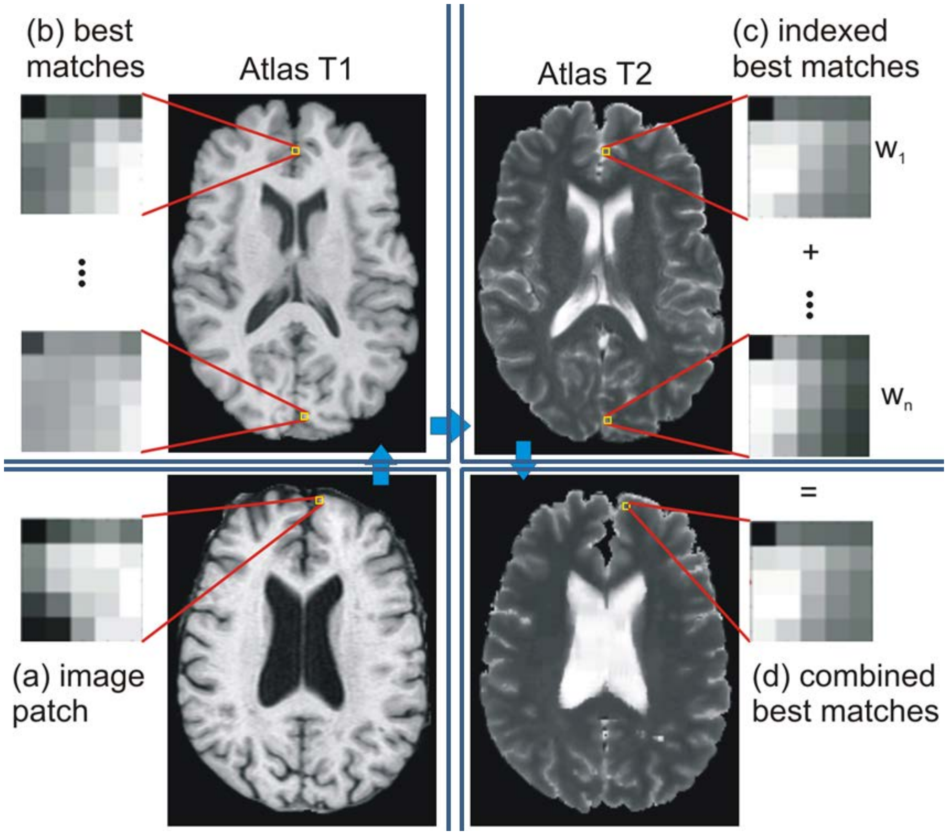
[nT1, sT2] $\Rightarrow$ [sT1, nT2]
CC

PSI-CLONE

Pulse sequence information-based contrast learning on neighborhood ensembles

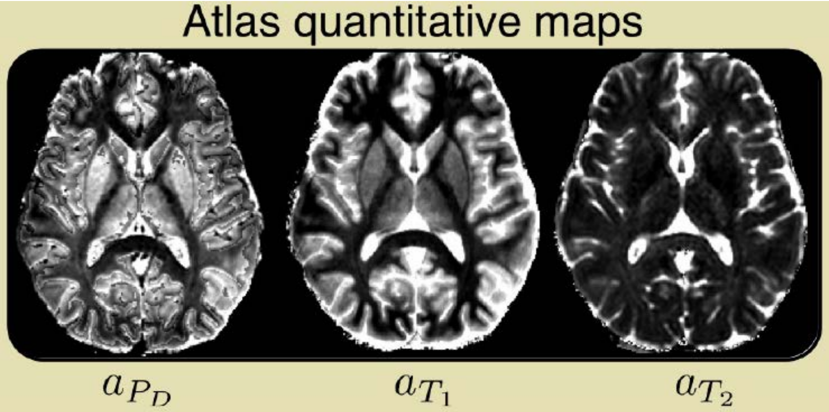
"Chicken and Egg" Problem

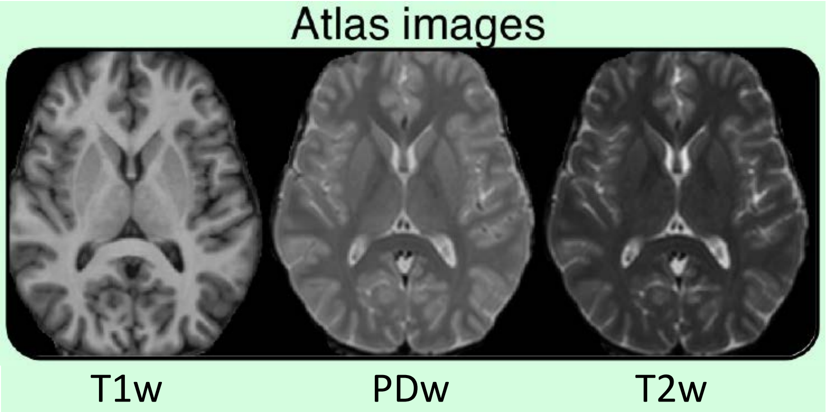
- The subject image must "match" an atlas image
  - In not, cannot choose good patches
- How to make subject image "match" the atlas?
  - Use MIMECS, GENESIS, or REPLICA ☺
- But this requires a matching atlas image
  - Uh oh… ☹



PSI-CLONE Framework

- Estimate subject pulse sequence parameters
  - E.g., TR, α, TE
- Synthesize a new ***atlas*** image a using pulse sequence parameters and atlas quantitative maps
- Use REPLICA training phase to learn a regression from a to the desired atlas contrast
- Use REPLICA synthesis process to synthesize a new subject image with the desired contrast





Estimating Pulse Sequence Parameters

- Underlying tissue properties

$$\boldsymbol{\beta}(\mathbf{x}) = [P_D(\mathbf{x}), T_1(\mathbf{x}), T_2(\mathbf{x})]$$

- Assume 3 unknown pulse sequence parameters, e.g.,

$$\boldsymbol{\Theta} = [T_E, T_R, \alpha]$$

- Imaging equations

$$b_i(\mathbf{x}) = \Gamma_i(\boldsymbol{\beta}(\mathbf{x}); \boldsymbol{\Theta}_i)$$

- Average tissue parameters in CSF, GM, and WM

$$\bar{\boldsymbol{\beta}}_C \qquad \bar{\boldsymbol{\beta}}_G \qquad \bar{\boldsymbol{\beta}}_W$$

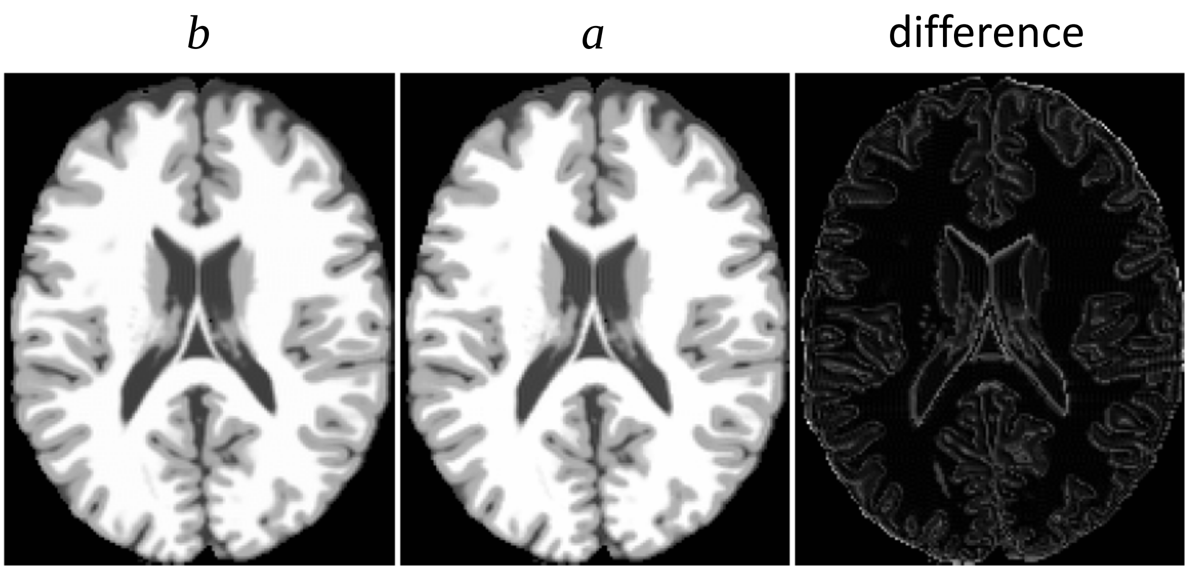
- Carry out 3-class classification of brain

$$\bar{b}_{iC} = \Gamma_i(\bar{\boldsymbol{\beta}}_C; \boldsymbol{\Theta}_i)$$
$$\bar{b}_{iG} = \Gamma_i(\bar{\boldsymbol{\beta}}_G; \boldsymbol{\Theta}_i)$$
$$\bar{b}_{iW} = \Gamma_i(\bar{\boldsymbol{\beta}}_W; \boldsymbol{\Theta}_i)$$

- Solve for Θ

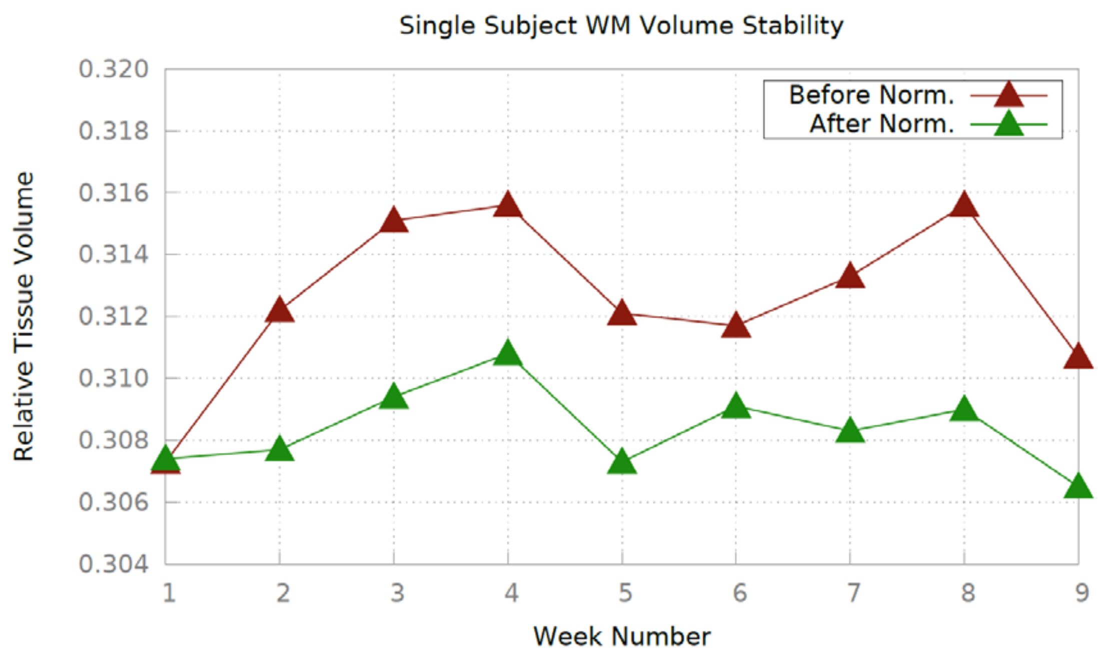
Experiment 8: BrainWeb Simulation

- Use quantitative maps from brainweb phantom
- Use Brainweb to synthesize a subject image: b
- Carry out Psi-CLONE on the subject to get an "atlas" image a with subject tissue contrast
- Result:



Experiment 9: WM Volume Stability

- Normal human imaged weekly on the same scanner for 9 weeks
- Atlas (different subject):
  - MPRAGE (TR=10.3ms, TE=6ms)
  - Quantitative T1, T2, PD
- Run Psi-CLONE to compute normalized MPRAGE images
- Segment MPRAGE images using TOADS
- Compute relative WM volume (w.r.t. ICV)
- Result:



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Summary

- Different methods for image synthesis based on patches:
  - MIMECS
  - GENESIS
  - REPLICA
  - Psi-CLONE
- Many potential applications:
  - Improve consistency of classification/segmentation
  - Stabilize longitudinal analysis
  - Generate high resolution alternative contrasts
  - Enhance abnormal features (e.g., lesions)
  - Improve cross modal registration
  - Reduce artifacts

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  - NIH/NINDS 5R01NS070906

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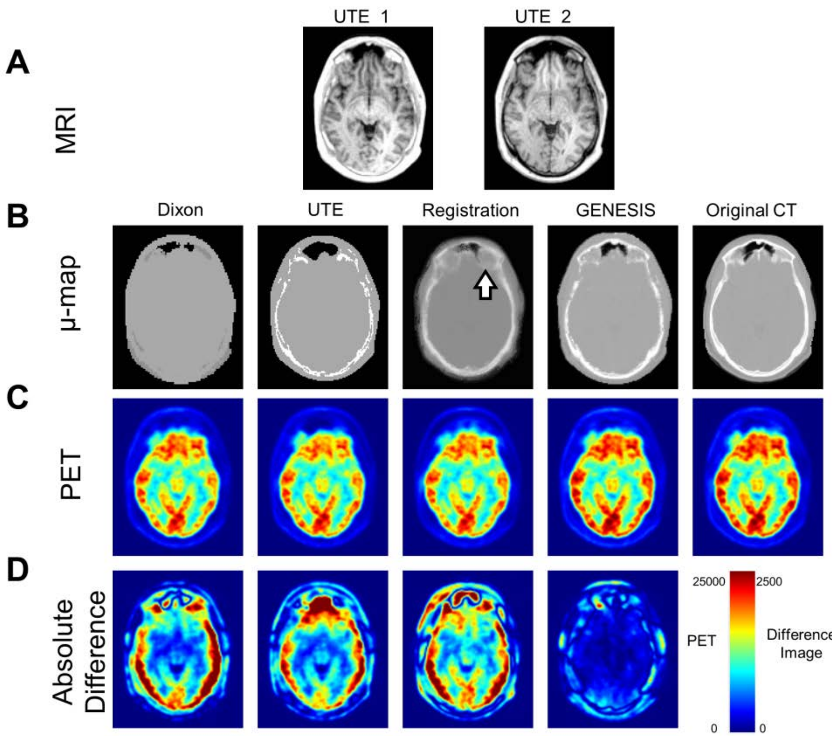
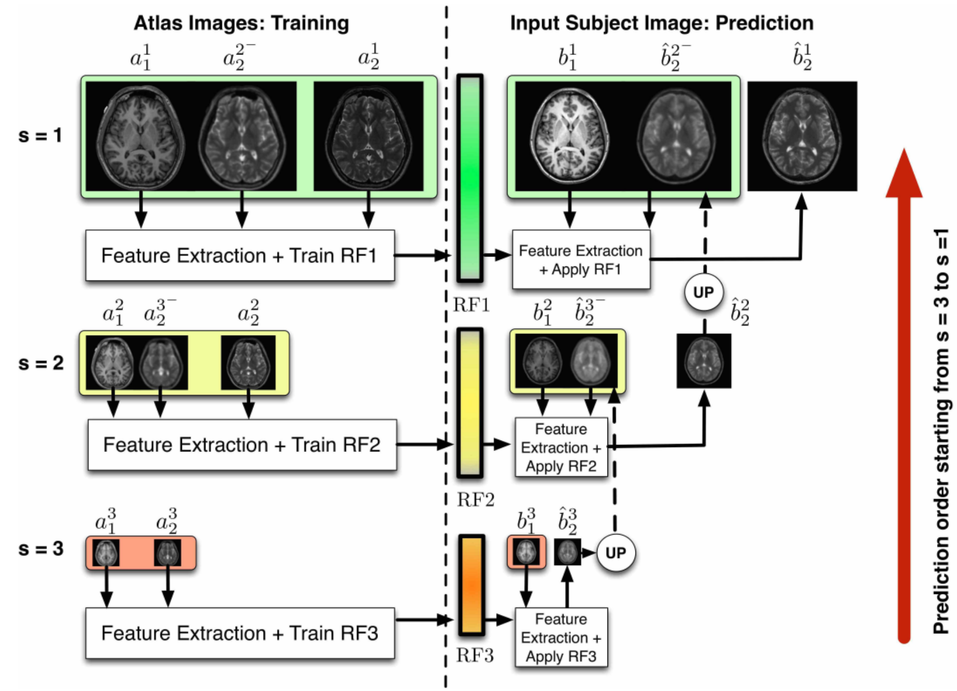
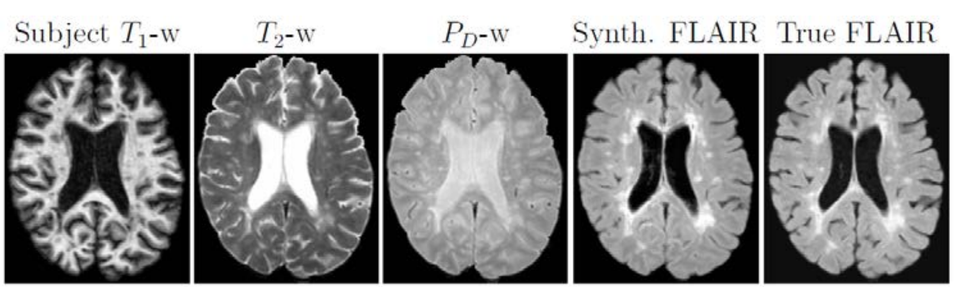
QUESTIONS?



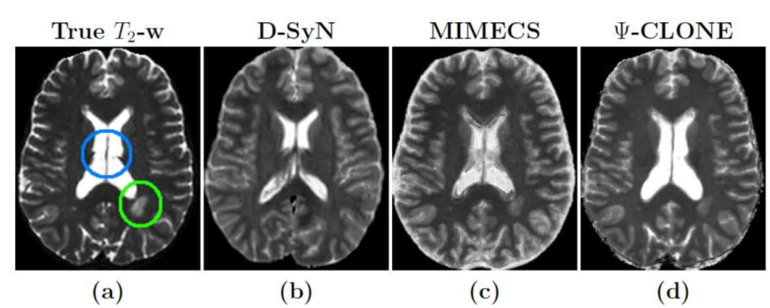
A
MRI
UTE 1
UTE 2
B
μ-map
Dixon
UTE
Registration
GENESIS
Original CT
C
PET
D
Absolute Difference
25000
2500
PET
Difference Image
0
0



Atlas Images: Training
Input Subject Image: Prediction
s = 1
s = 2
s = 3
Feature Extraction + Train RF1
Feature Extraction + Train RF2
Feature Extraction + Train RF3
Feature Extraction + Apply RF1
Feature Extraction + Apply RF2
Feature Extraction + Apply RF3
RF1
RF2
RF3
UP
Prediction order starting from s = 3 to s =1



Subject T_1-w
T_2-w
P_D-w
Synth. FLAIR
True FLAIR



True T_2-w
D-SyN
MIMECS
Ψ-CLONE
(a)
(b)
(c)
(d)