

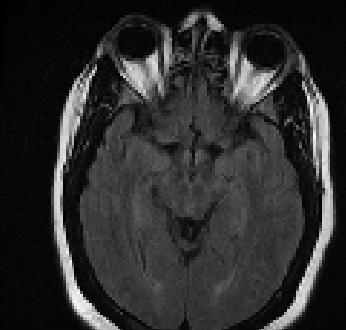
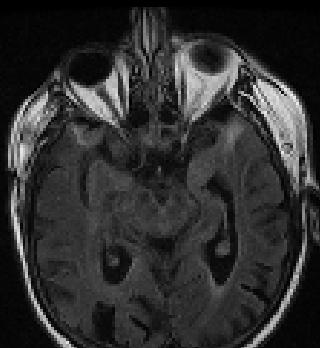
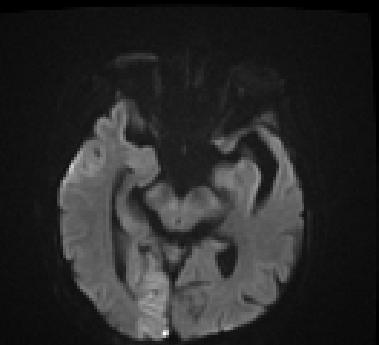
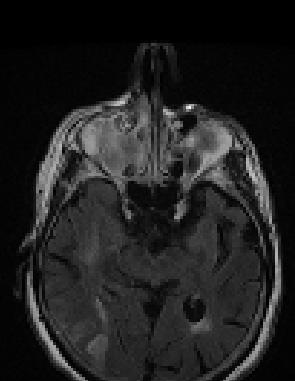
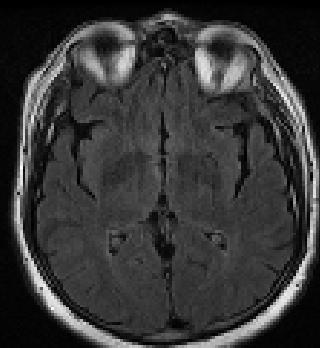
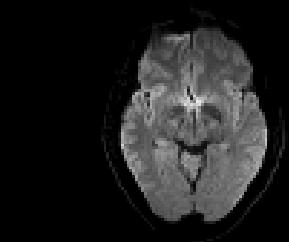
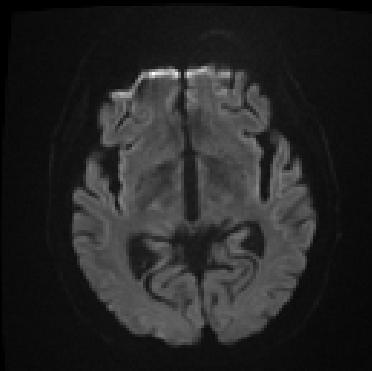
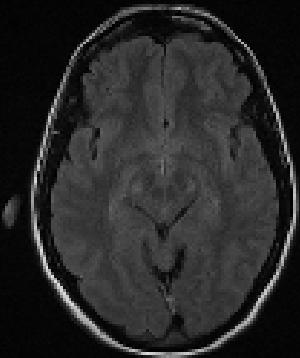
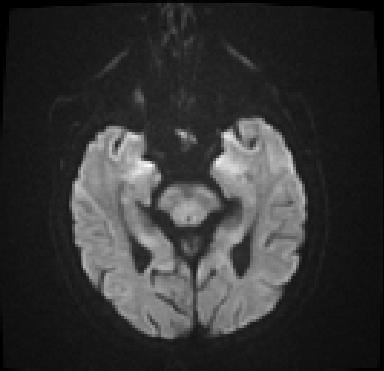
[voxelmorph.mit.edu](http://voxelmorph.mit.edu)

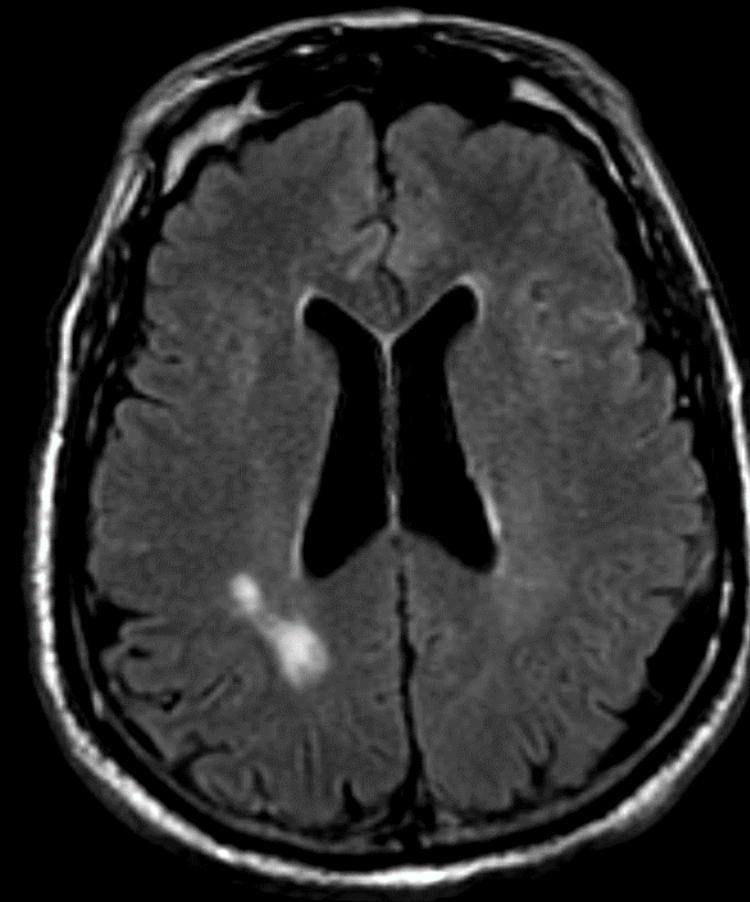
+ in future FreeSurfer release

# Unsupervised Learning of Image Correspondences in Medical Imaging Analysis

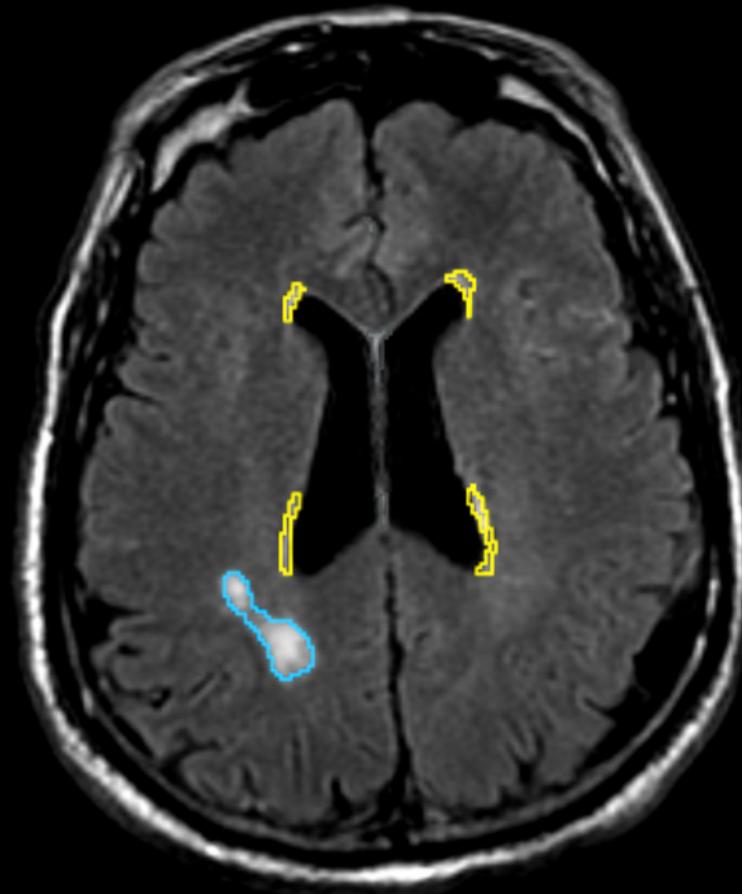
---

Adrian V. Dalca  
HMS, MIT





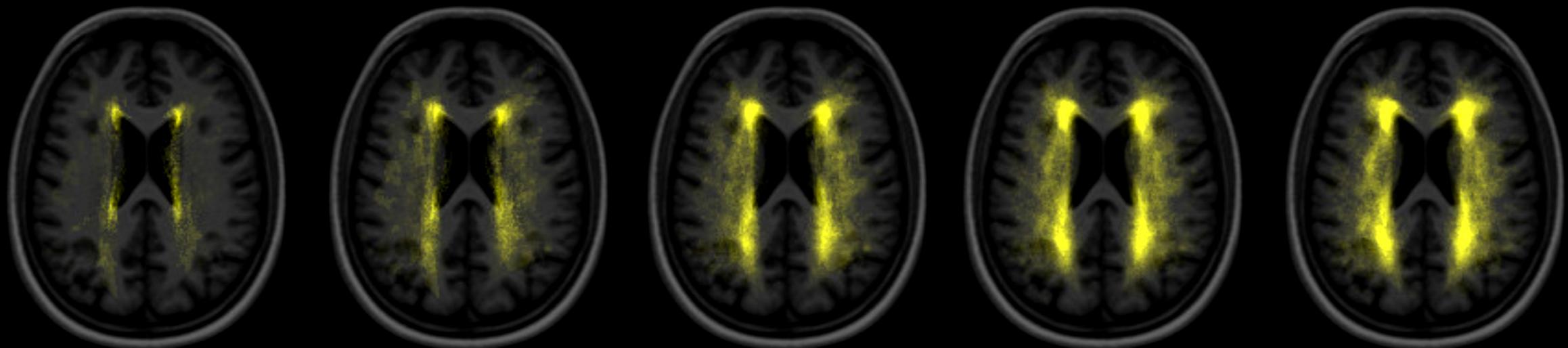
Stroke



Small vessel disease

# Progression with age

---



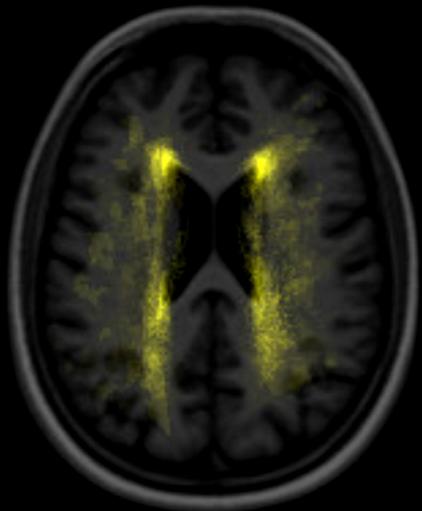
31 years  
average

42.5 years  
average

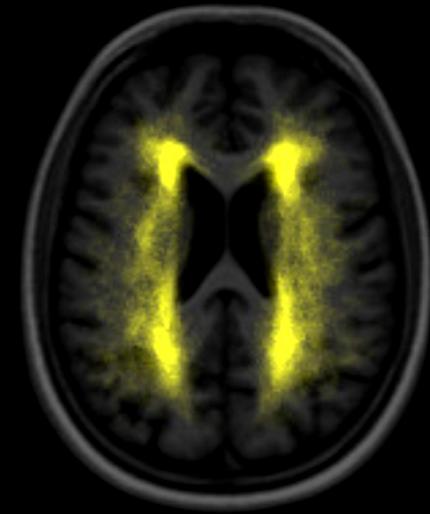
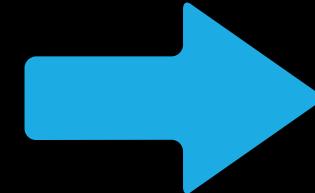
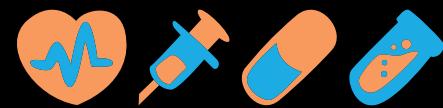
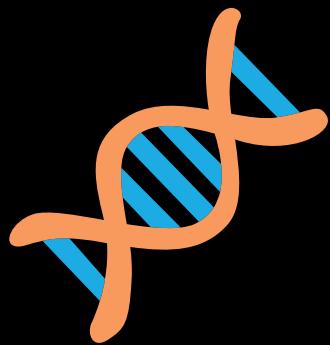
54 years  
average

65.5 years  
average

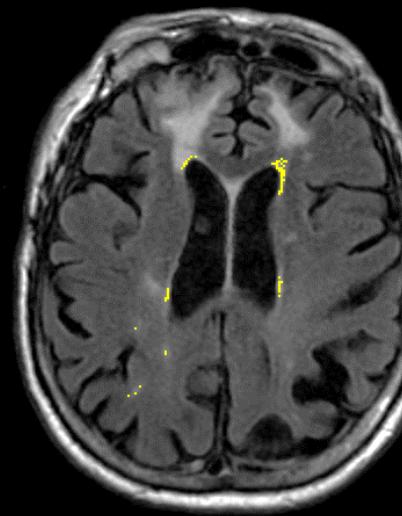
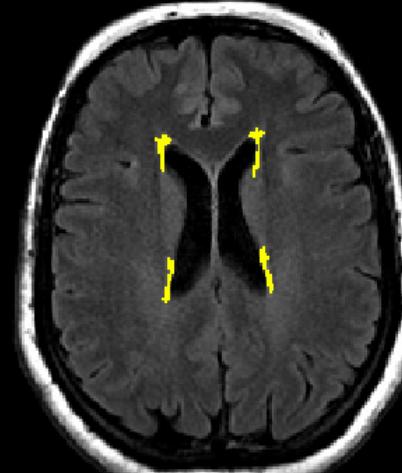
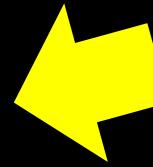
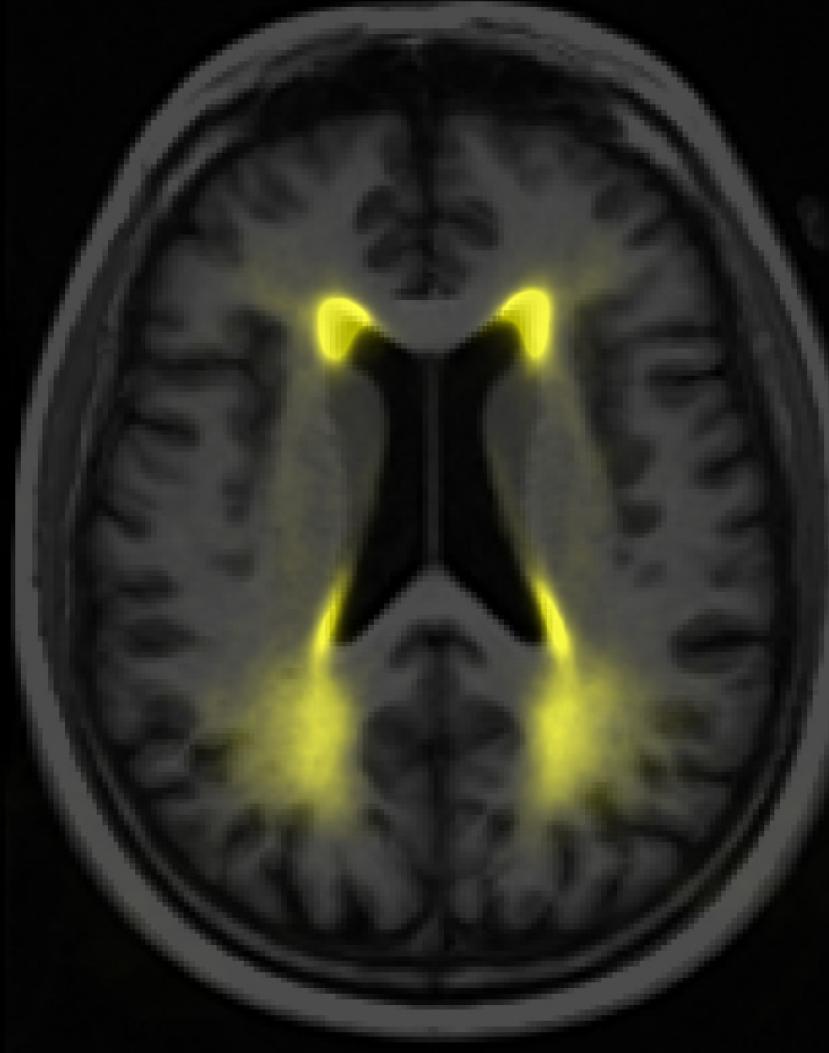
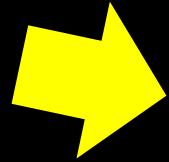
77 years  
average

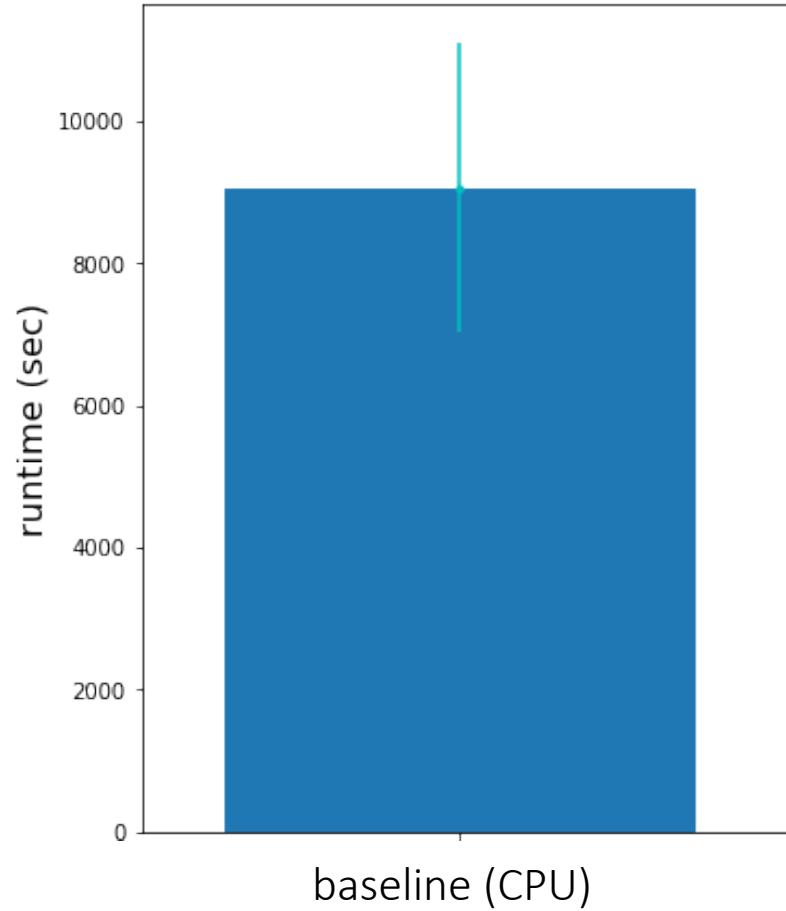


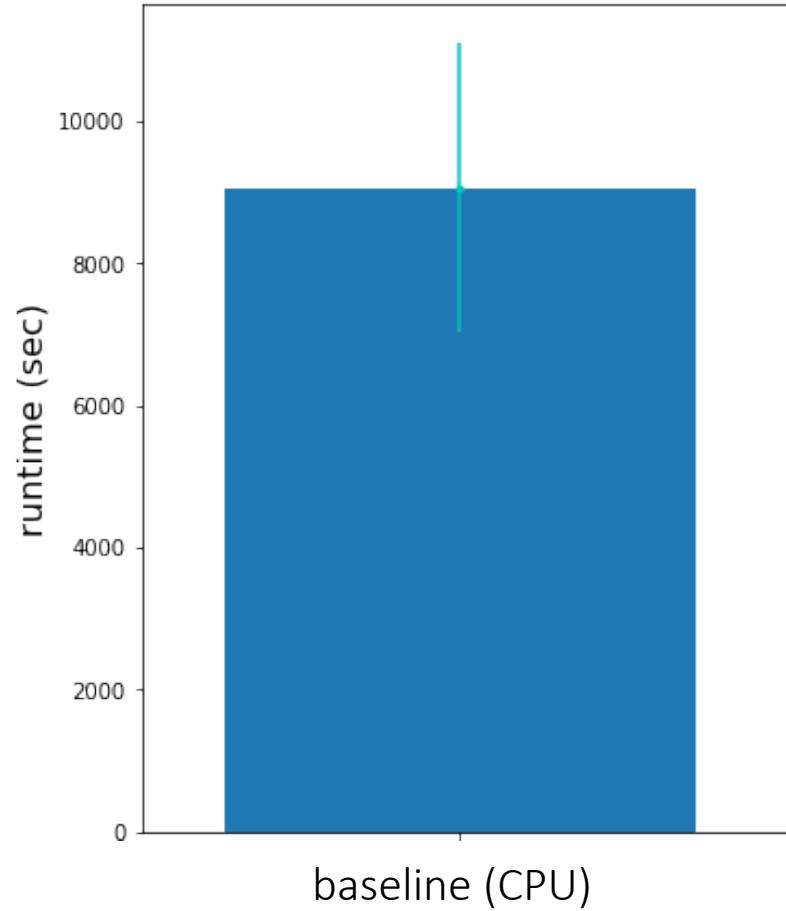
Scan at age 50



Scan at age 60

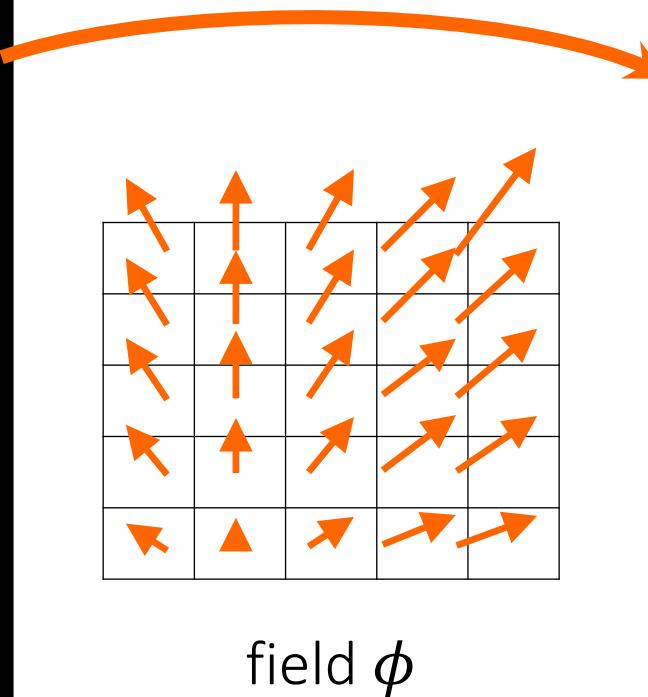




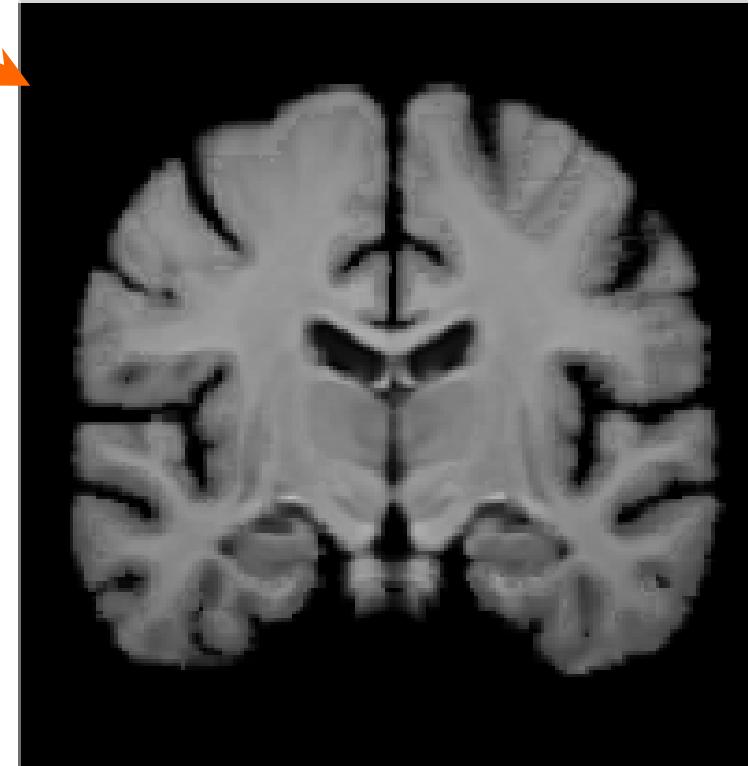


# Registration

---



moving scan  $m$



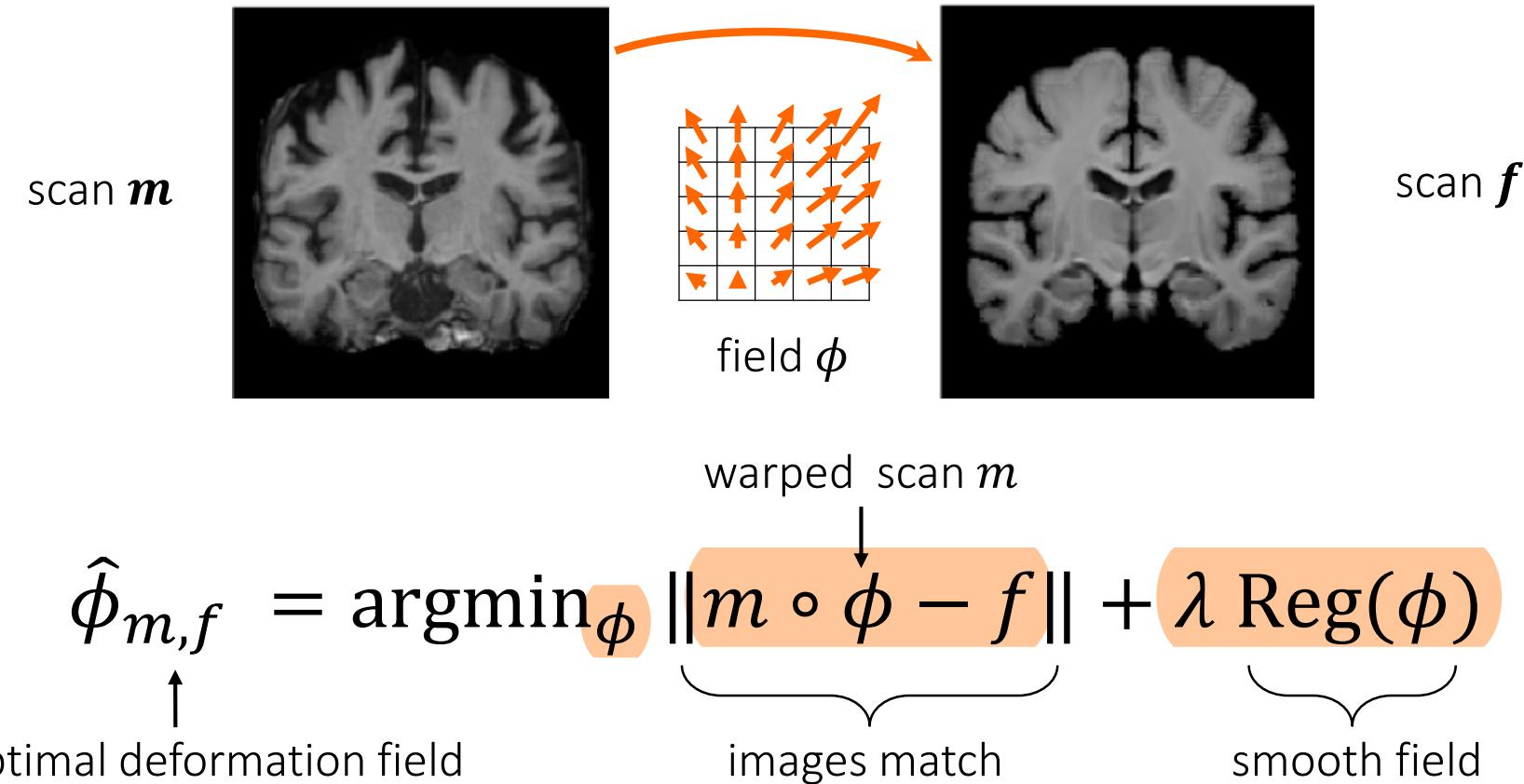
fixed scan  $f$

# Registration is fundamental in MIA

---

- Register scans to a template for analysis
- Register subject scans to each other for direct comparison
- Clinical data alignment  
e.g. before and after surgery
- Segmentation  
propagate anatomical labels
- Related to alignment in other fields  
computer vision, 1D signals, computational biology

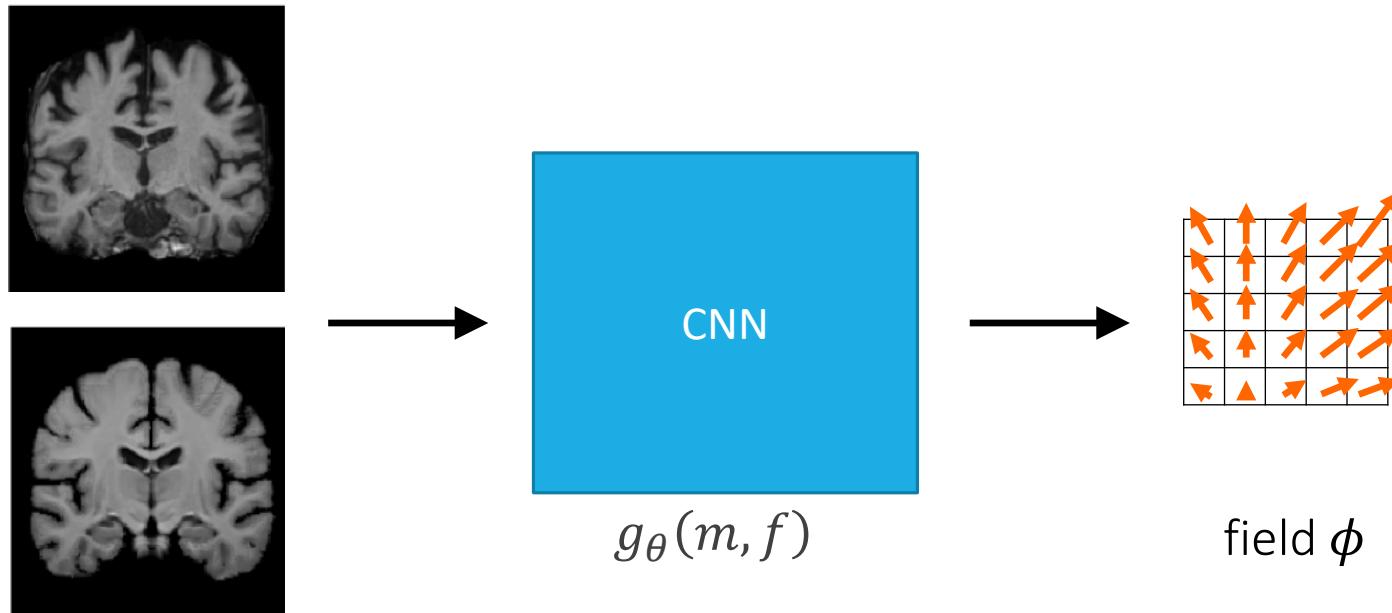
# Pairwise optimization



- significant development
- slow for two images

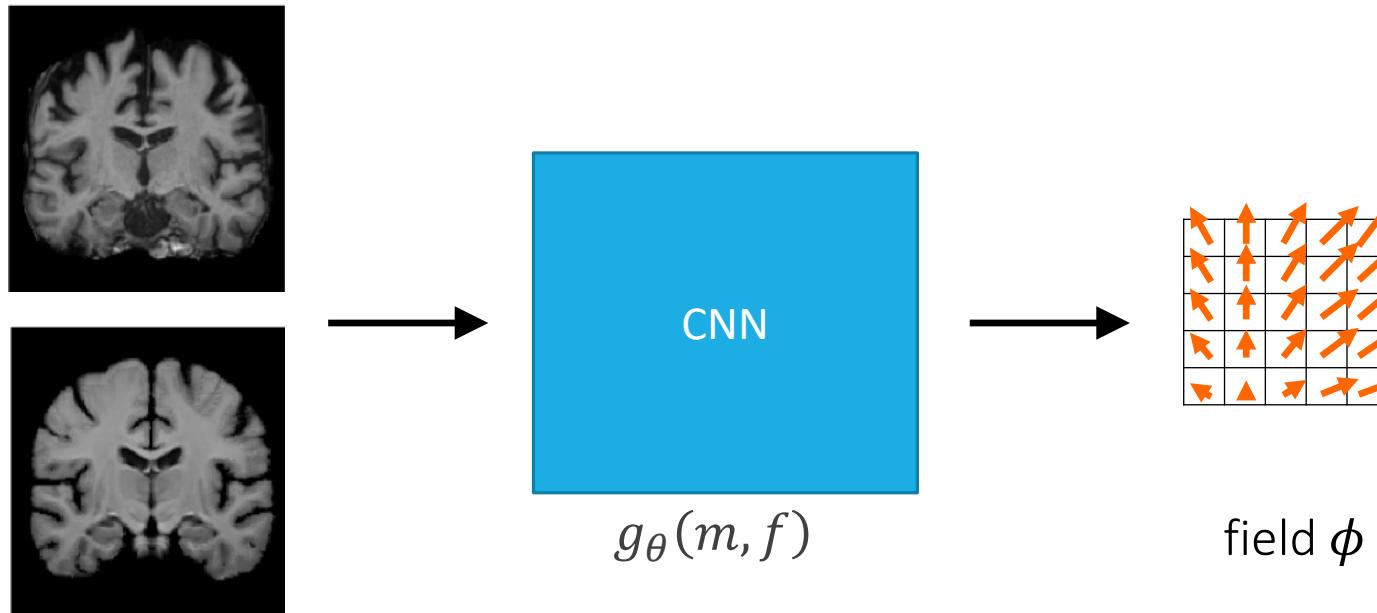
# Learning-based methods

---



- Supervised (have example triplets  $\{m, f, \phi\}$ )
- Unsupervised (only have images  $\{m, f\}$ ) (**voxelmorph**)

# Learning-based methods



- Supervised (have example triplets  $\{m, f, \phi\}$ )
- Unsupervised (only have images  $\{m, f\}$ ) (**voxelmorph**)

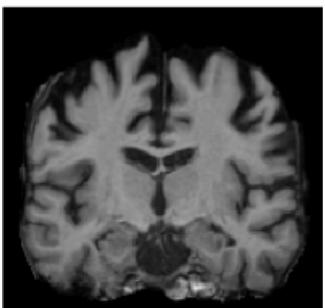
- limited use of classical modelling
- **fast** for new image pair

# Outline

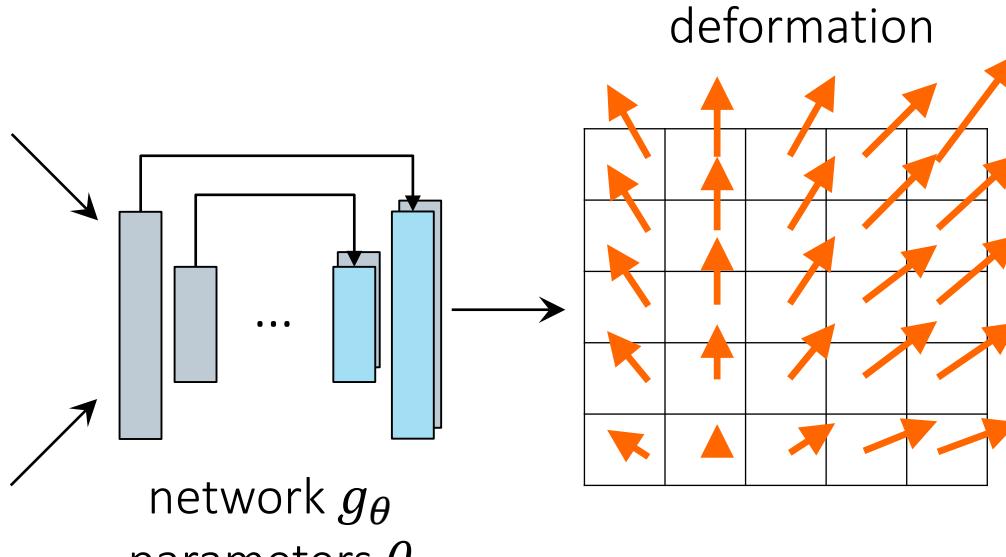
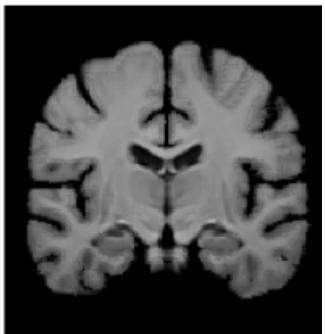
---

# Framework

Moving image  
( $m$ )



Fixed image  
( $f$ )



deformation

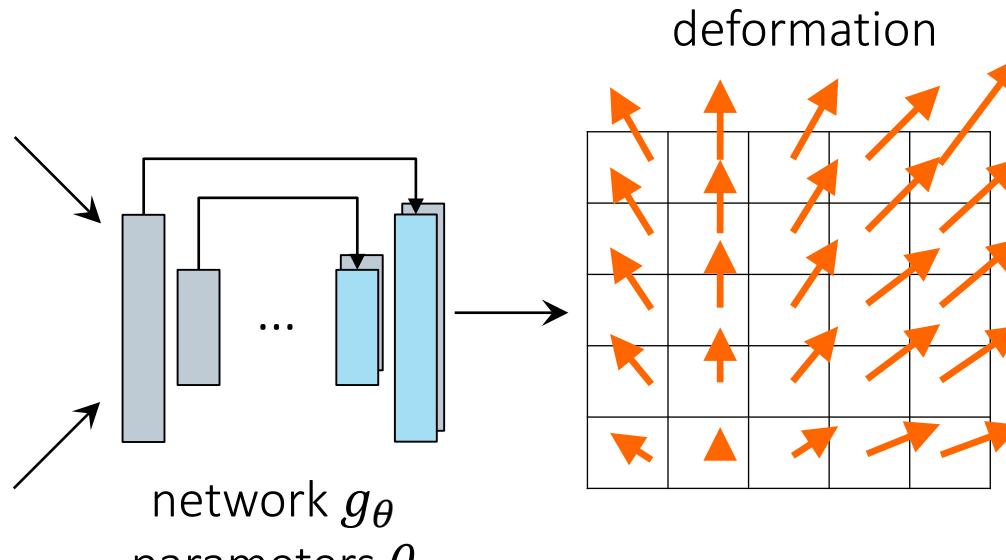
network  $g_\theta$   
parameters  $\theta$

Supervised:

$$\mathcal{L} = \|\phi - \phi_{gt}\|^2$$

# VoxelMorph

Moving image  
( $m$ )

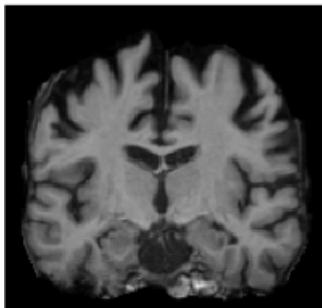


Unsupervised:

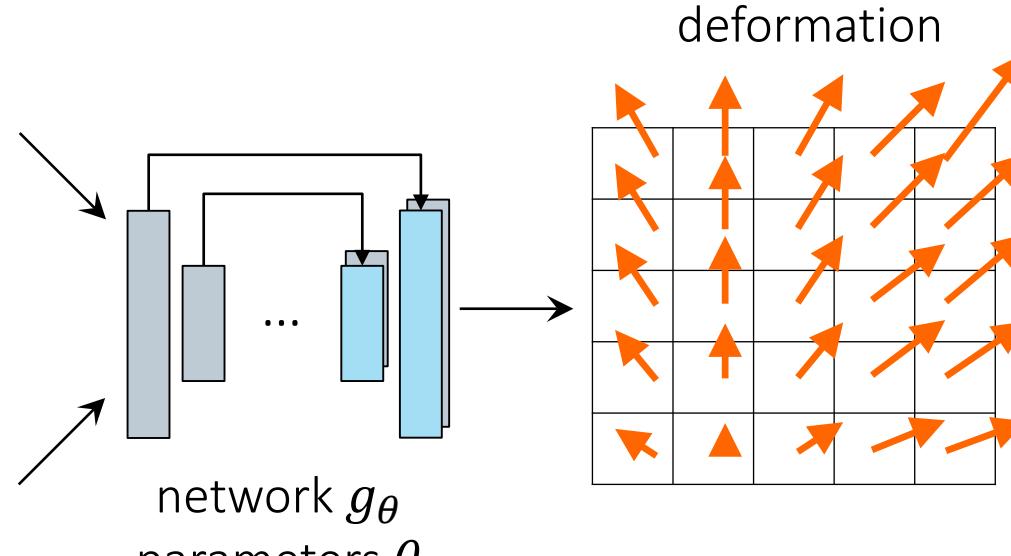
$$\mathcal{L} = \underbrace{\|m \circ \phi - f\|}_{\text{images match}} + \lambda \underbrace{\text{Reg}(\phi)}_{\text{smooth field}}$$

# VoxelMorph Loss

Moving image  
( $m$ )

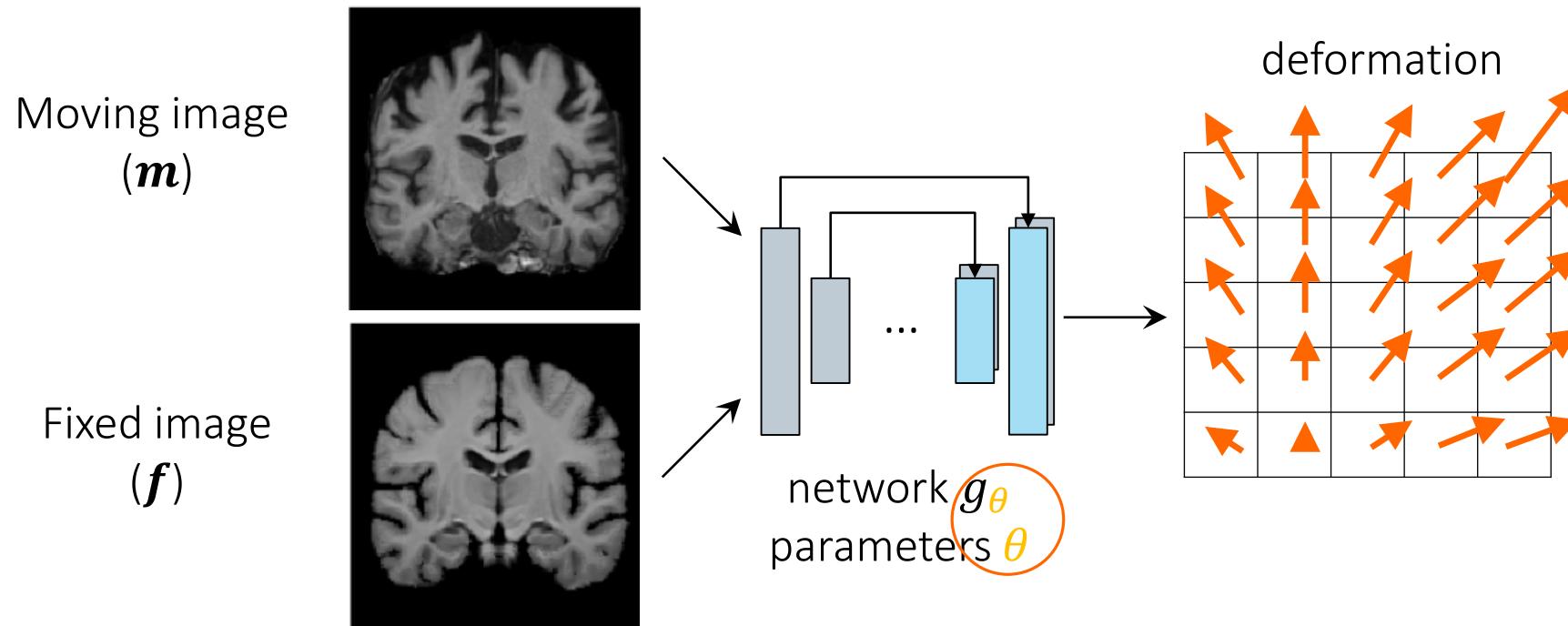


Fixed image  
( $f$ )



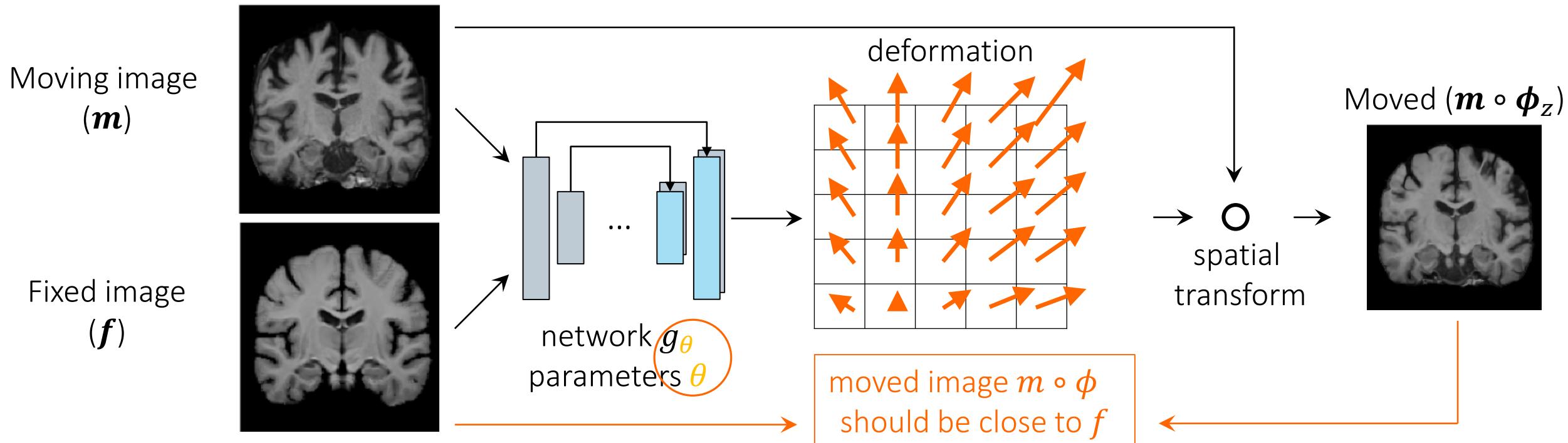
$$\mathcal{L} = \sum_{i,j} \|m_i \circ \phi_{ij} - f_{ij}\| + \lambda \text{Reg}(\phi_{ij})$$

# VoxelMorph Loss



$$\mathcal{L}(\theta; \text{data}) = \sum_{i,j} \| m_i \circ \underbrace{g_\theta(m_i.f_i)}_{\phi_{ij}} - f_{ij} \| + \lambda \operatorname{Reg}(\underbrace{g_\theta(m_i.f_i)}_{\phi_{ij}})$$

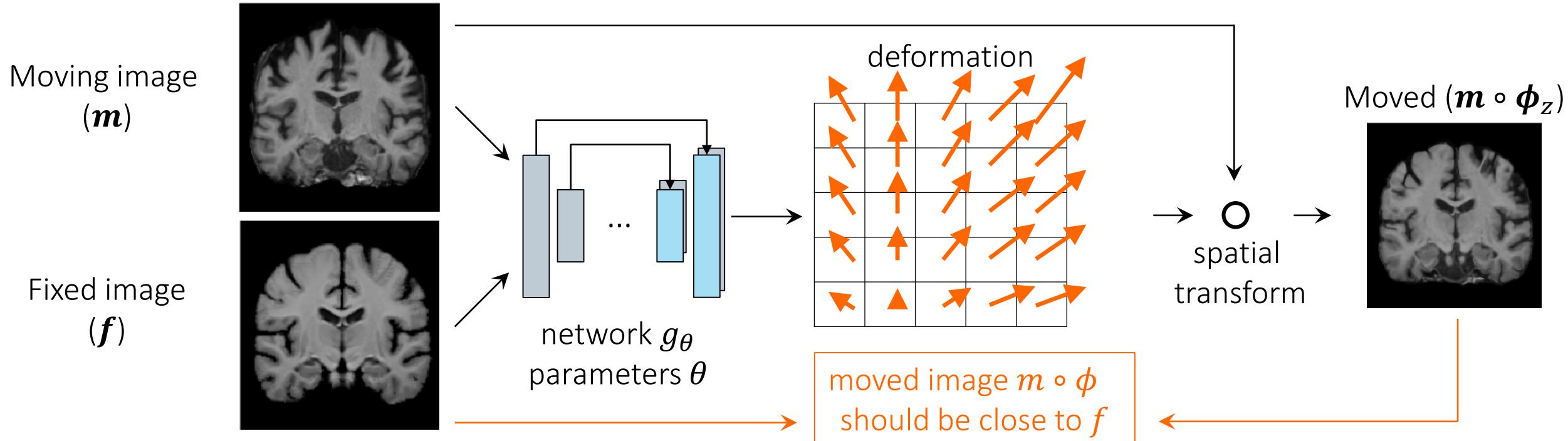
# VoxelMorph Loss



$$\mathcal{L}(\theta; \text{data}) = \sum_{i,j} \|m_i \circ g_\theta(m_i, f_i) - f_{ij}\| + \lambda \text{Reg}(g_\theta(m_i, f_i))$$

$\underbrace{\phi_{ij}}_{\phi_{ij}}$        $\underbrace{\phi_{ij}}_{\phi_{ij}}$

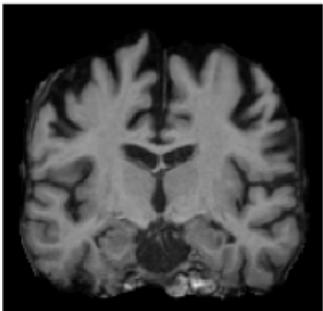
# Training



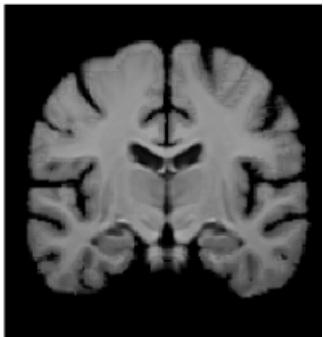
- SGD based techniques
- Each image pair contributes **slightly** to  $\theta$   
Classical optimization: slightly update  $\phi$  for an image pair

# Registration

Moving image  
 $(m)$

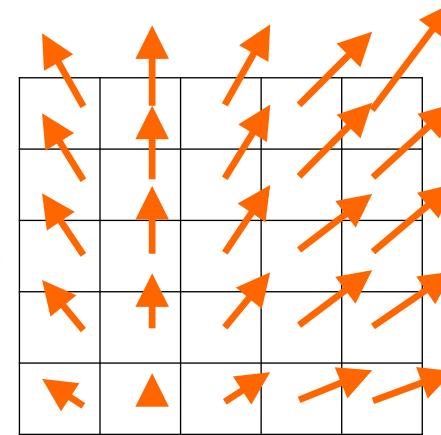


Fixed image  
 $(f)$

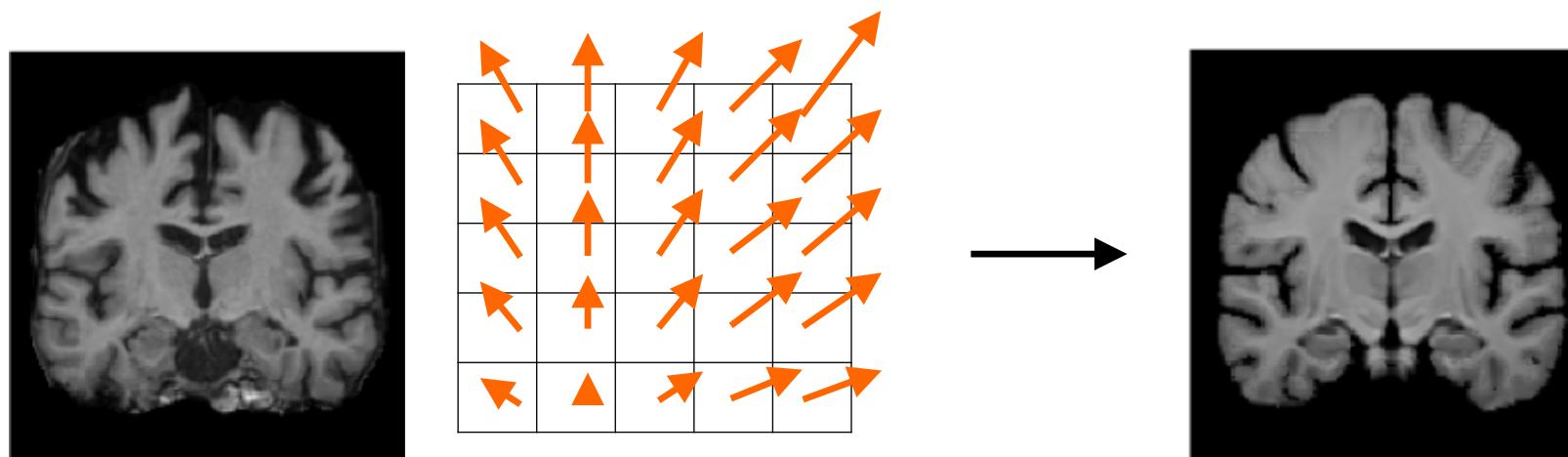


network  $g_\theta$   
parameters  $\theta$

deformation



# Probabilistic model



$$m \circ \phi_z + \epsilon = f$$

$$\hookrightarrow z \sim \mathcal{N}(z; 0, \Lambda^{-1})$$

stationary velocity field

smoothness via Laplacian

Goal:  $p(z|m, f)$  posterior probability of registration

# Atlas-based registration

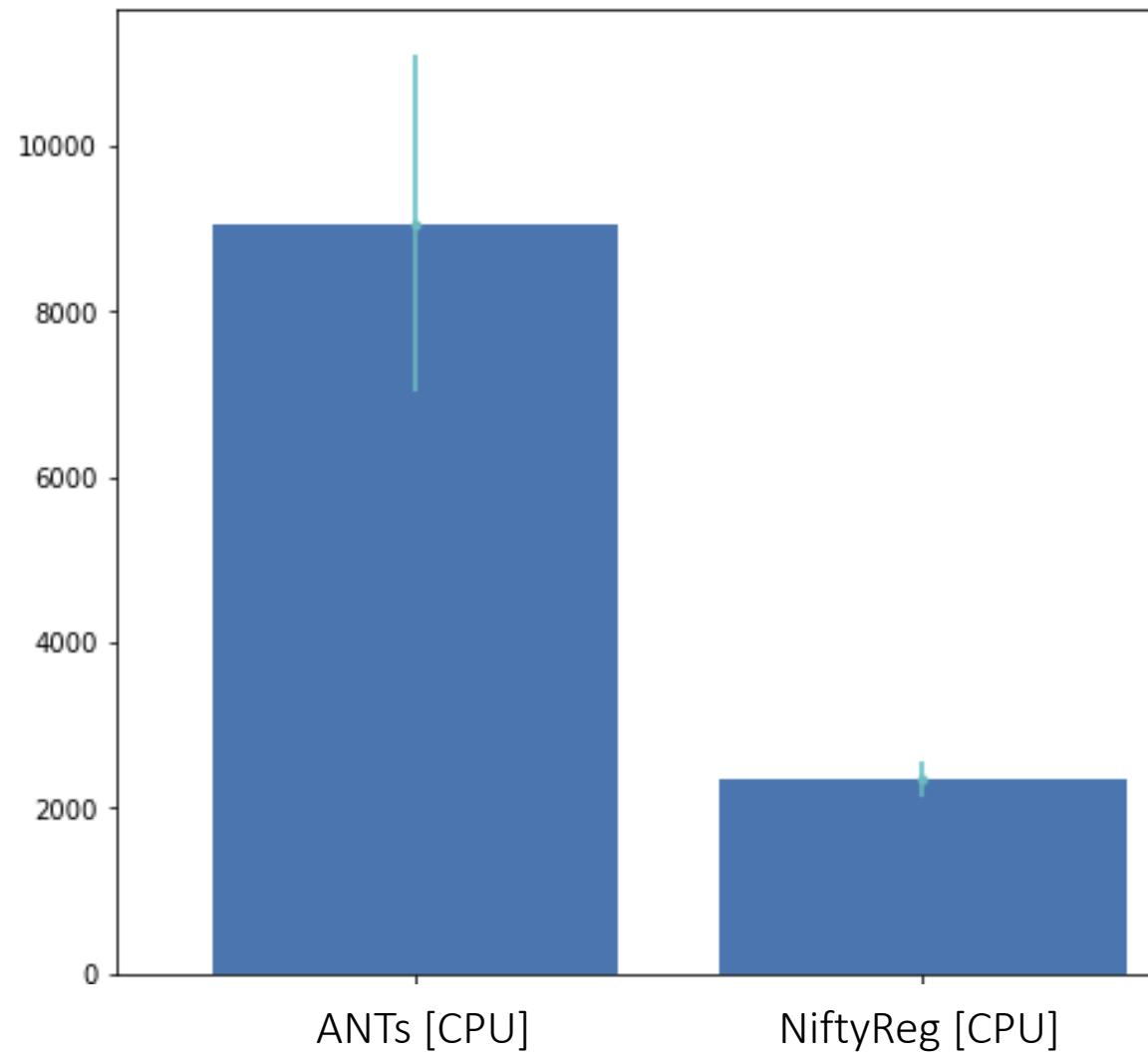
---

Data: 7000 training volumes, 250 validate, 250 test

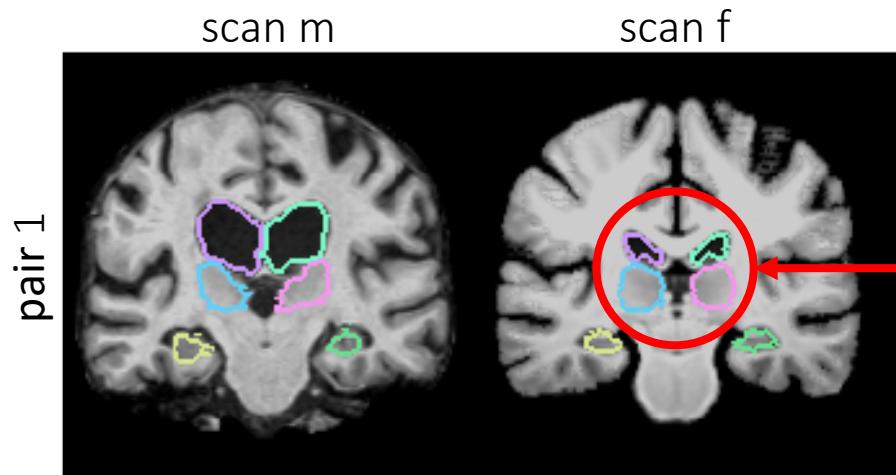
Baseline: ANTs optimization method

# Runtime for a new 3D image pair

---

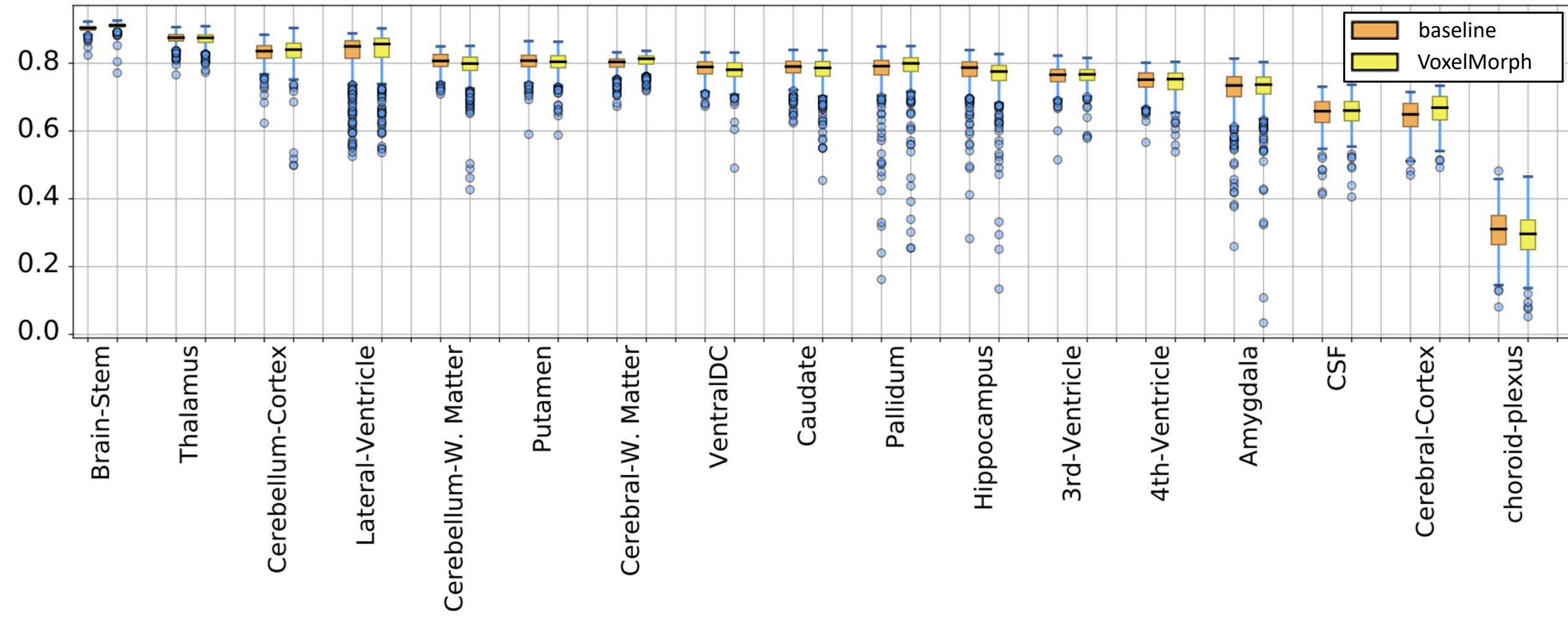


# Anatomical volume overlap



\*algorithms only see images, no segmentation maps

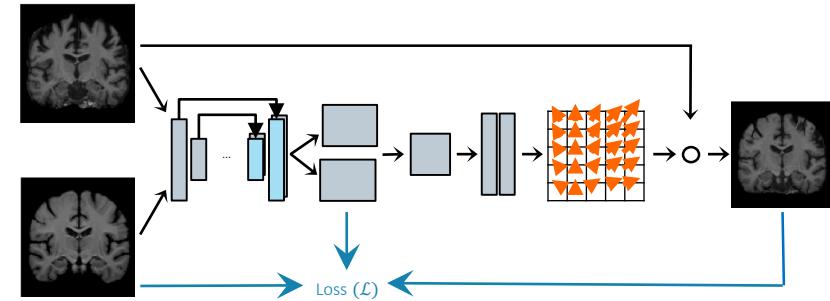
# Accuracy via volume overlap (Dice)



# Outline

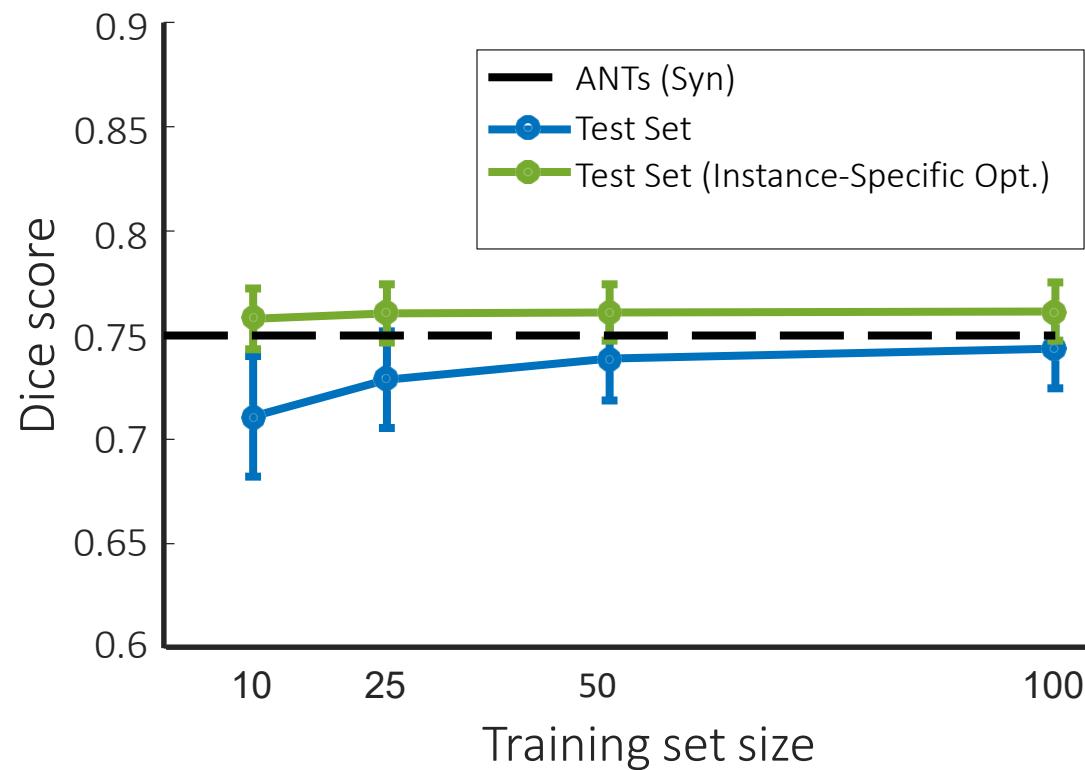
---

- Model
  - Variational Inference with neural networks
  - Optimization interpretation
  - Results (runtime and accuracy)

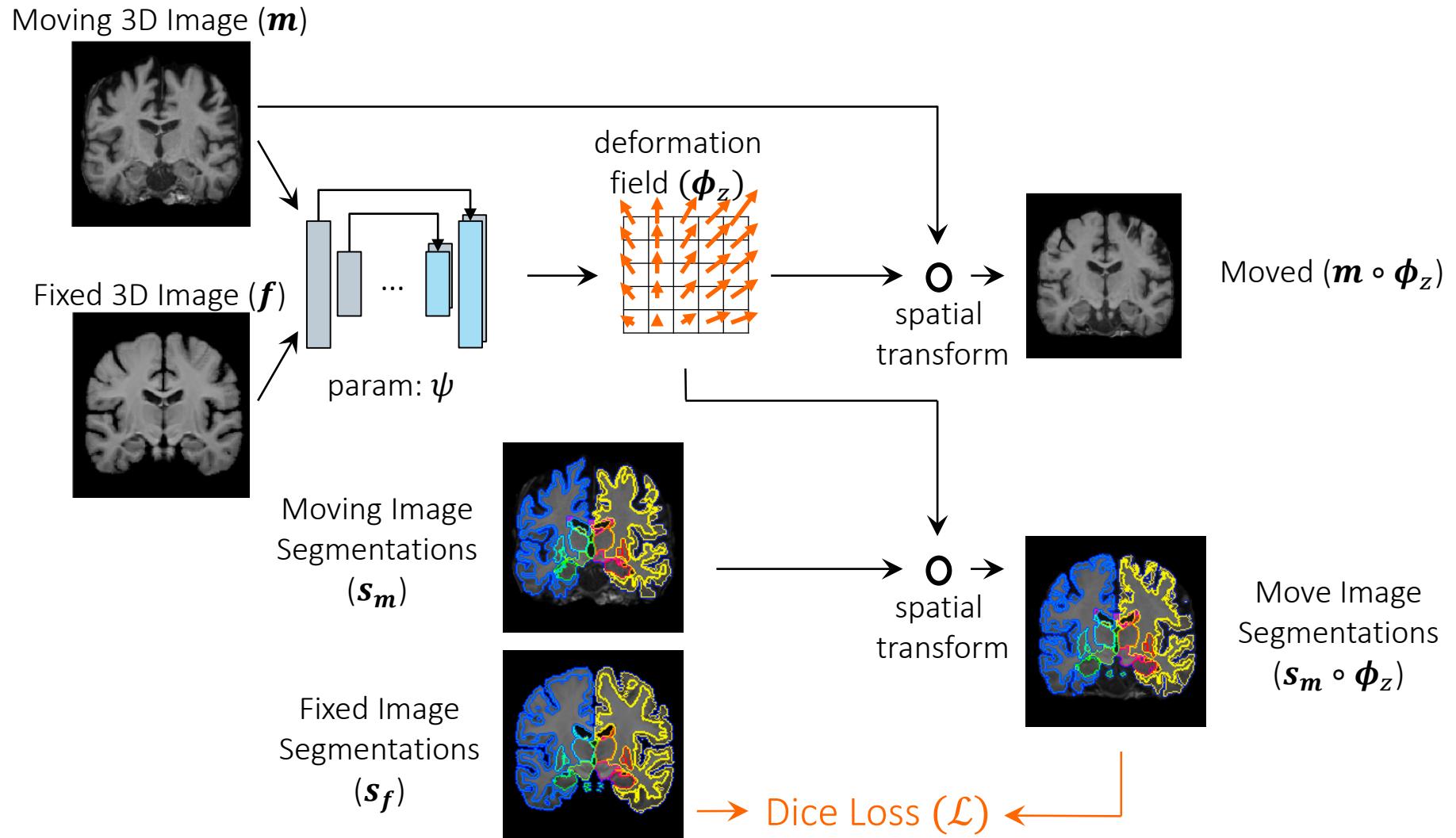


# Amortized analysis: training with limited data

---

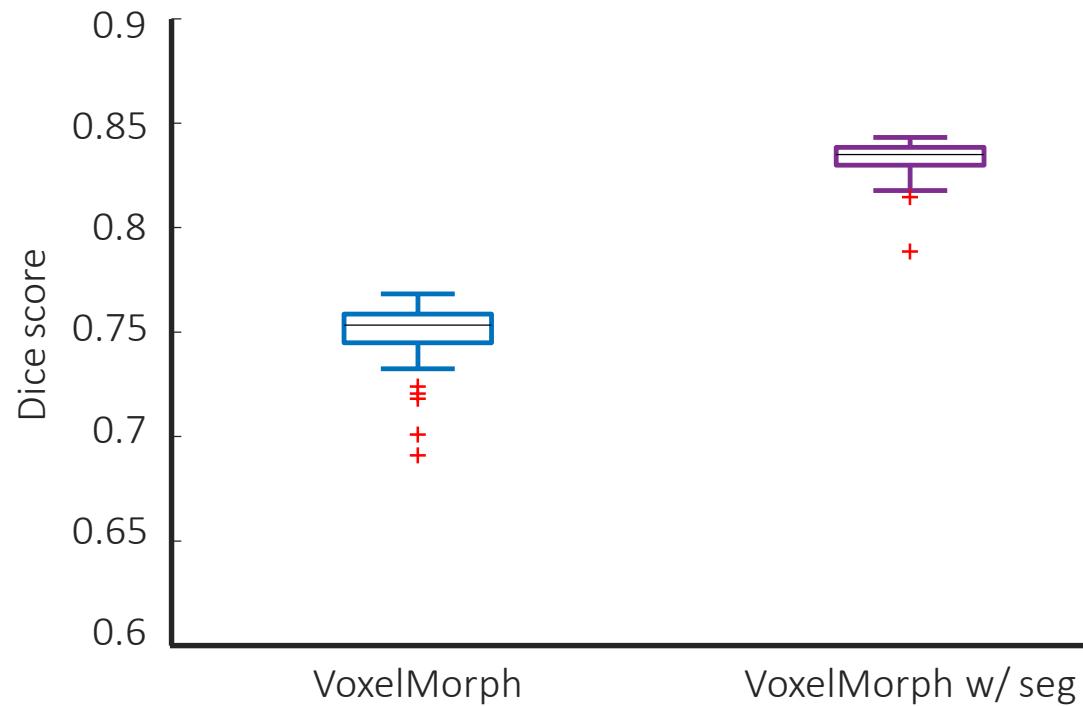


# Segmentation Maps available at training



# Test time performance

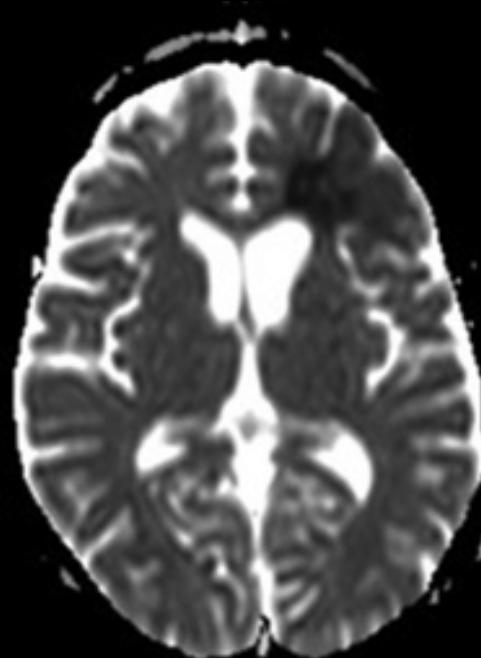
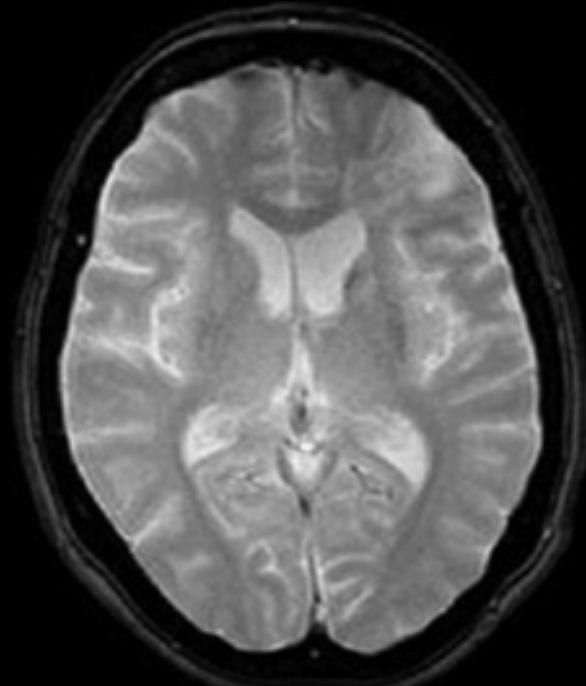
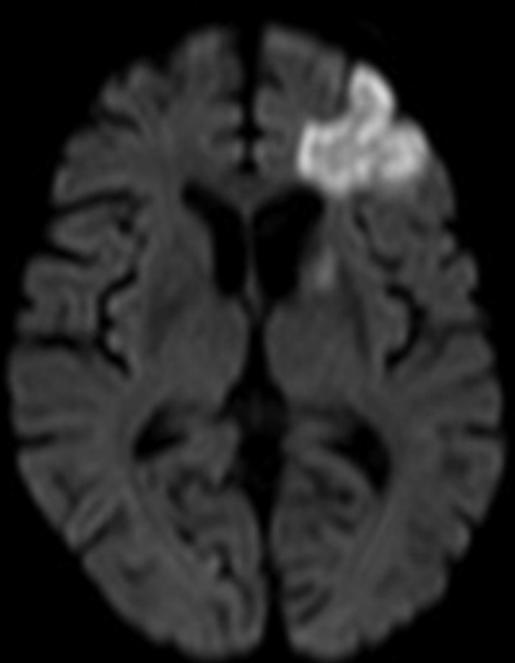
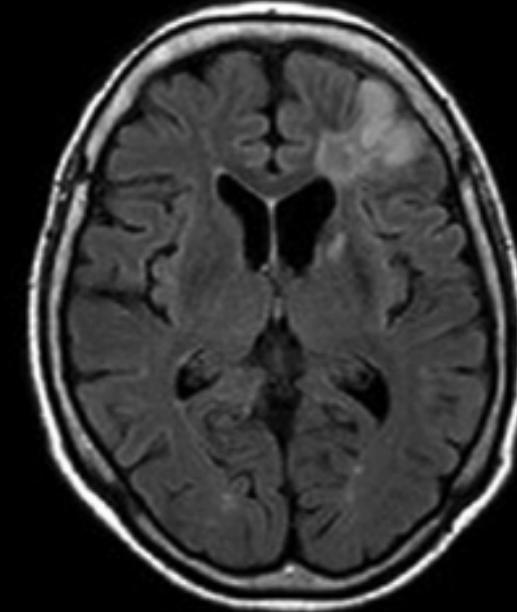
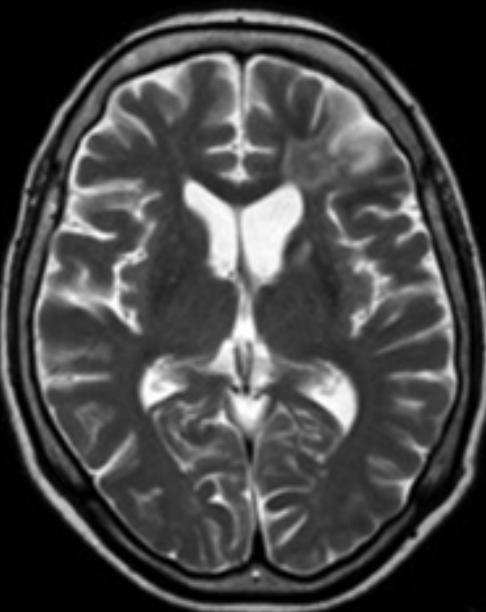
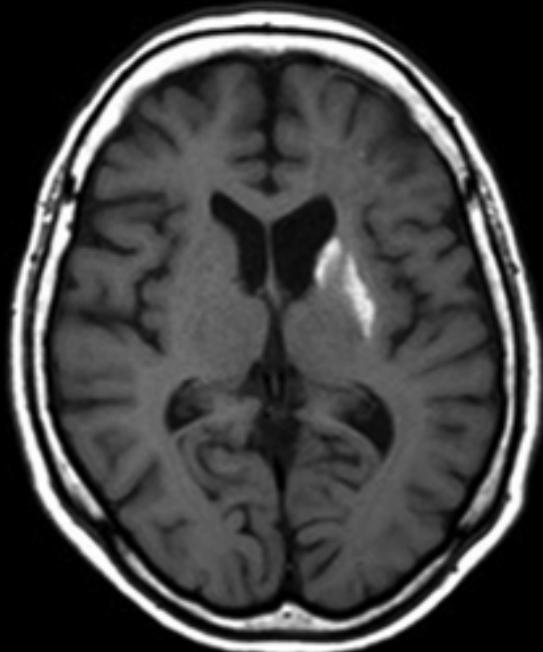
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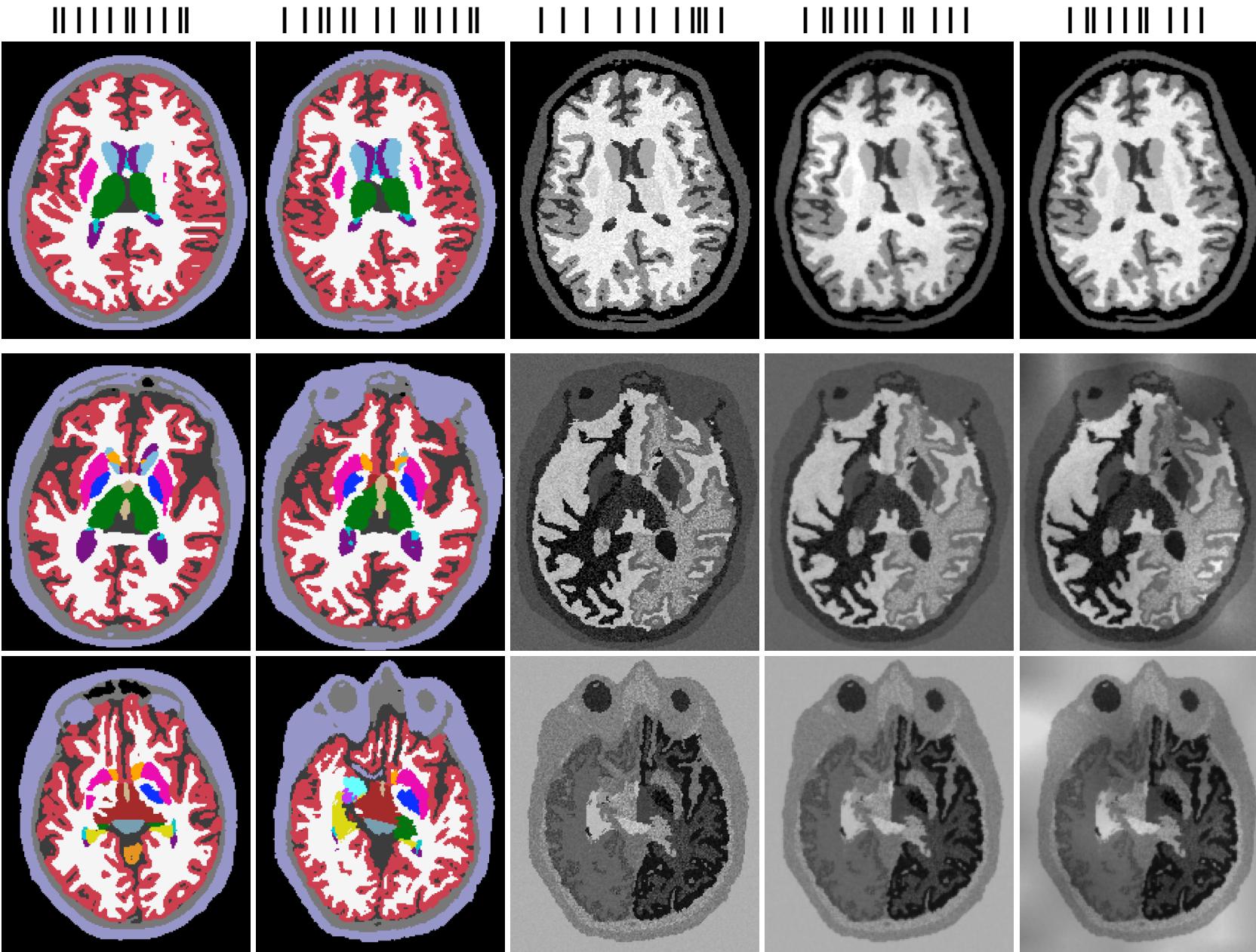


# SynthMorph (do we need real data?)

---

Hoffmann et al in submission





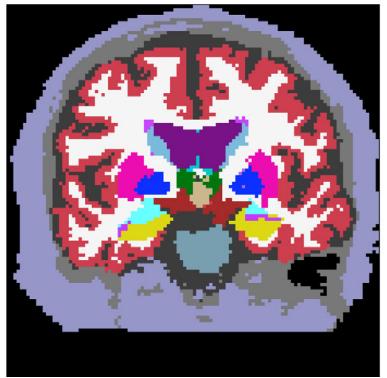
<https://github.com/BBillot/lab2im>

Billot MIDL 2020  
Billot MICCAI 2020

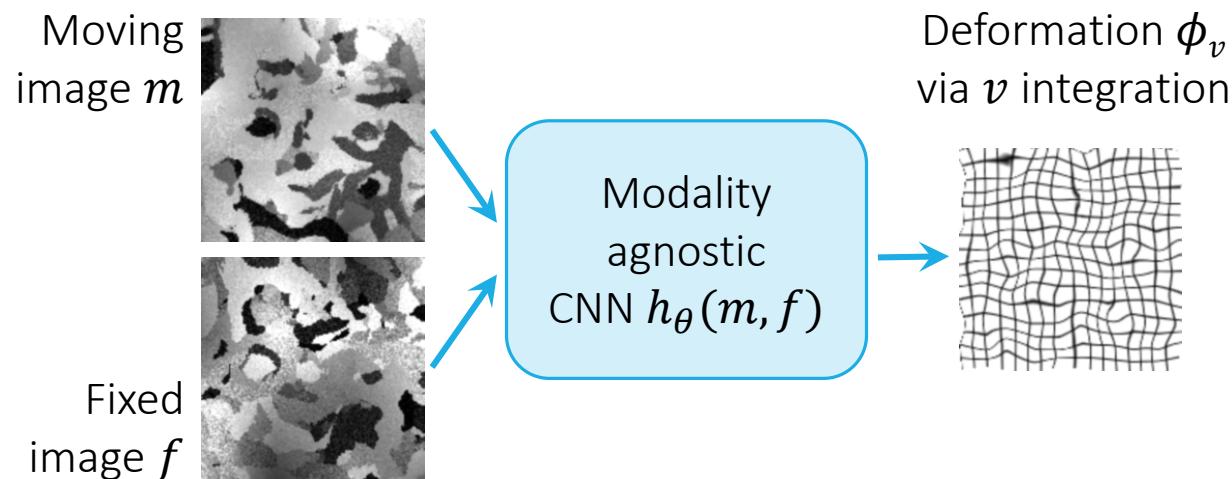
# Do we need anatomical images to train?

---

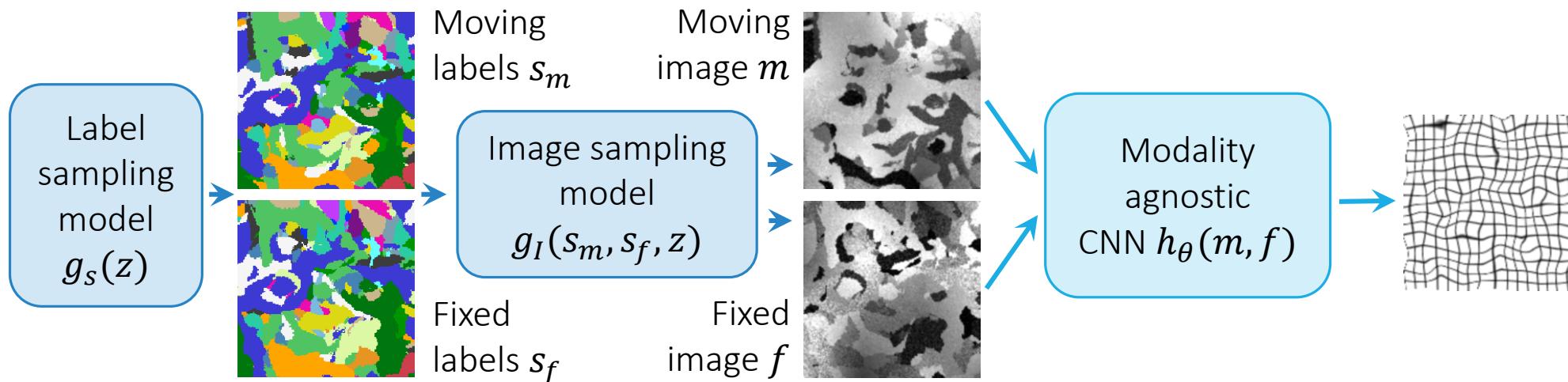
Brains



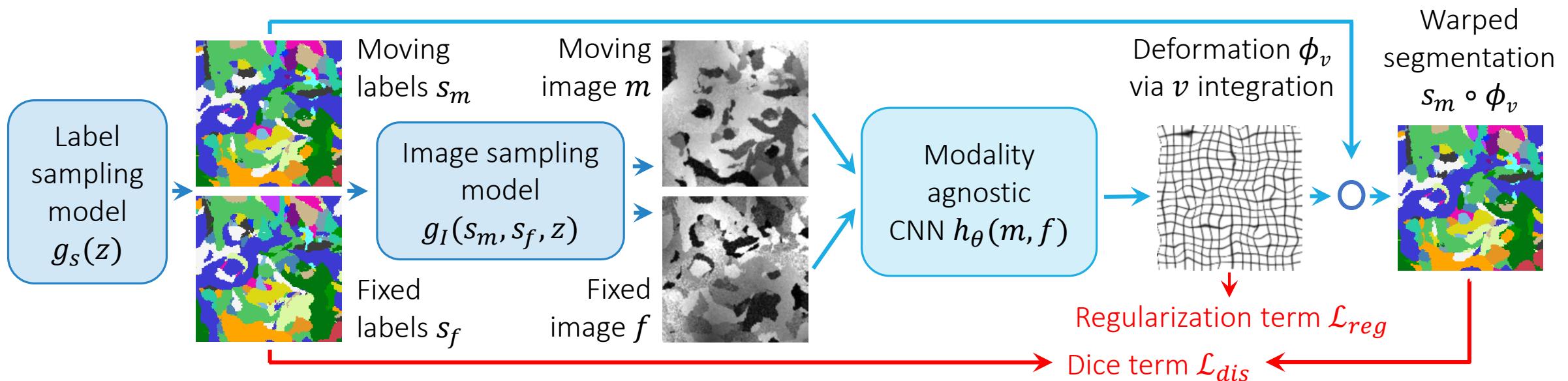
# Do we need anatomical images to train?



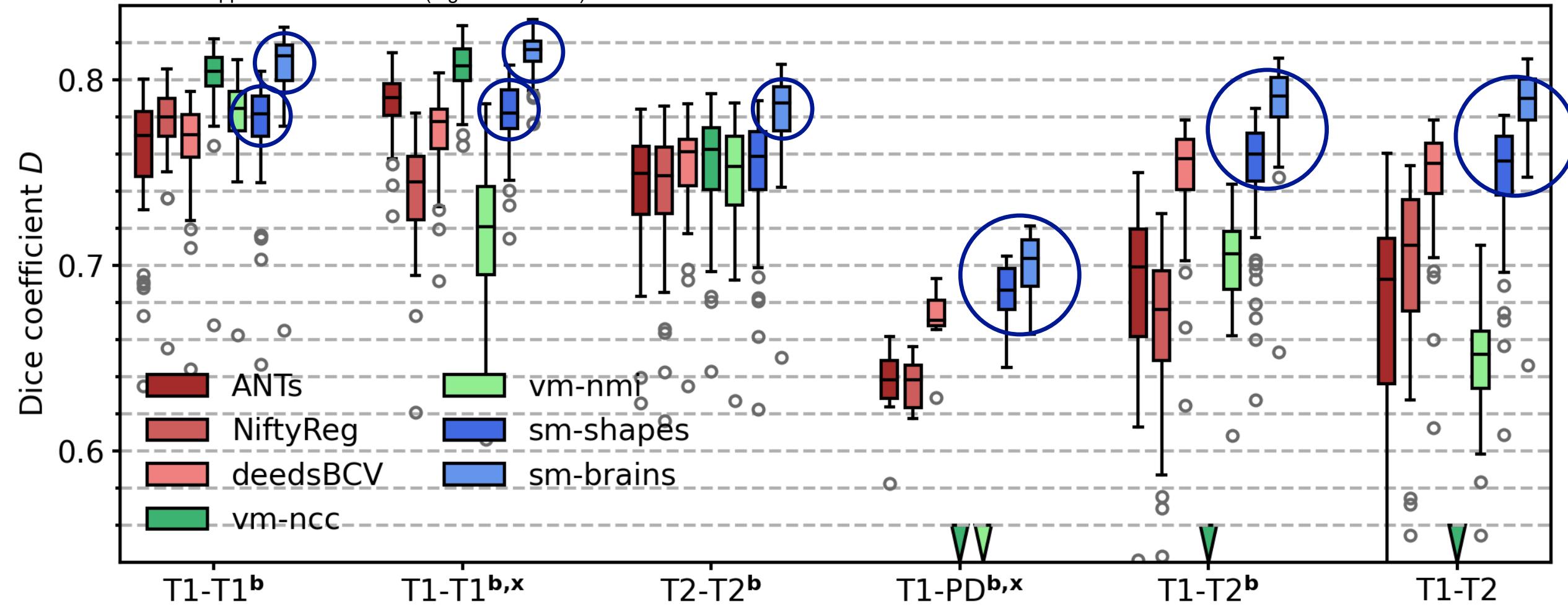
# Do we need anatomical images to train?

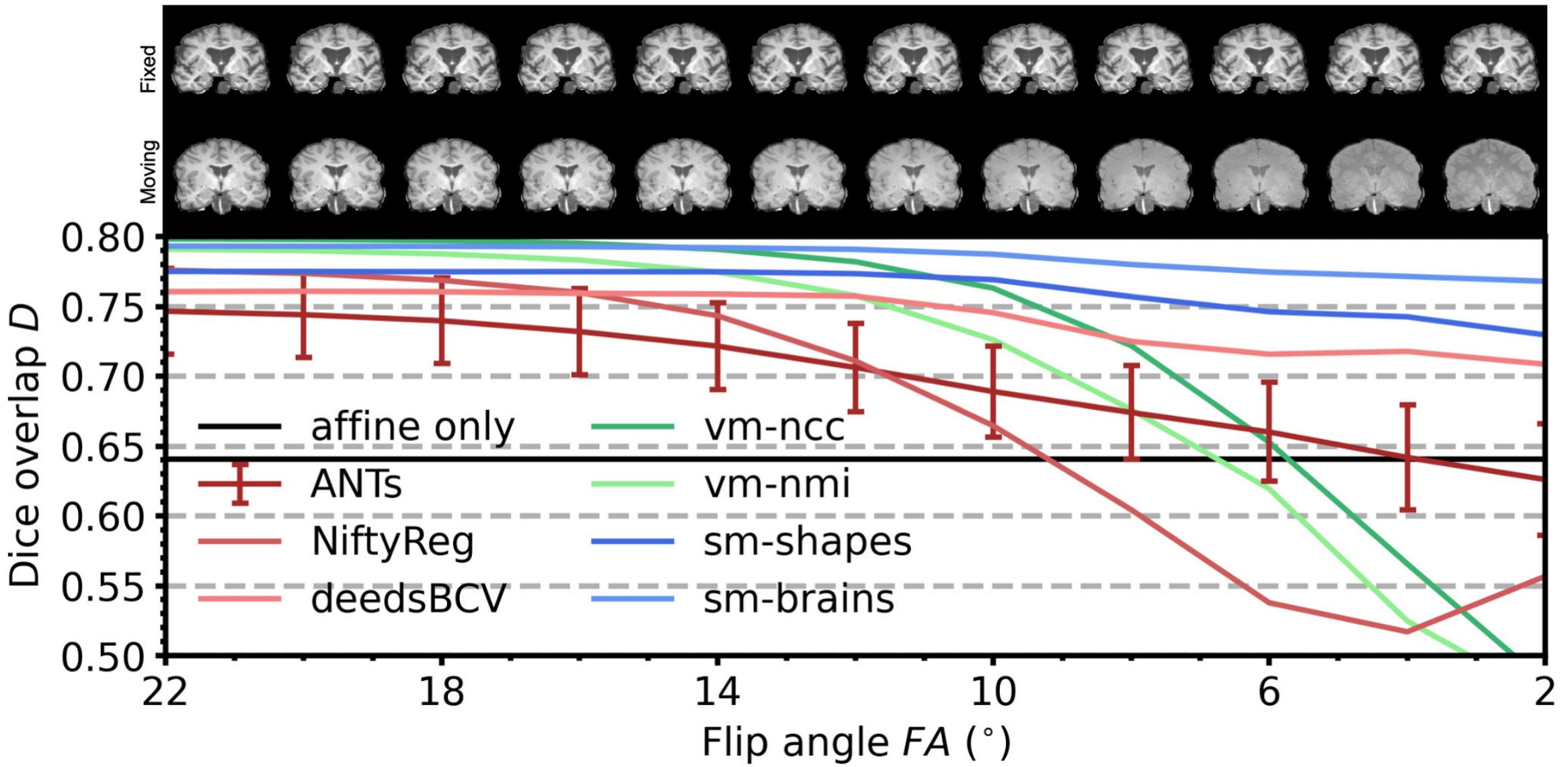


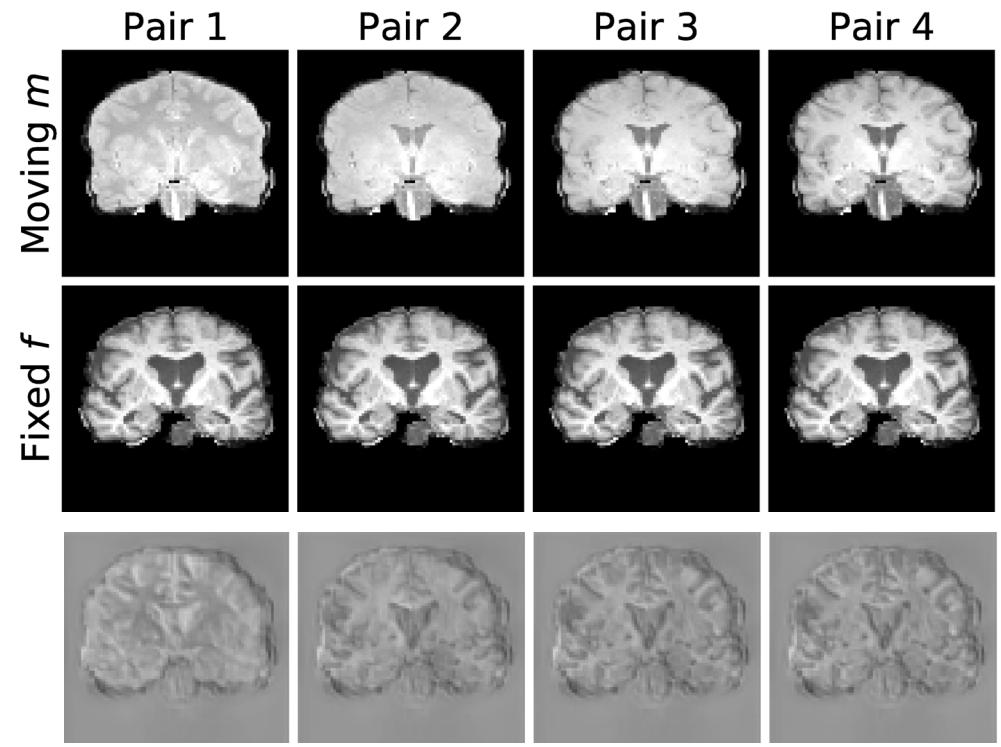
# Do we need anatomical images to train?



**b** Skull-stripped  $\times$  Cross-dataset (e.g. HCP-OASIS)







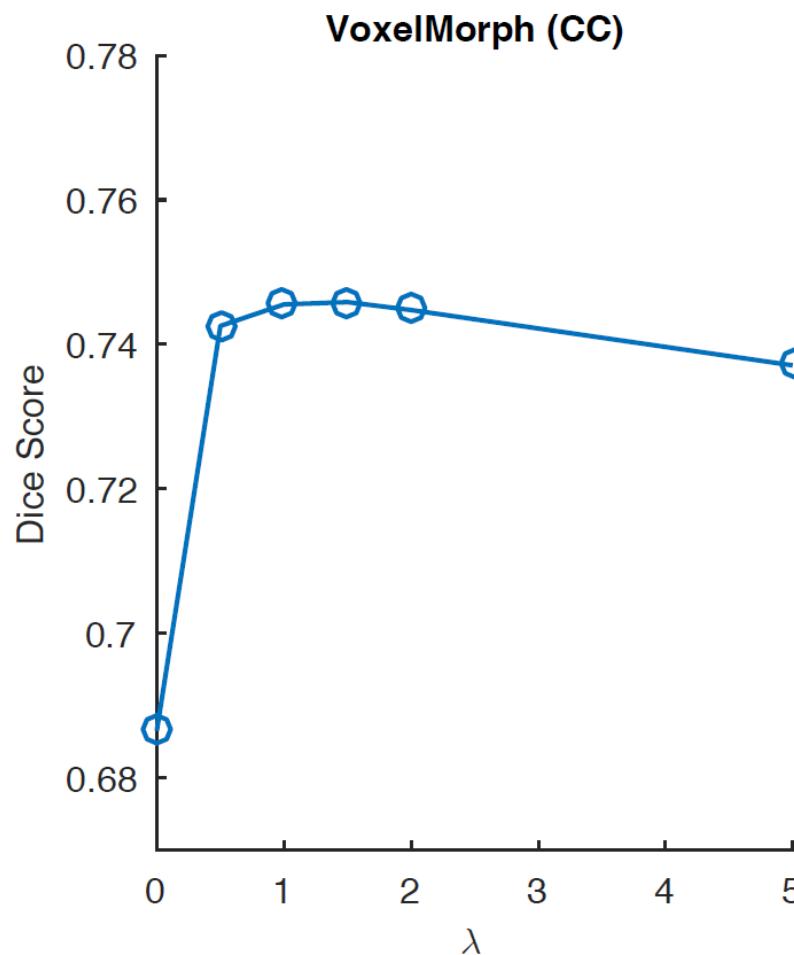
VoxelMorph - NMI

# HyperMorph: Amortized parameter learning

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Hoopes, Hoffmann, Fischl, Guttag, Dalca, IPMI 2021

# Regularization Analysis (hyperparameters)



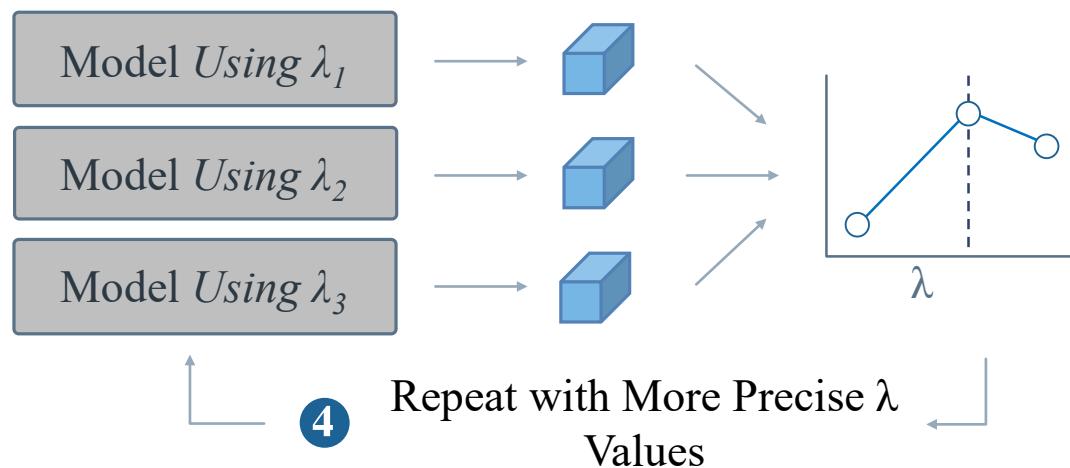
$$\mathcal{L} = \underbrace{\|m \circ \phi - f\|}_{\text{images match}} + \underbrace{\lambda \text{Reg}(\phi)}_{\text{smooth field}}$$

# HyperMorph

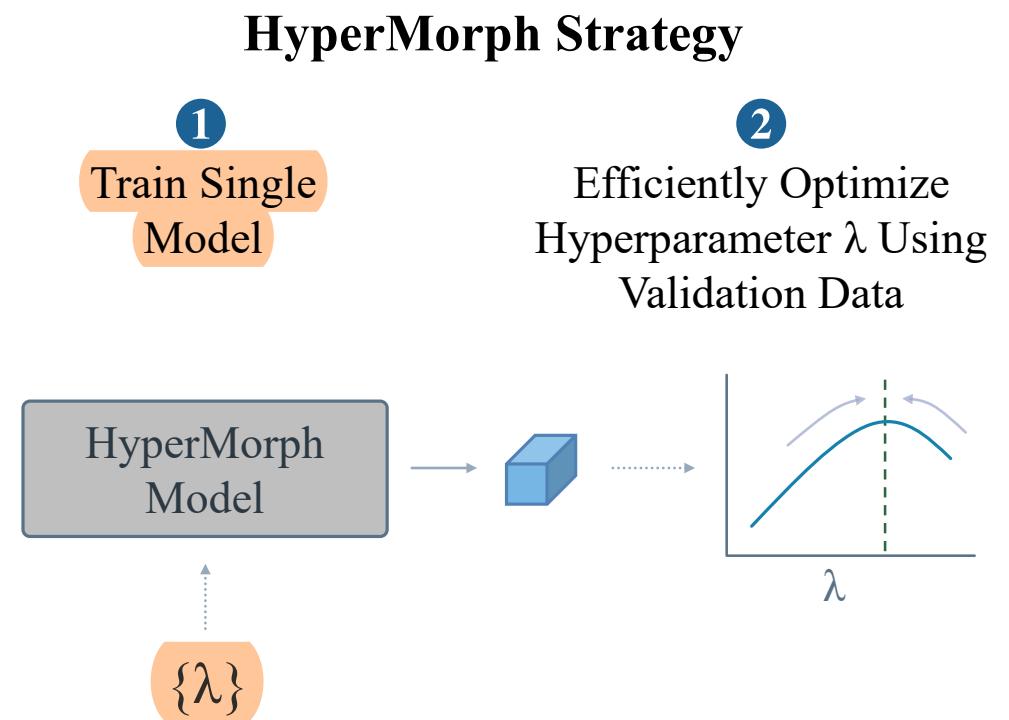
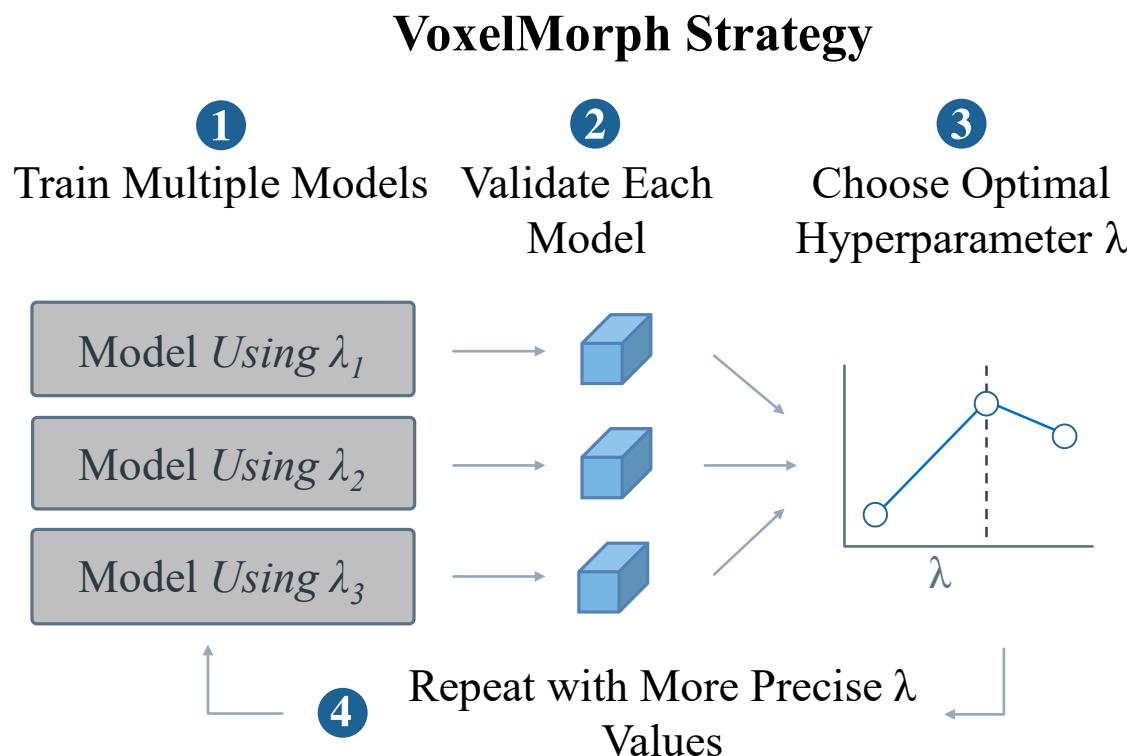
---

## VoxelMorph Strategy

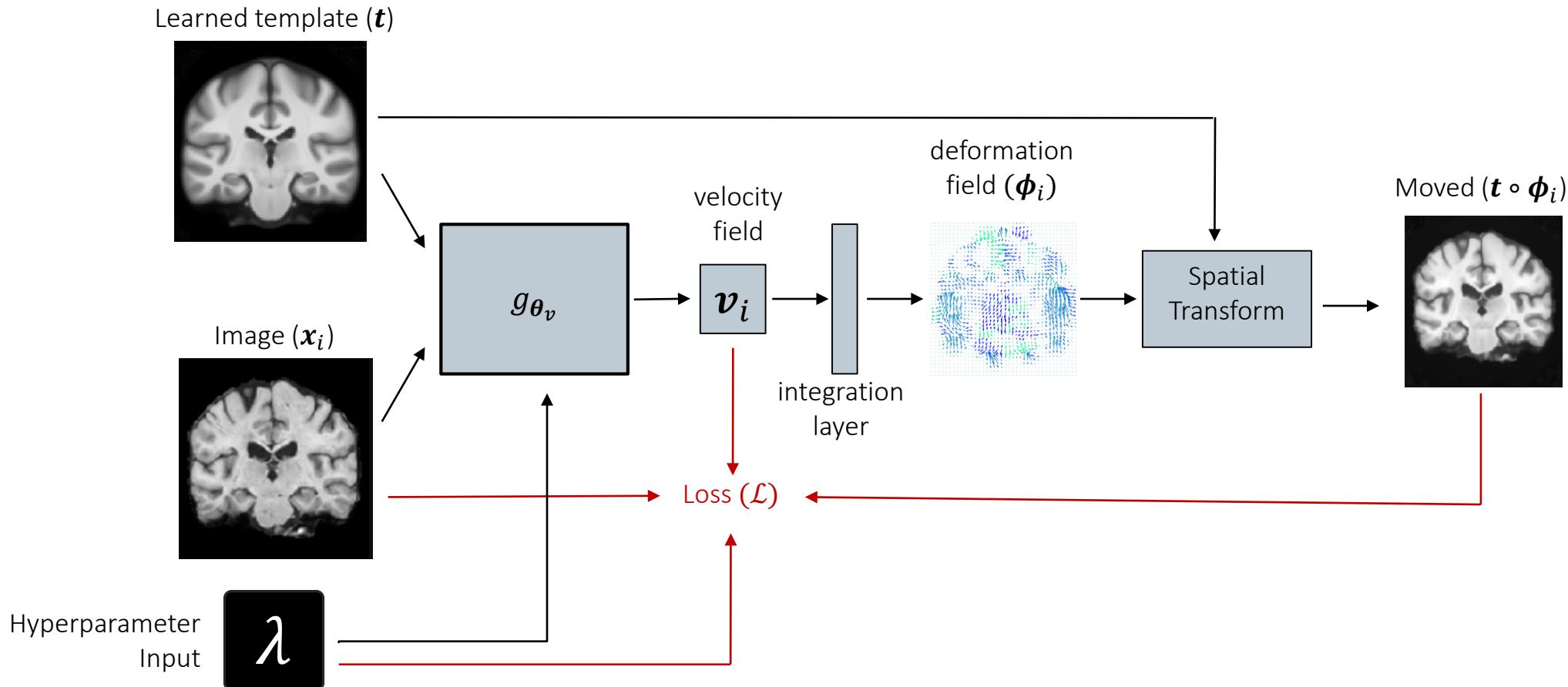
- 1 Train Multiple Models
- 2 Validate Each Model
- 3 Choose Optimal Hyperparameter  $\lambda$



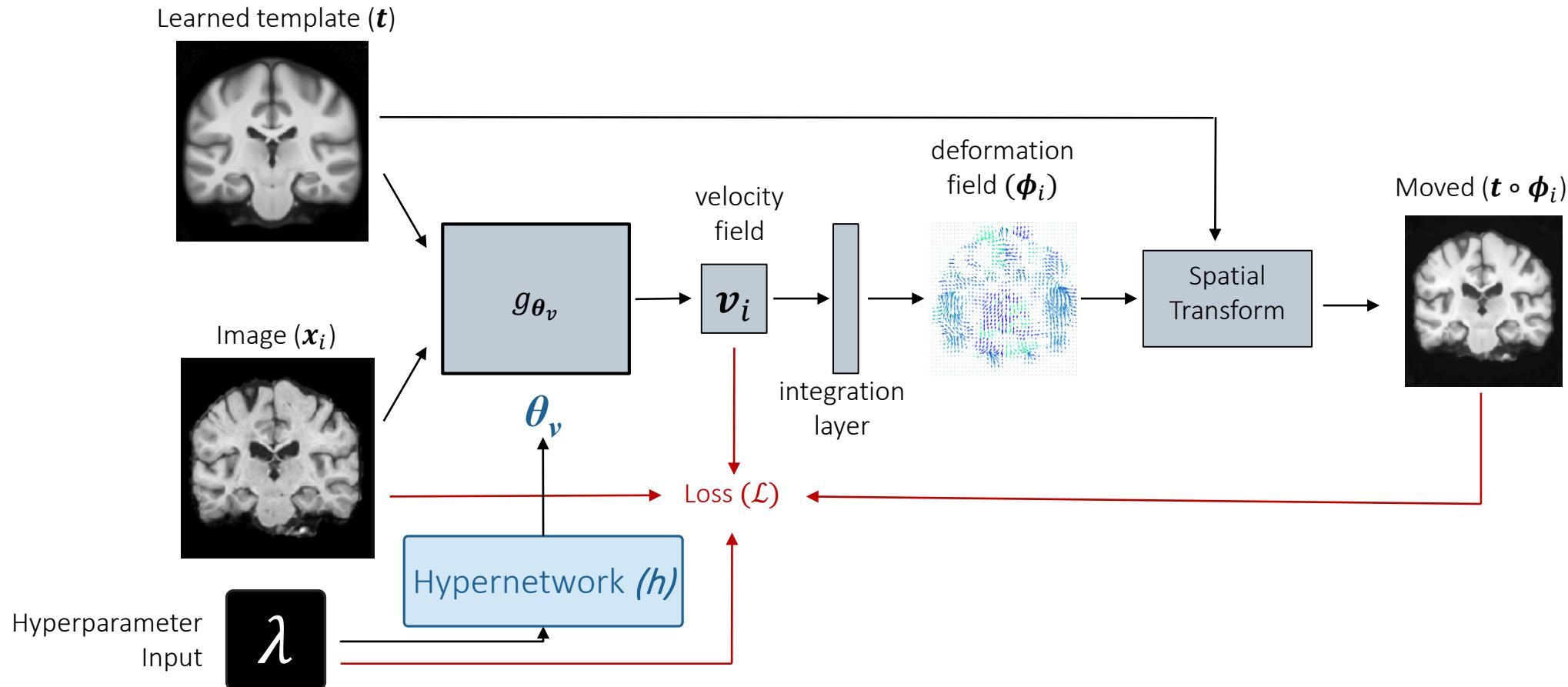
# HyperMorph



# HyperMorph

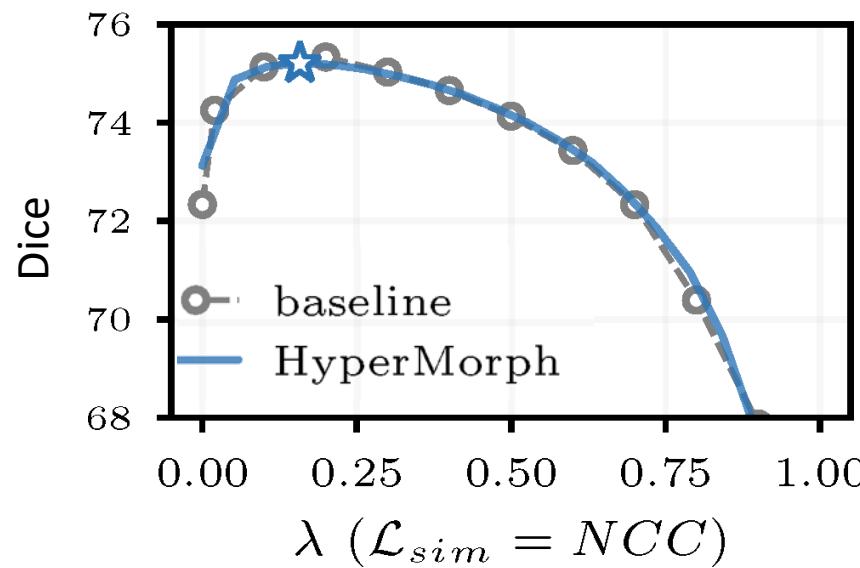


# HyperMorph



# Baseline Comparison

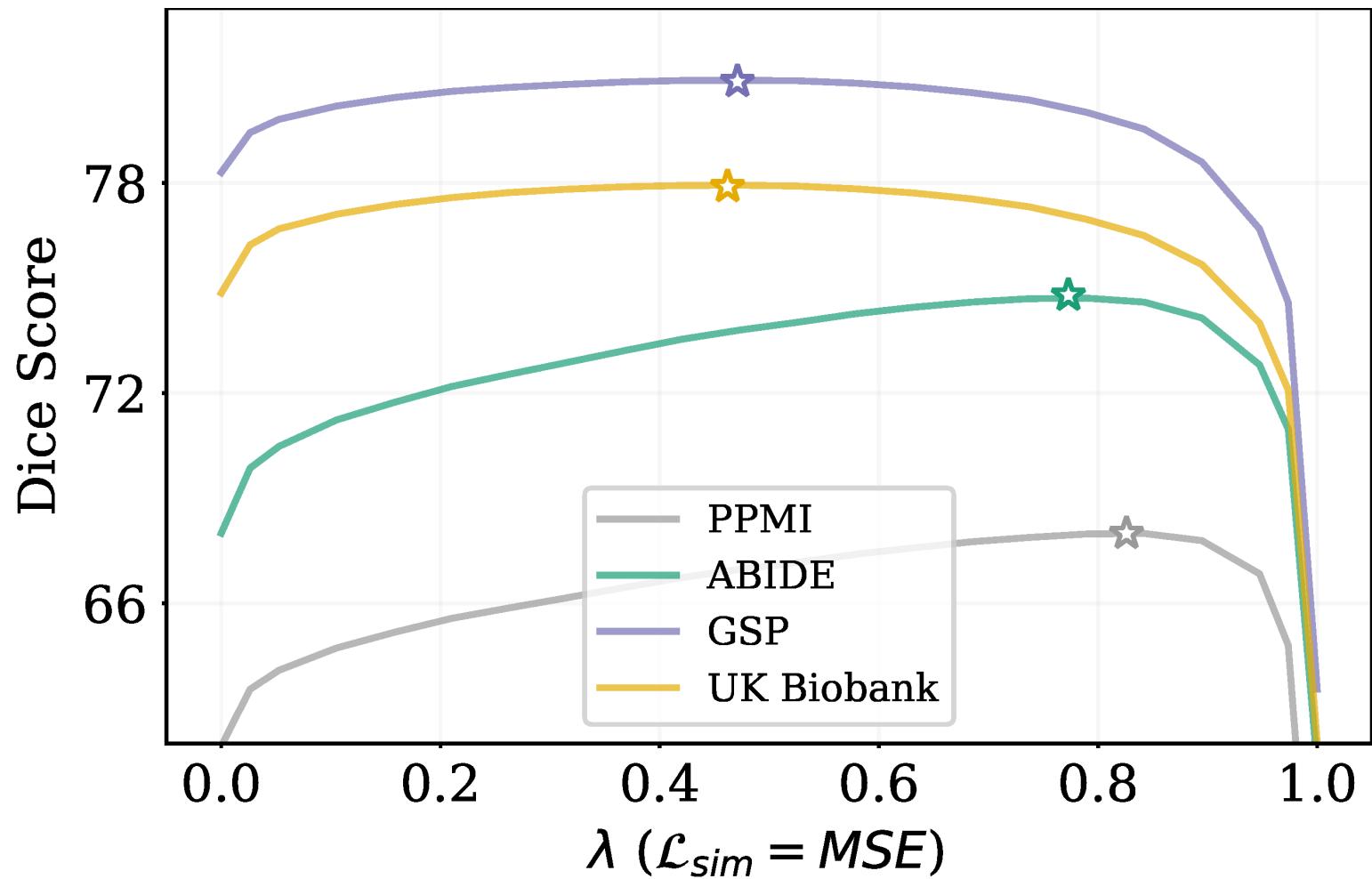
---



Runtime (GPU-hours)  
VoxelMorph (~10 models): 765  
HyperMorph: **147**

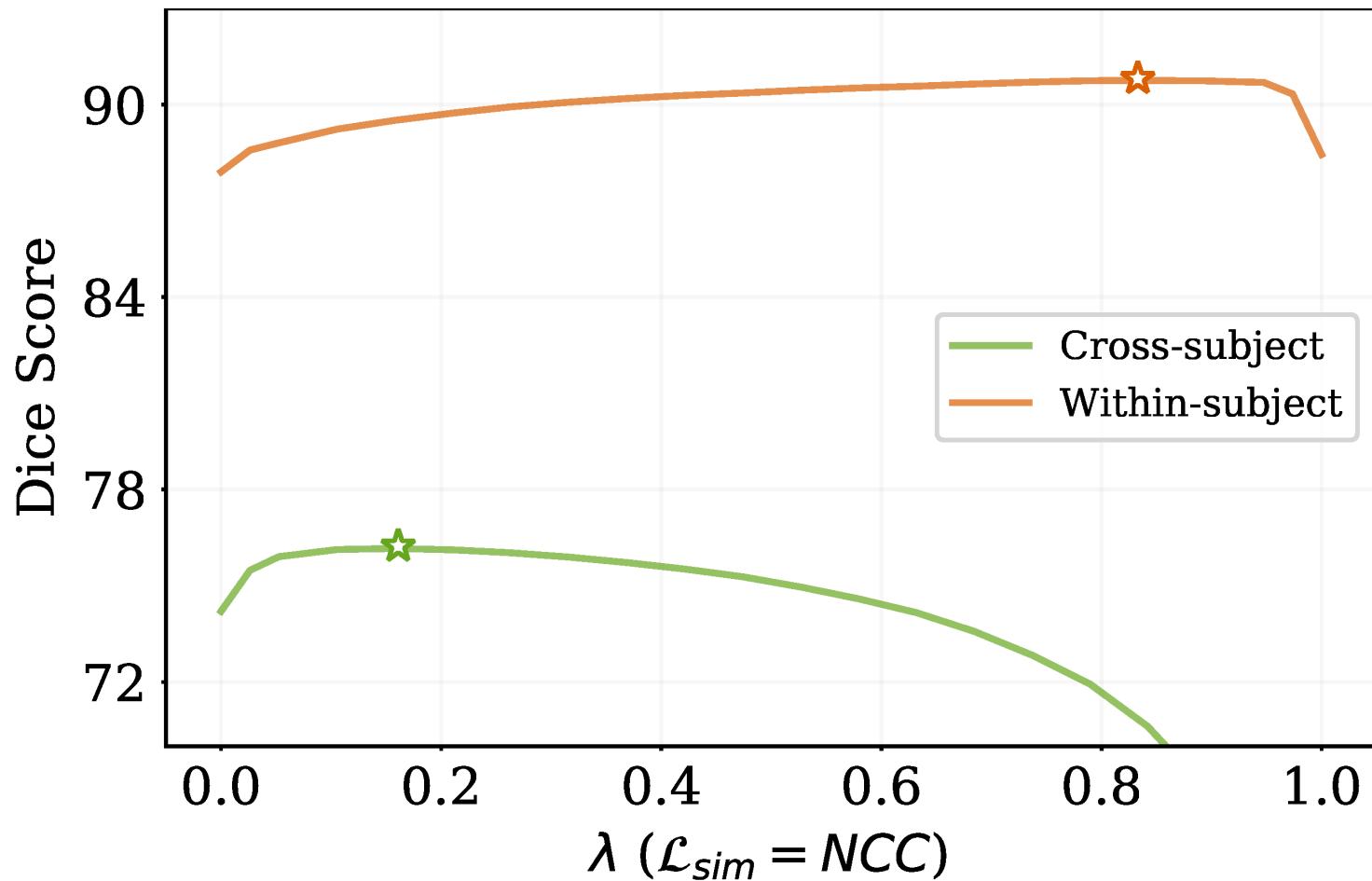


# Optimal Hyperparameters vary by dataset



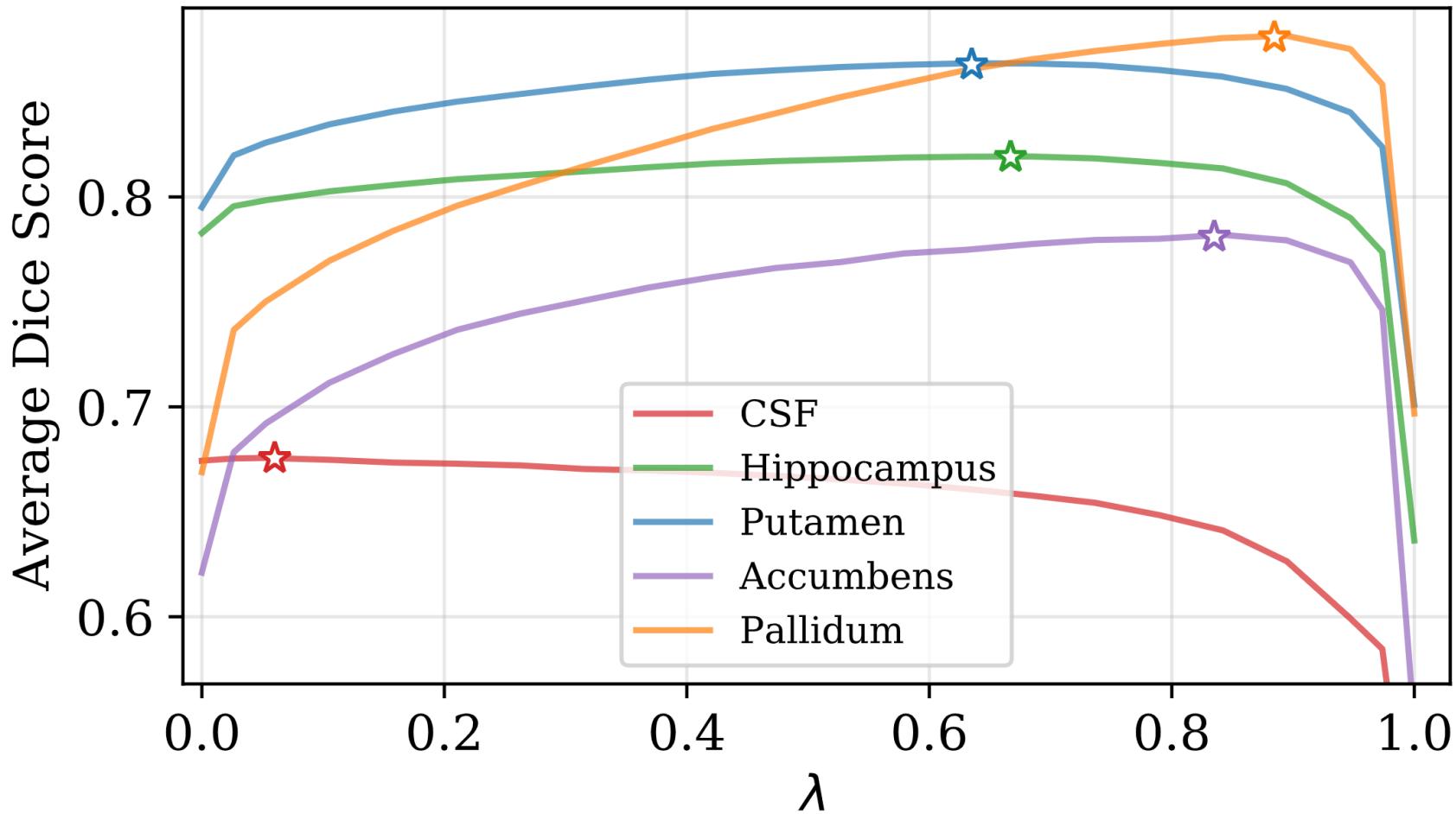
# Optimal Hyperparameters vary by task

---



... even by anatomical region!

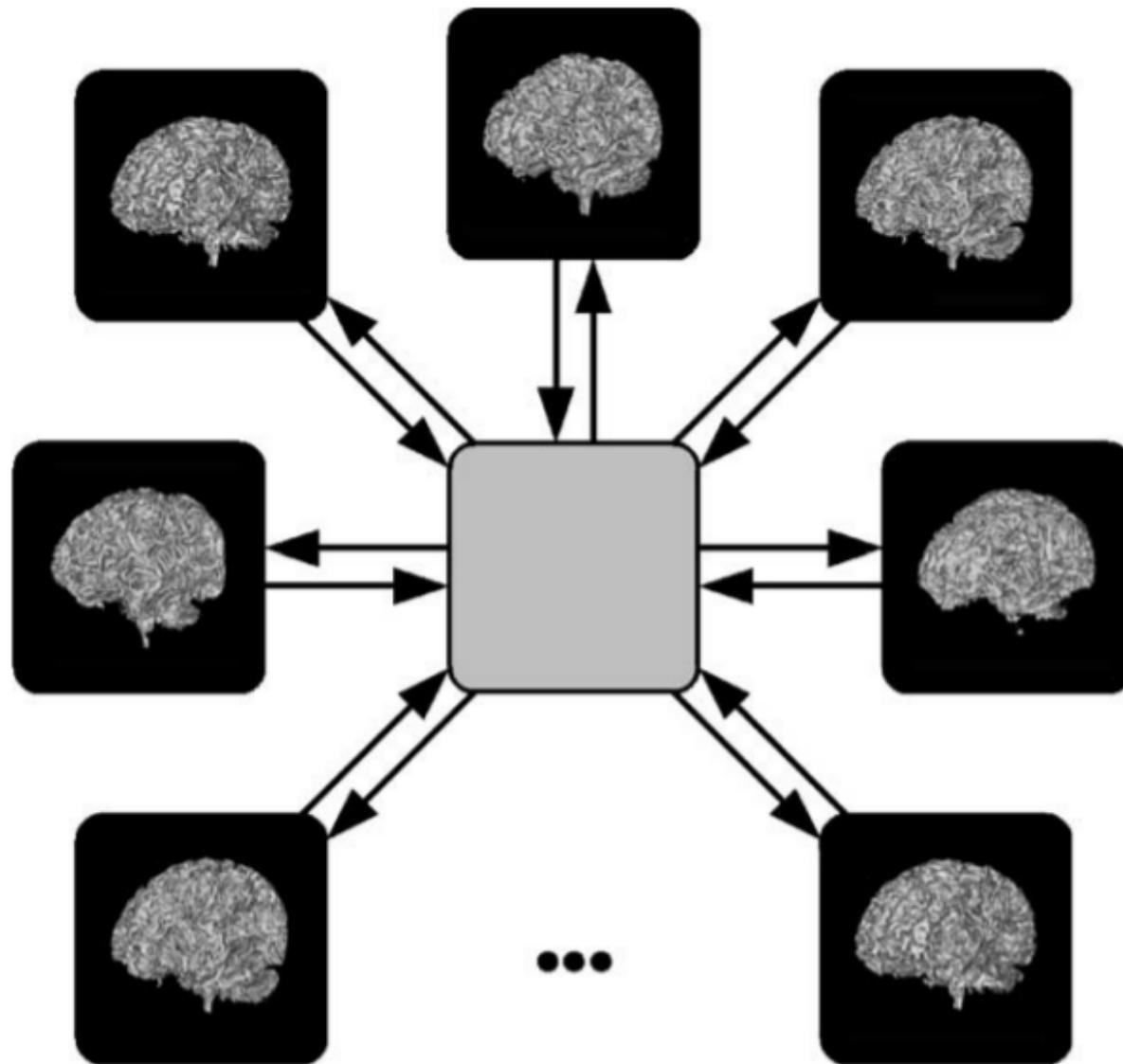
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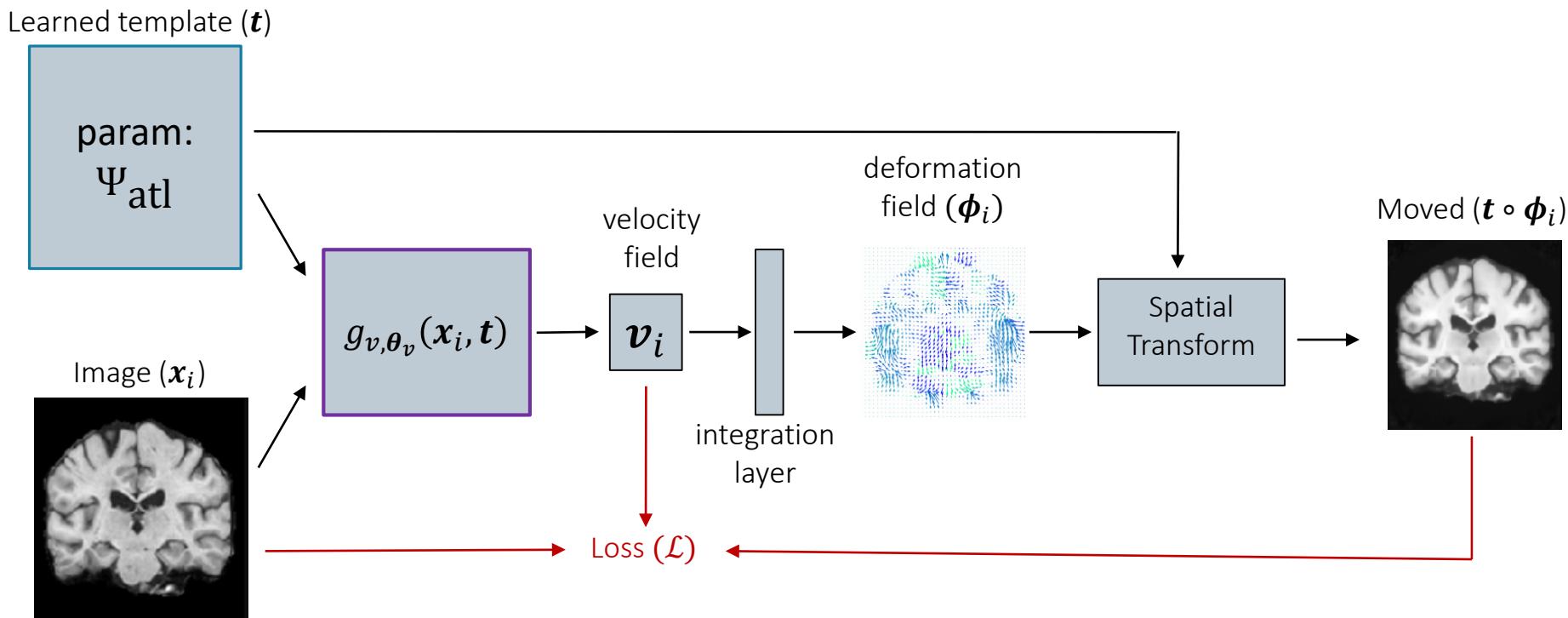
# Template construction

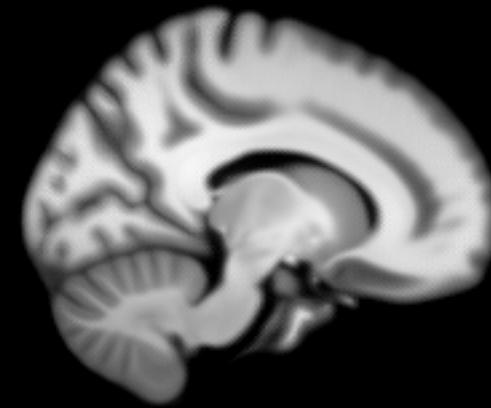
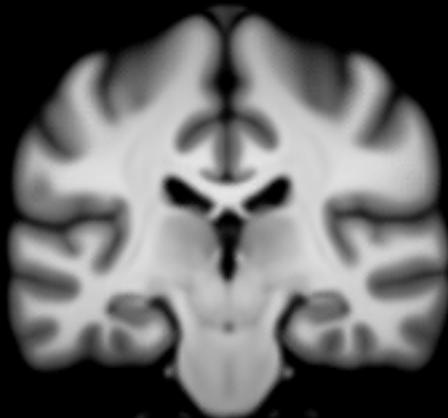
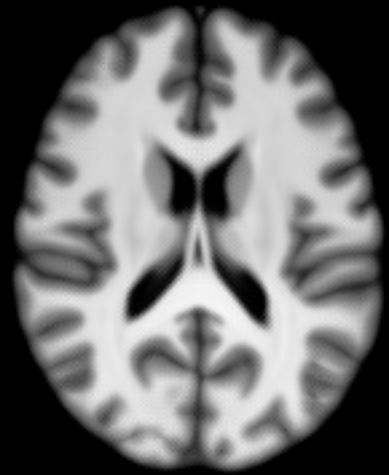
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Dalca, Rakic, Guttag, Sabuncu, NeurIPS 2019

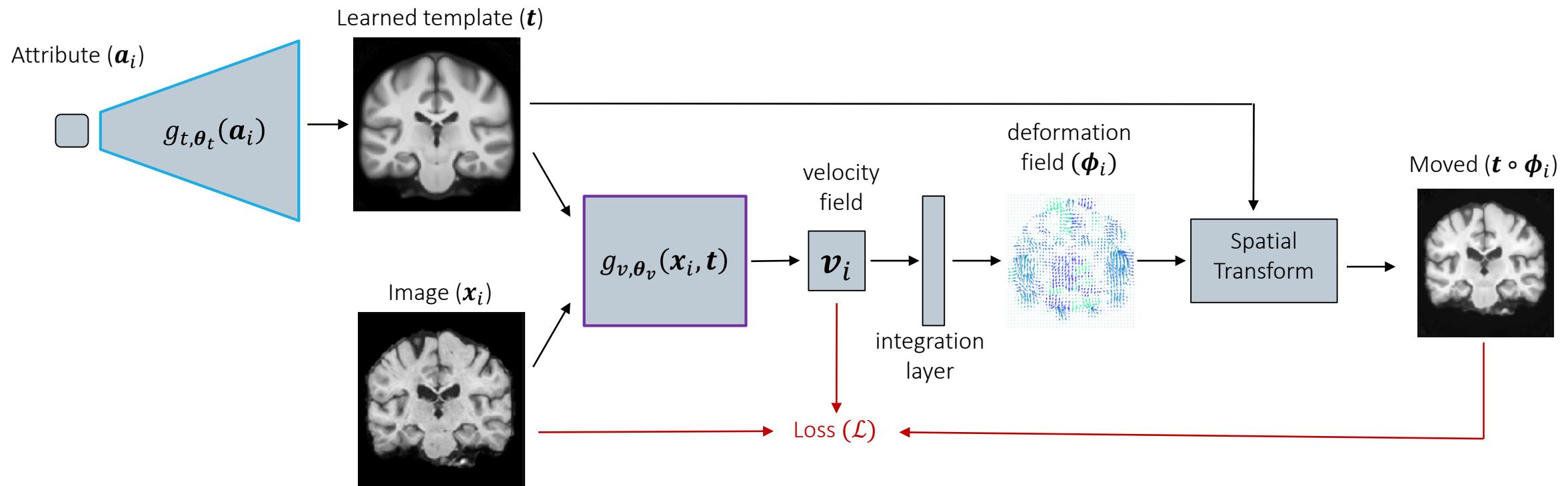


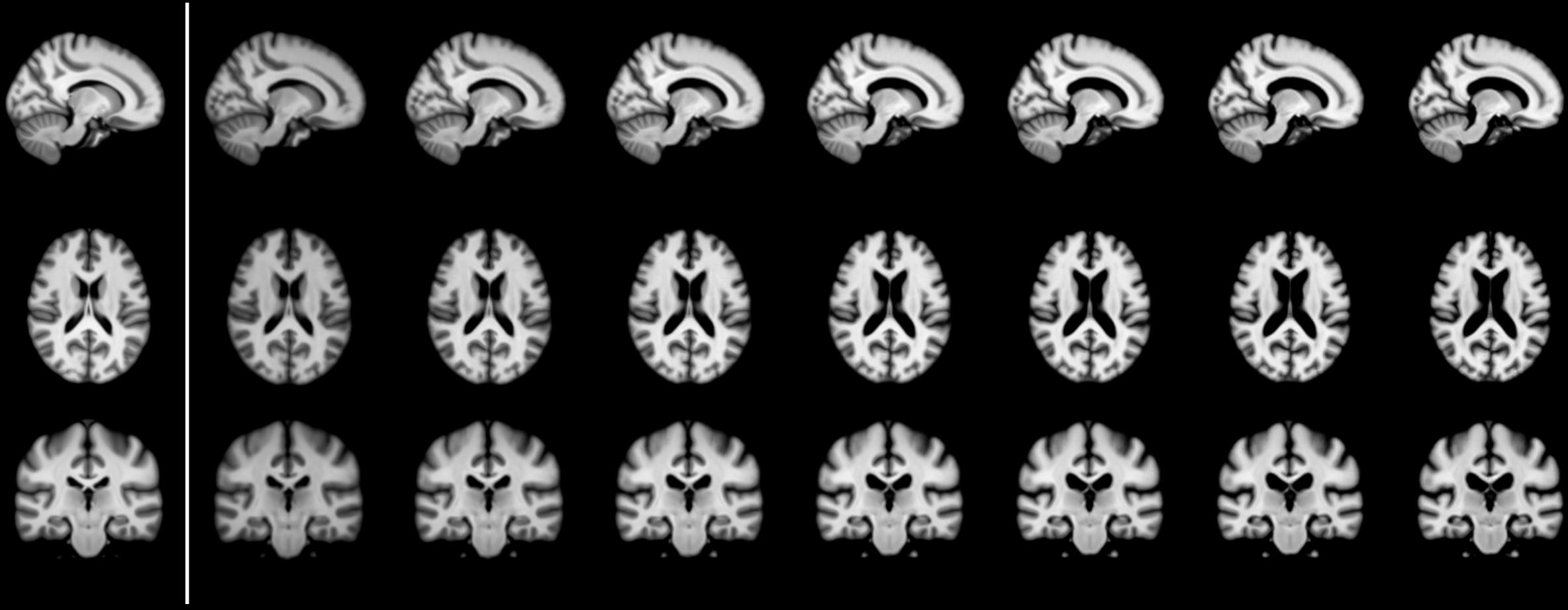
# Template Construction





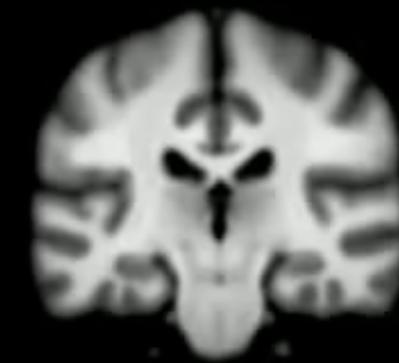
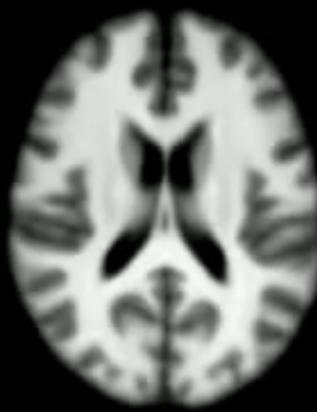
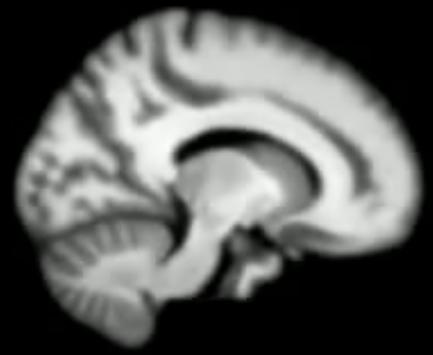
# Conditional template construction

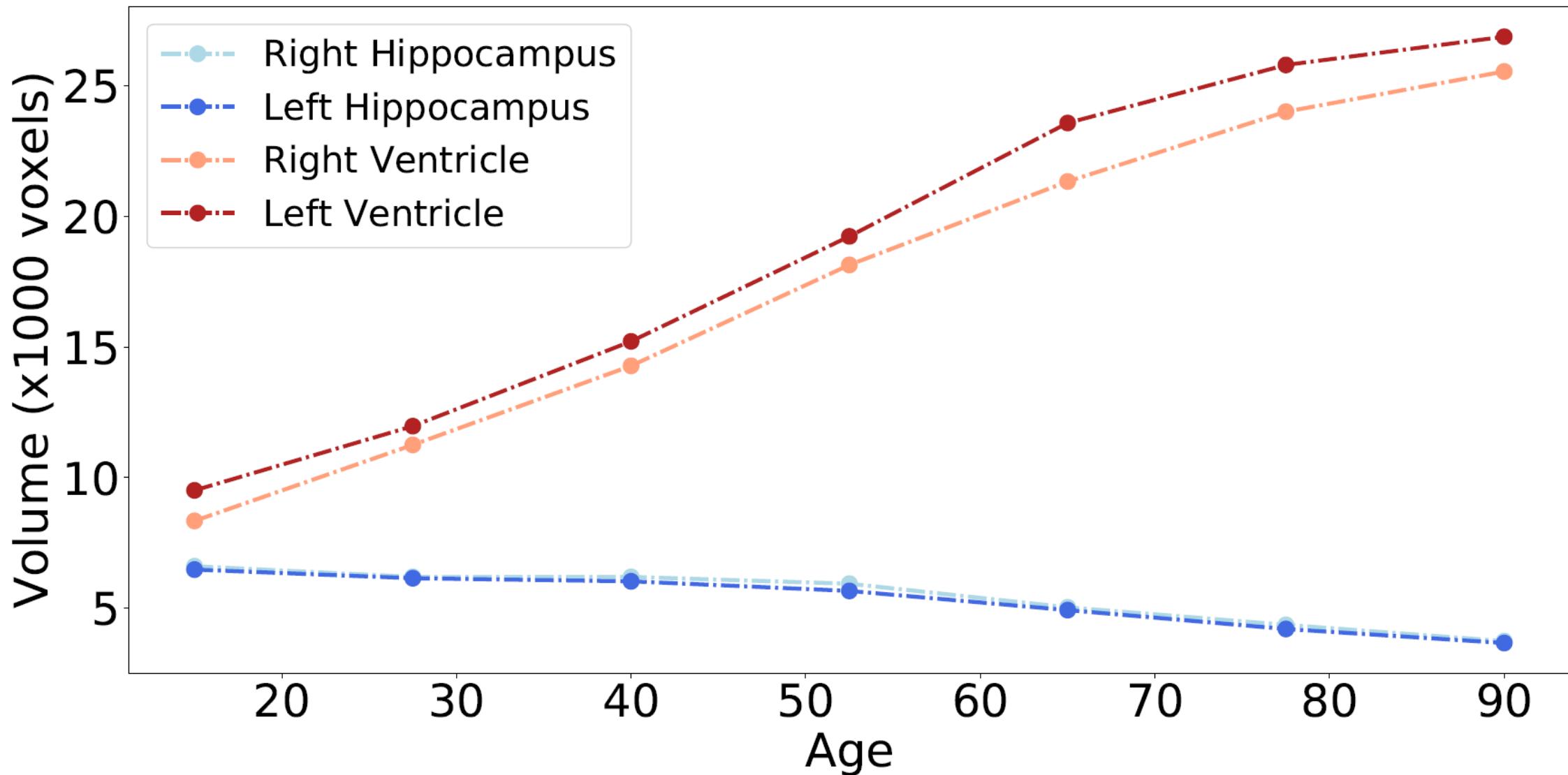


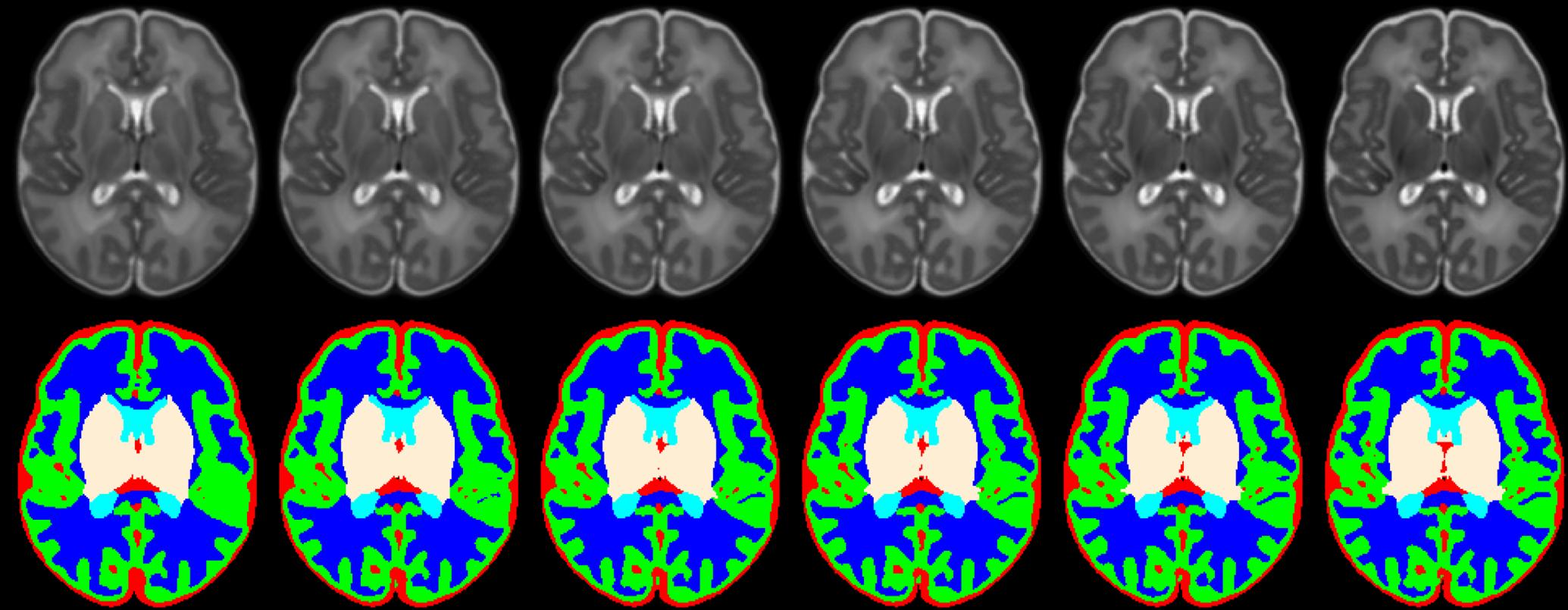


15 ← → 90

age: 15.0







29 weeks

32

35

38

41

44

# Acknowledgements

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Andrew Hoopes (MGH LCN)

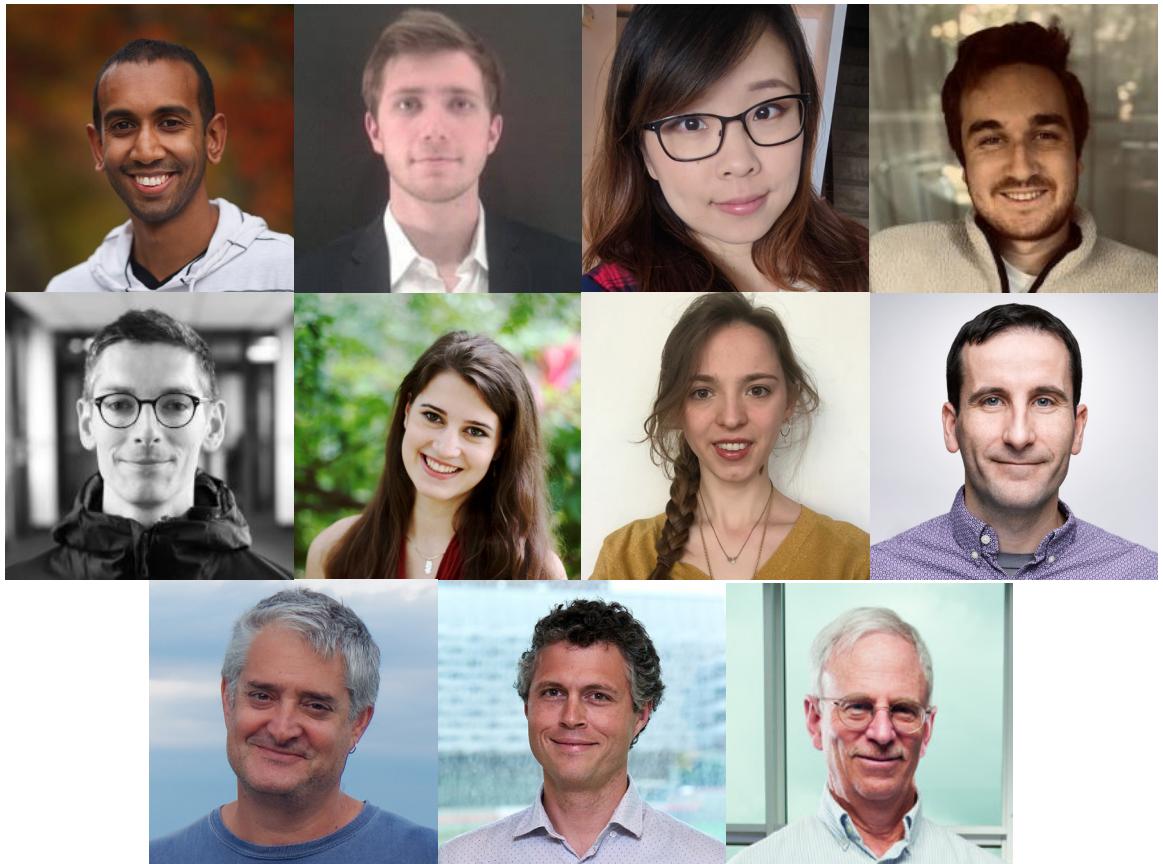
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Mert Sabuncu (Cornell ECE, HMS/MGH LCN)

Amy Zhao (MIT CSAIL DDIG)



# voxelmorph

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- Probabilistic generative model for diffeomorphisms
- Variational Inference
- Unsupervised Neural Network

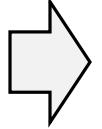


- Very **fast** for new image pair
- State-of-the-art **accuracy**
- **Diffeomorphic** deformations
- **Uncertainty** estimation

[voxelmorph.mit.edu](http://voxelmorph.mit.edu)

# voxelmorph

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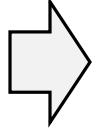
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- Limited training data → use VM as initialization
- Segmentation at training → better test Dice performance
- No atlas → construct atlas automatically
- Synthesis → invariant representations
- Can apply to wider domains

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