

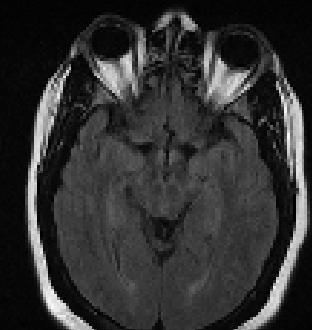
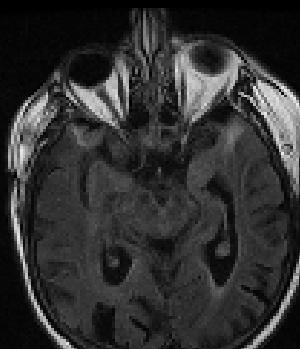
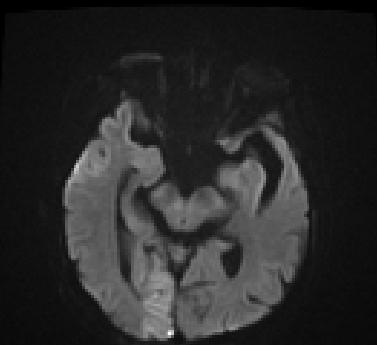
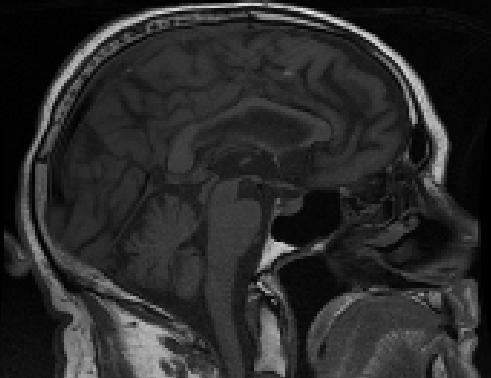
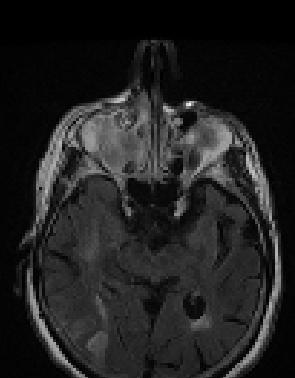
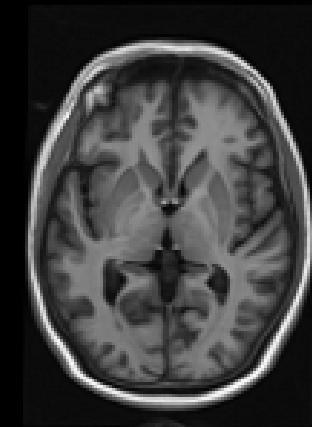
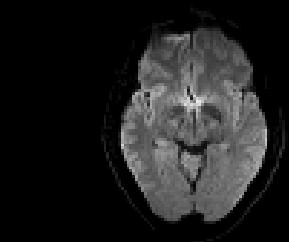
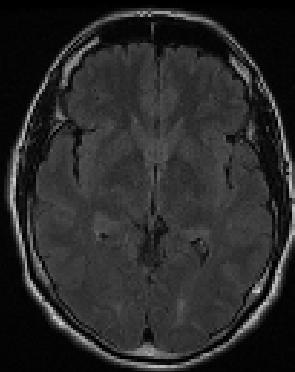
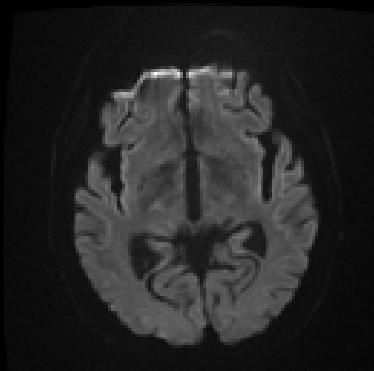
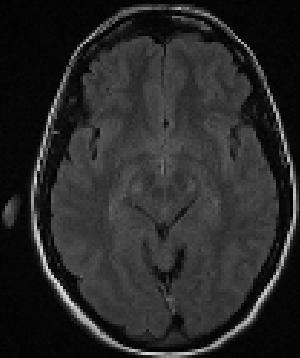
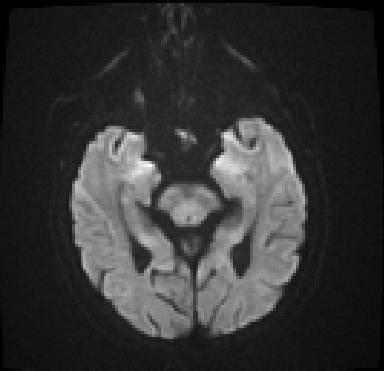
[voxelmorph.mit.edu](http://voxelmorph.mit.edu)

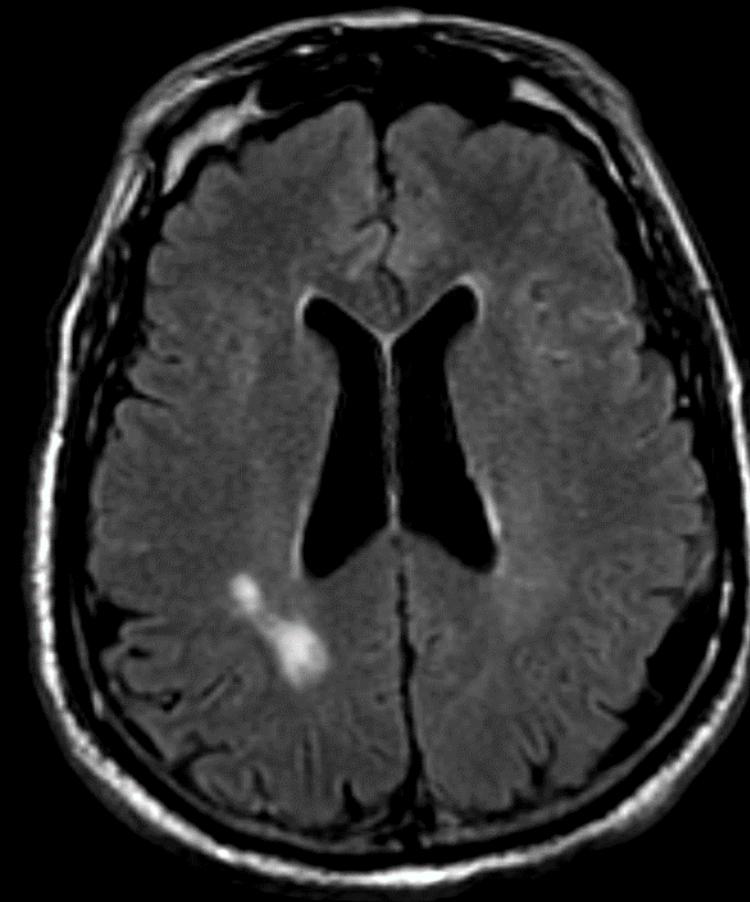
+ in future FreeSurfer release

# Unsupervised Learning of Image Correspondences in Medical Imaging Analysis

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Adrian V. Dalca  
HMS, MIT





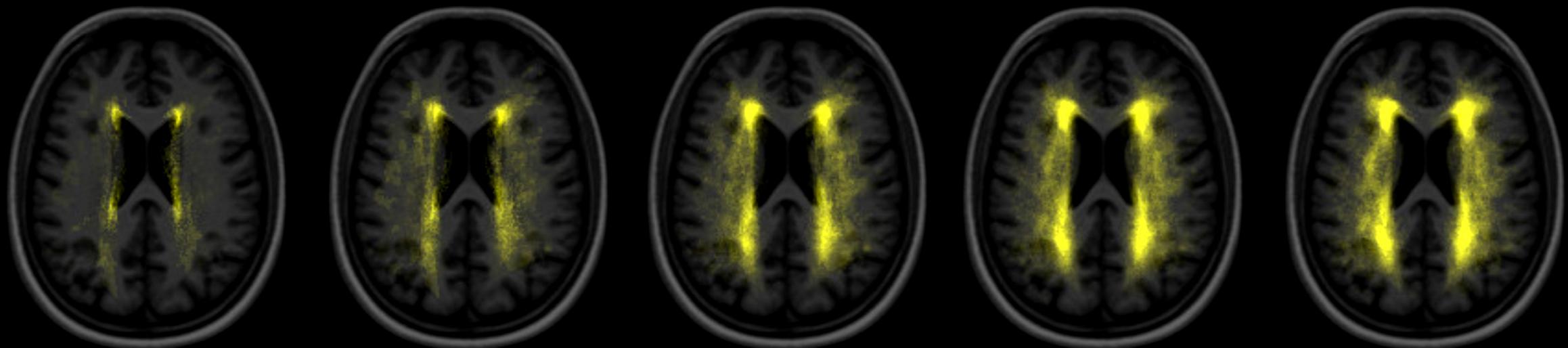
Stroke



Small vessel disease

# Progression with age

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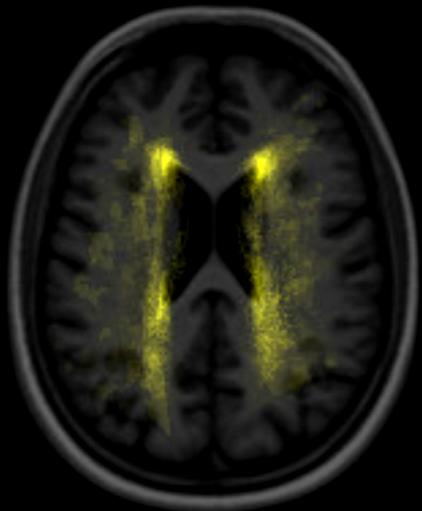
31 years  
average

42.5 years  
average

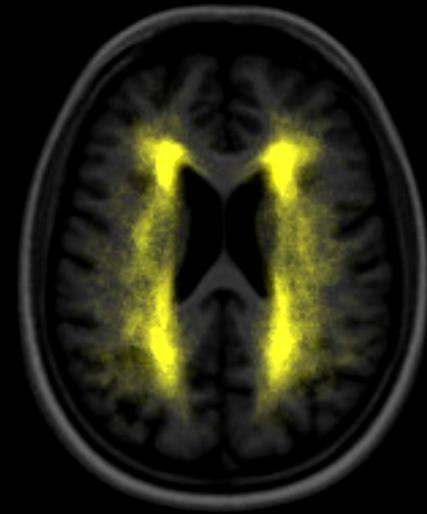
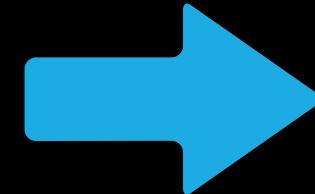
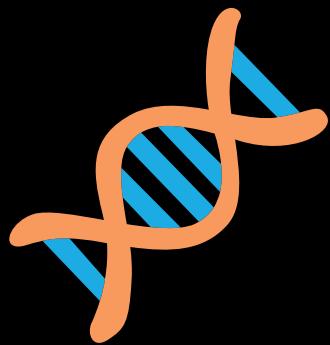
54 years  
average

65.5 years  
average

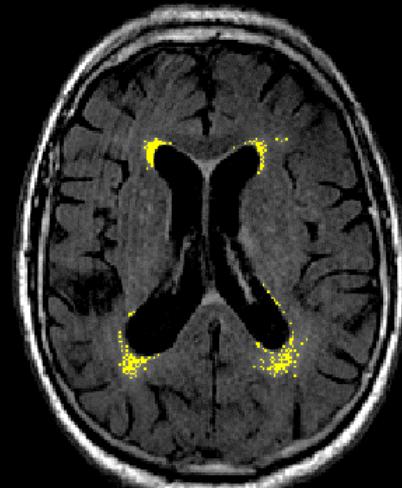
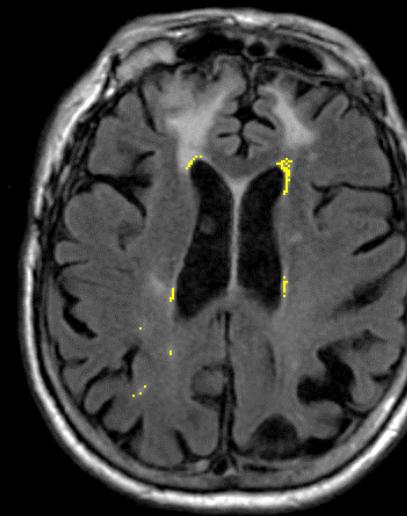
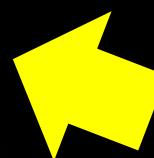
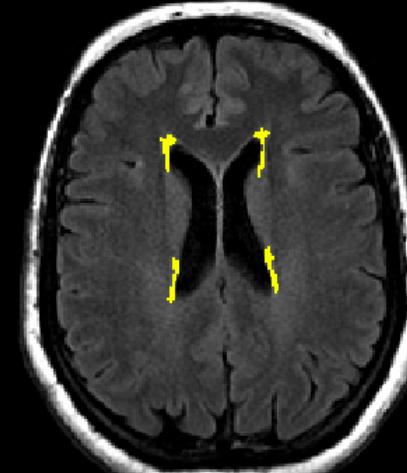
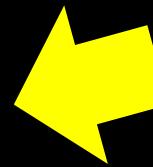
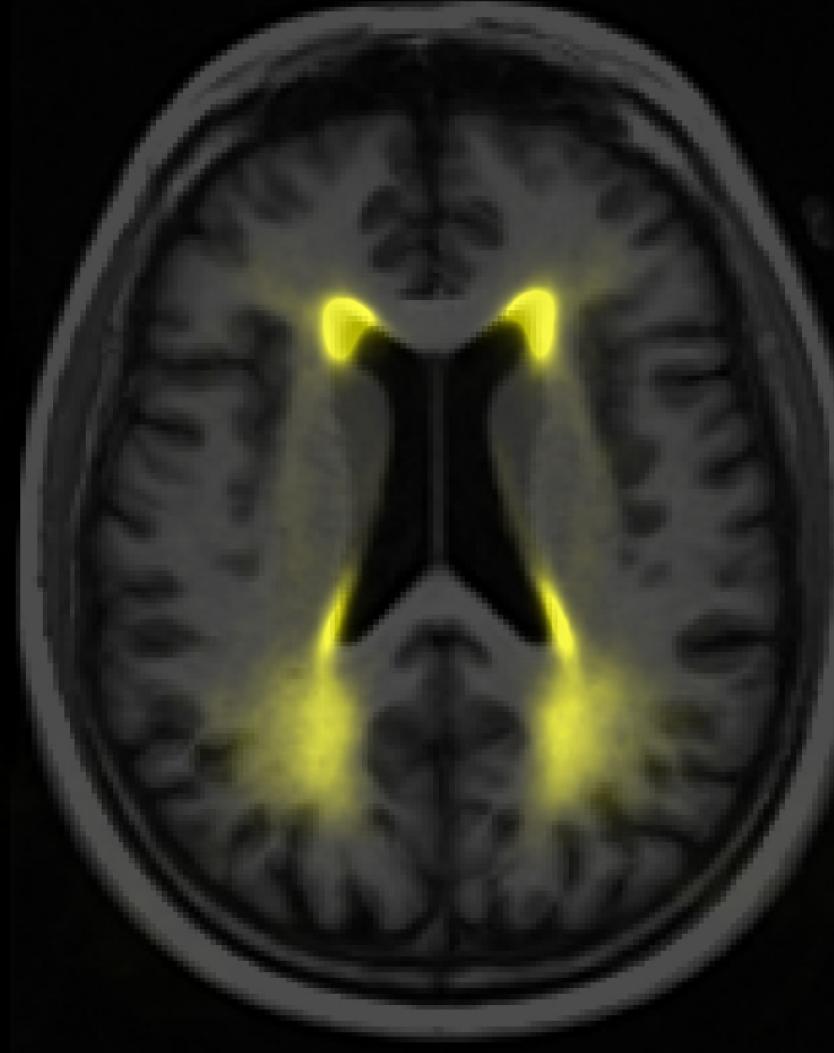
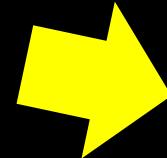
77 years  
average

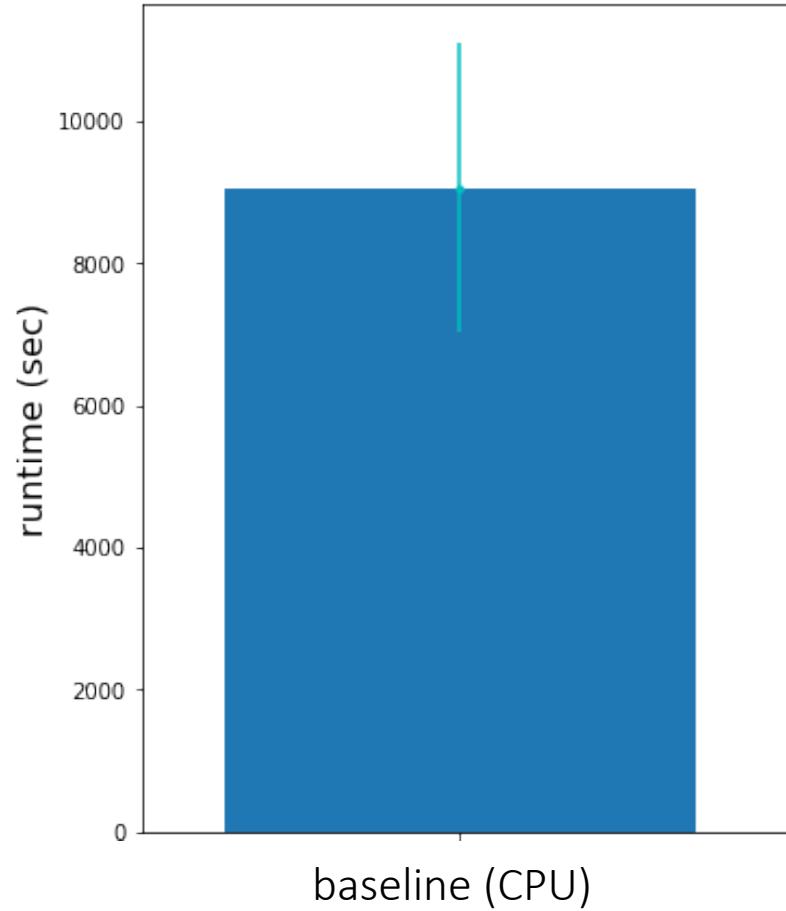


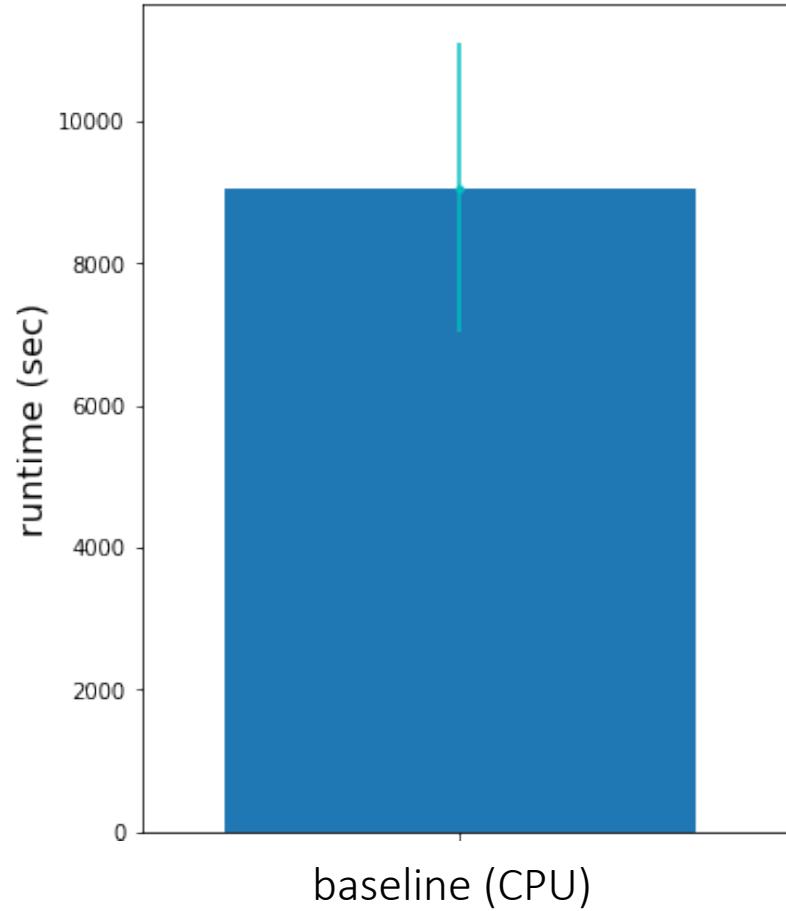
Scan at age 50



Scan at age 60

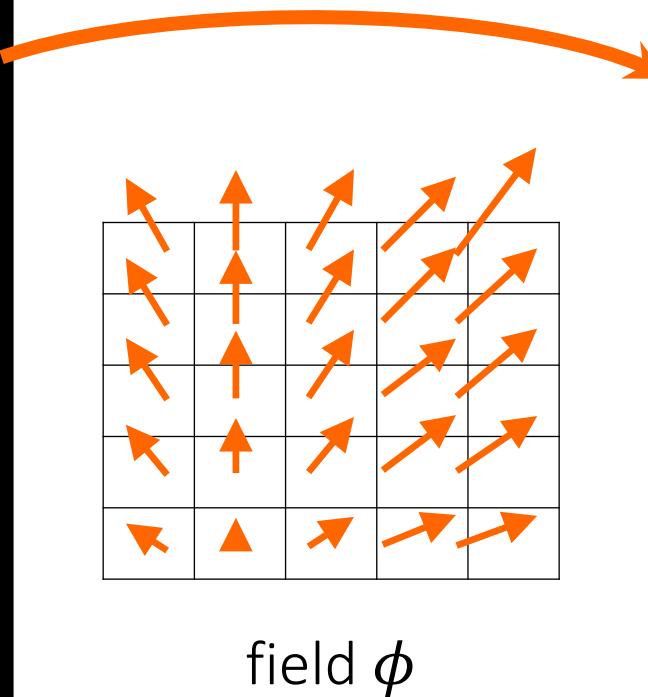






# Registration

---



moving scan  $m$



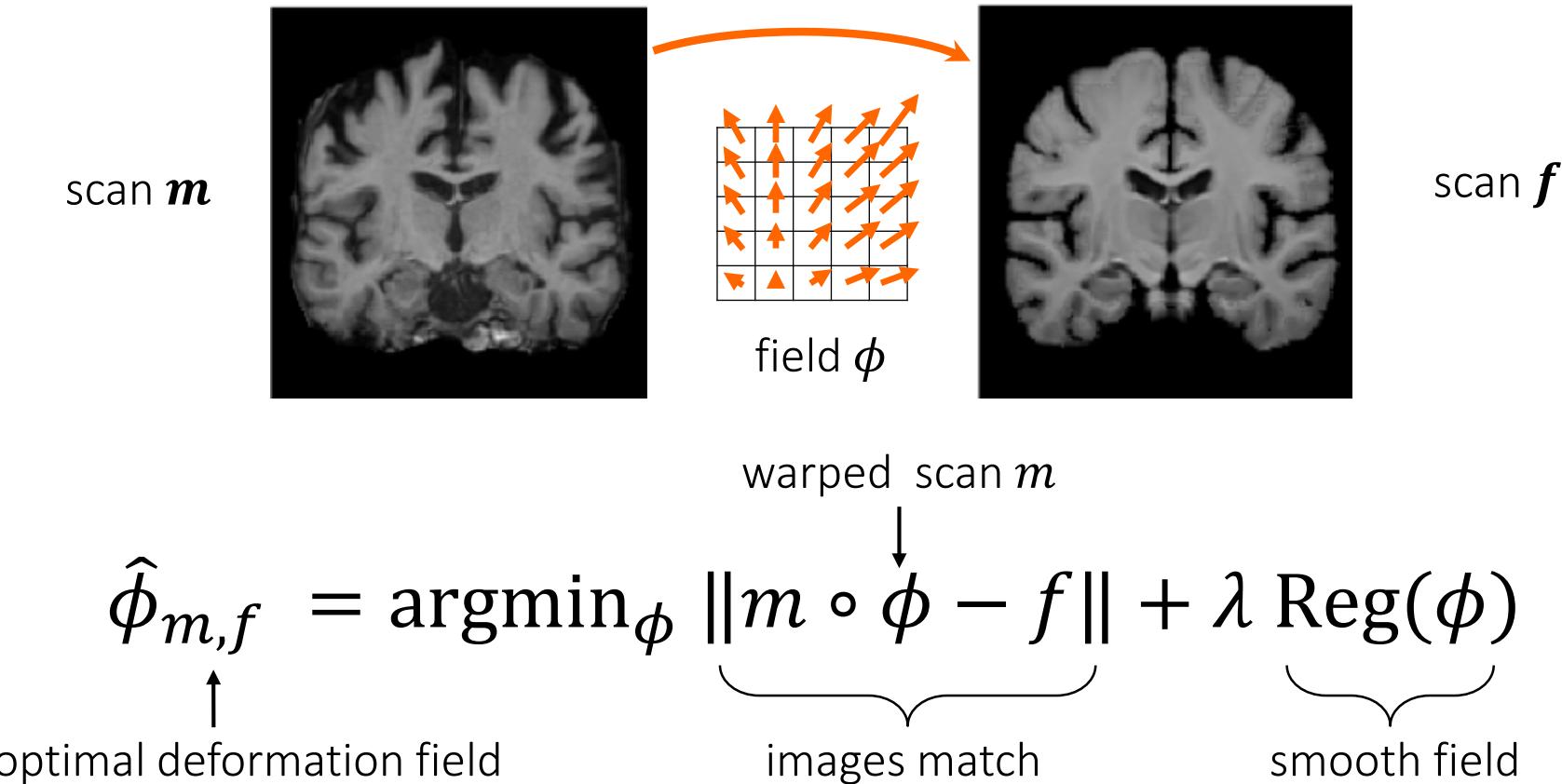
fixed scan  $f$

# Registration is fundamental in MIA

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- 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

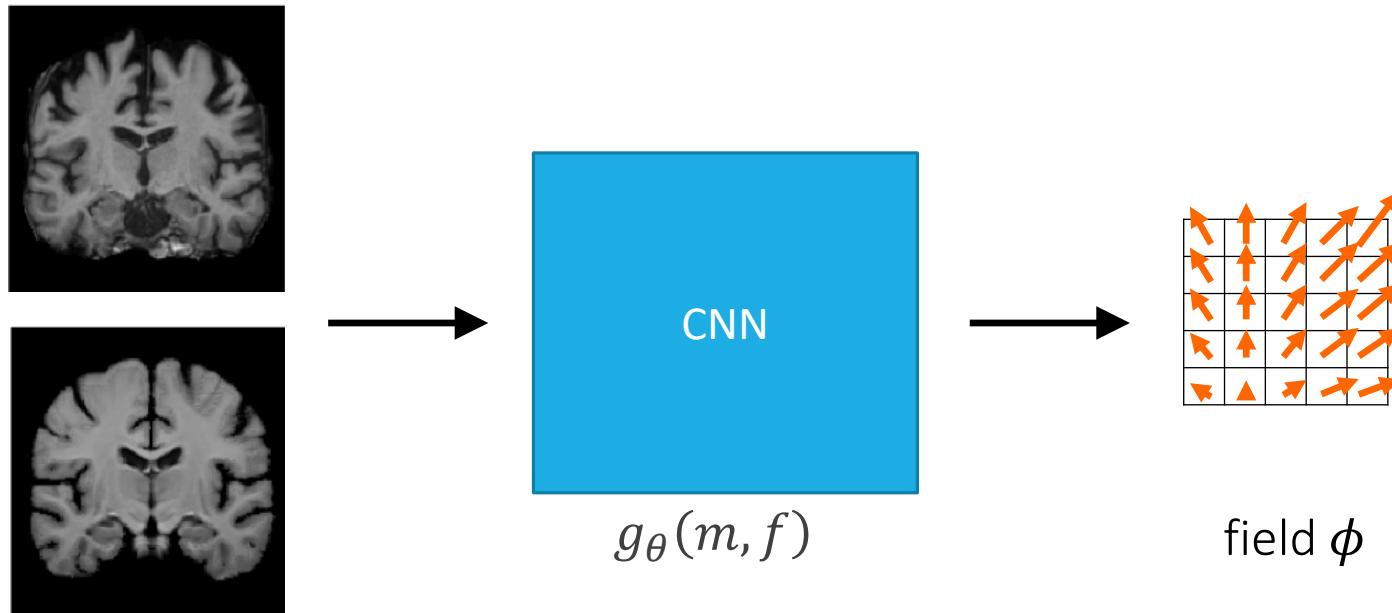
# Pairwise optimization



- significant development
- slow for two images

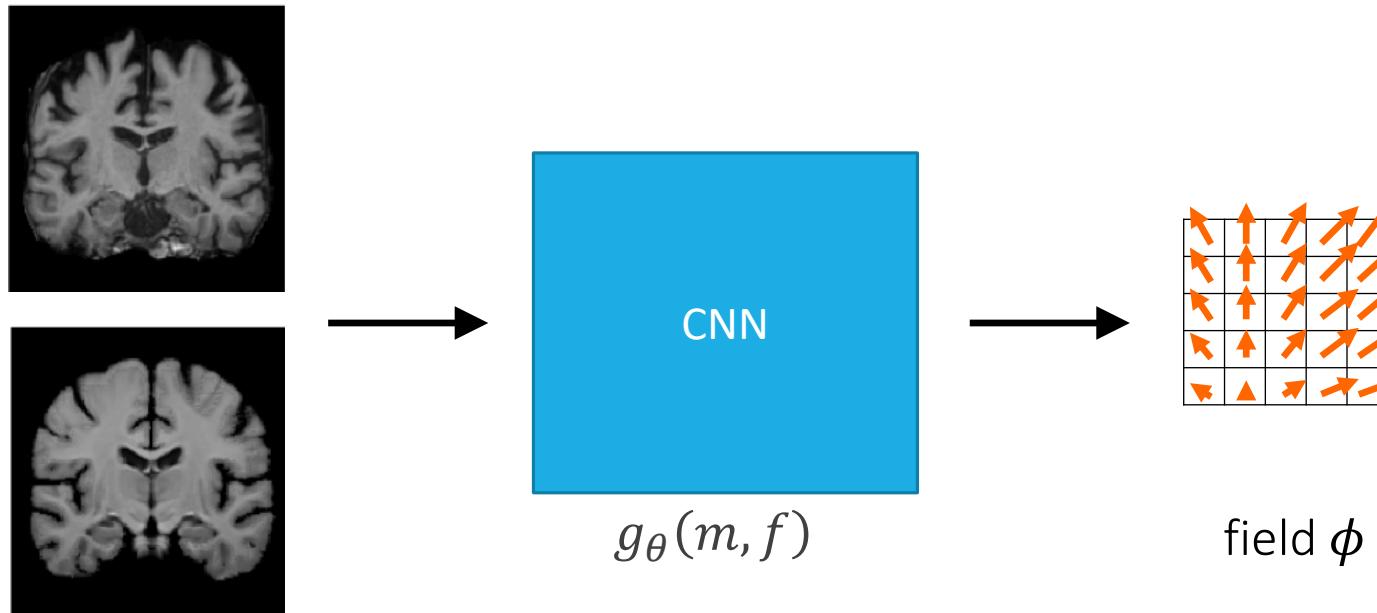
# Learning-based methods

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- 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**)

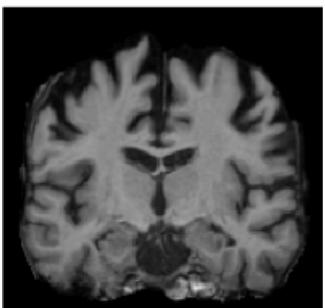
- limited use of classical modelling
- **fast** for new image pair

# Outline

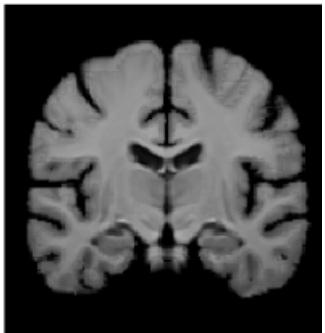
---

# Framework

Moving image  
( $m$ )

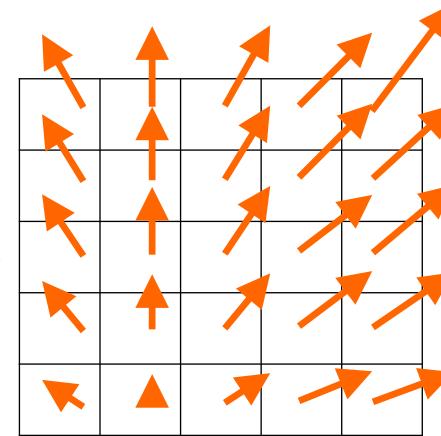


Fixed image  
( $f$ )



network  $g_\theta$   
parameters  $\theta$

deformation

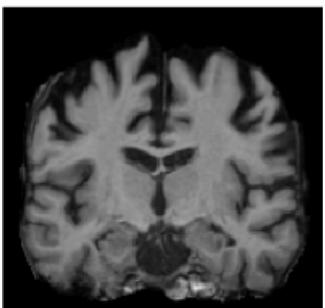


Supervised:

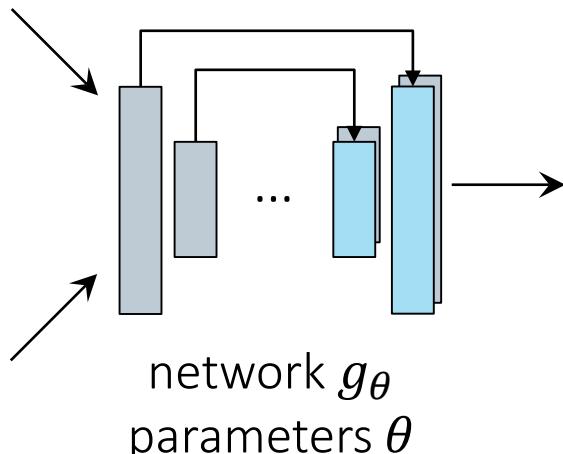
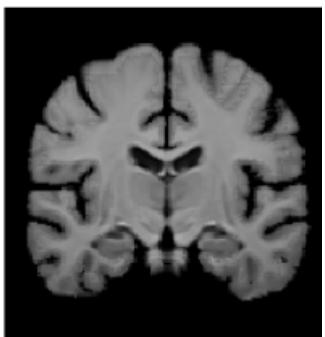
$$\mathcal{L} = \|\phi - \phi_{gt}\|^2$$

# VoxelMorph

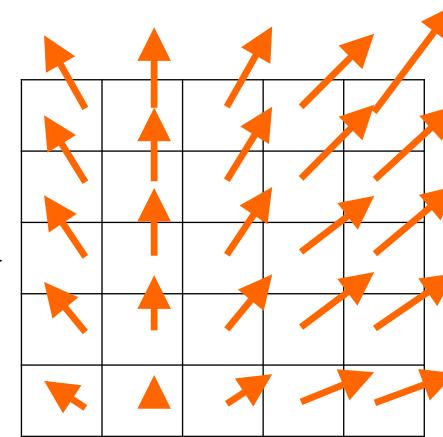
Moving image  
( $m$ )



Fixed image  
( $f$ )



deformation

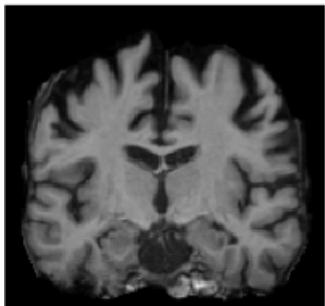


Unsupervised:

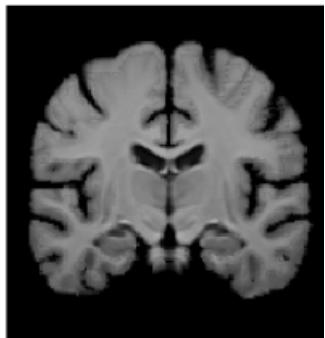
$$\mathcal{L} = \underbrace{\|m \circ \phi - f\|}_{\text{images match}} + \lambda \underbrace{\text{Reg}(\phi)}_{\text{smooth field}}$$

# VoxelMorph Loss

Moving image  
( $m$ )

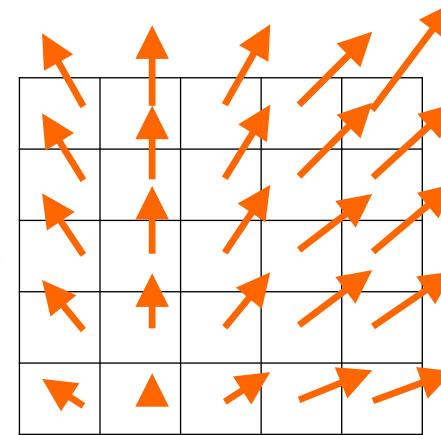


Fixed image  
( $f$ )



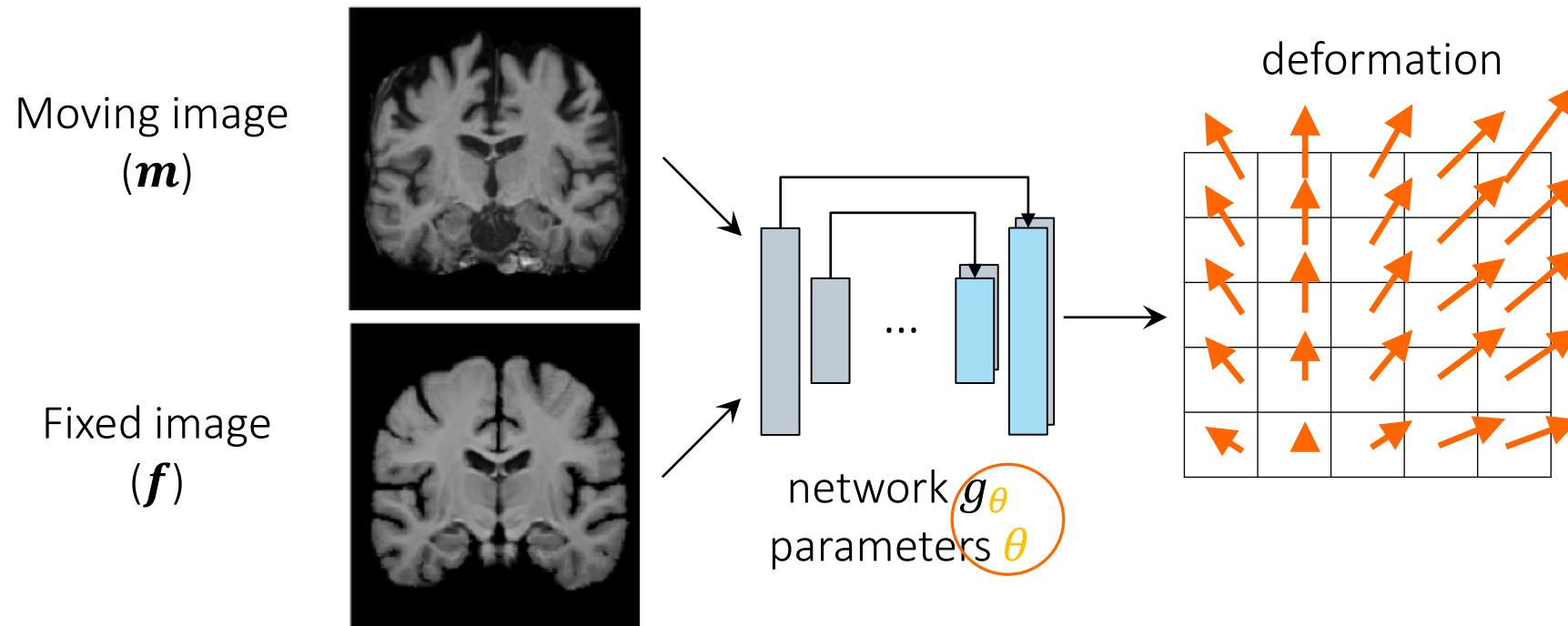
network  $g_\theta$   
parameters  $\theta$

deformation



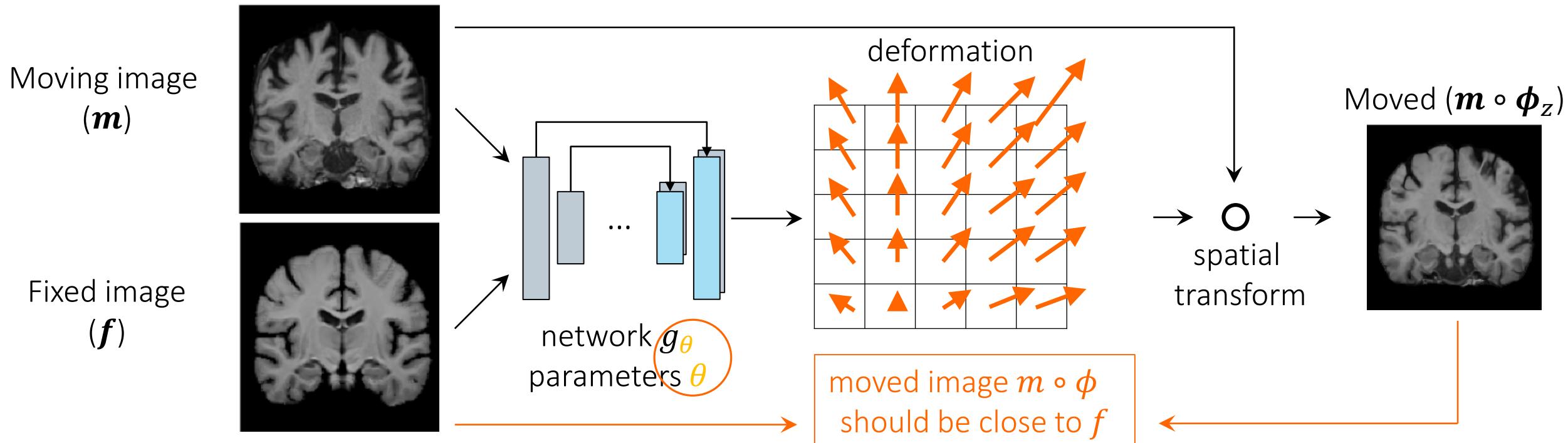
$$\mathcal{L} = \sum_{i,j} \|m_i \circ \phi_{ij} - f_{ij}\| + \lambda \text{Reg}(\phi_{ij})$$

# VoxelMorph Loss



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

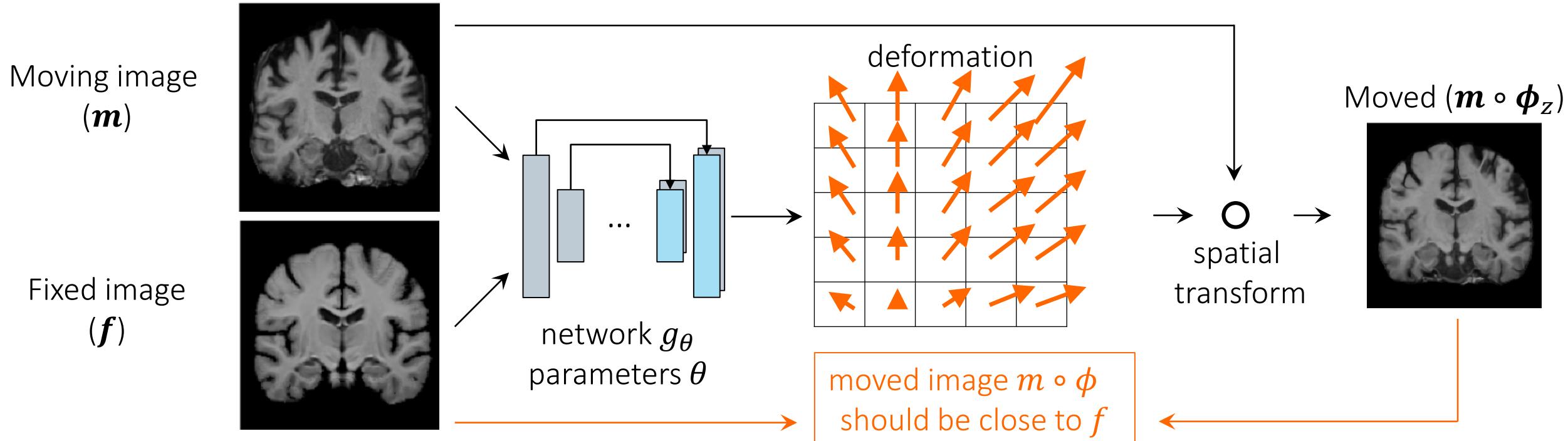
# VoxelMorph Loss



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

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

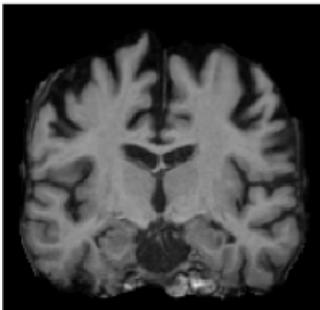
# Training



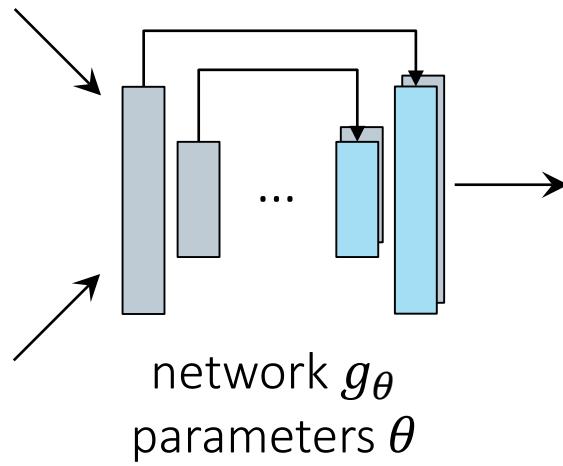
- SGD based techniques
- Each image pair contributes **slightly** to  $\theta$   
Classical optimization: slightly update  $\phi$  for an image pair

# Registration

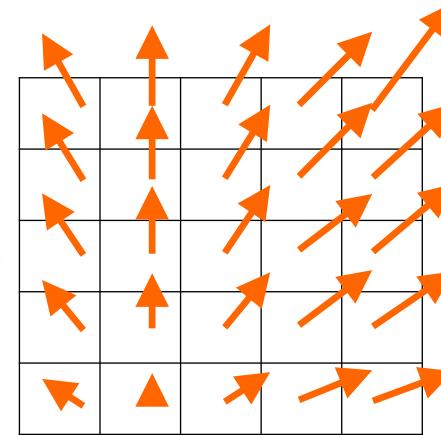
Moving image  
 $(m)$



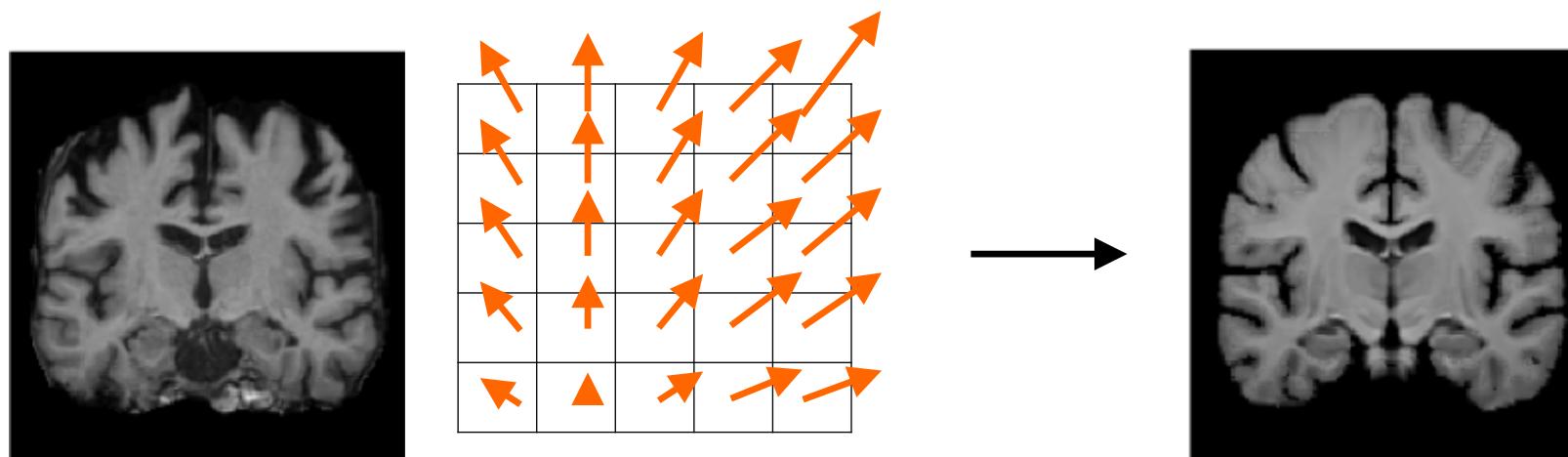
Fixed image  
 $(f)$



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

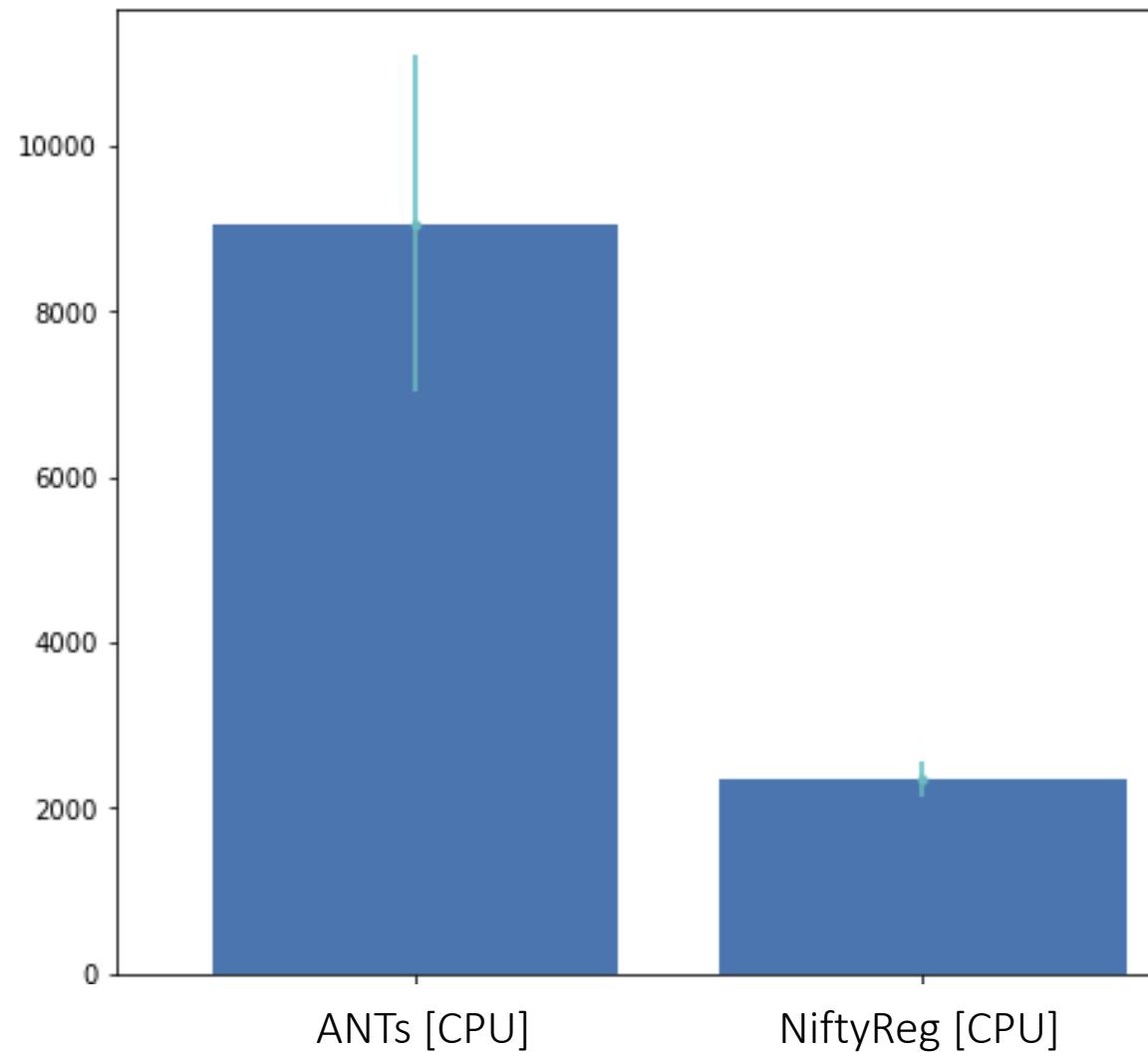
---

Data: 7000 training volumes, 250 validate, 250 test

Baseline: ANTs optimization method

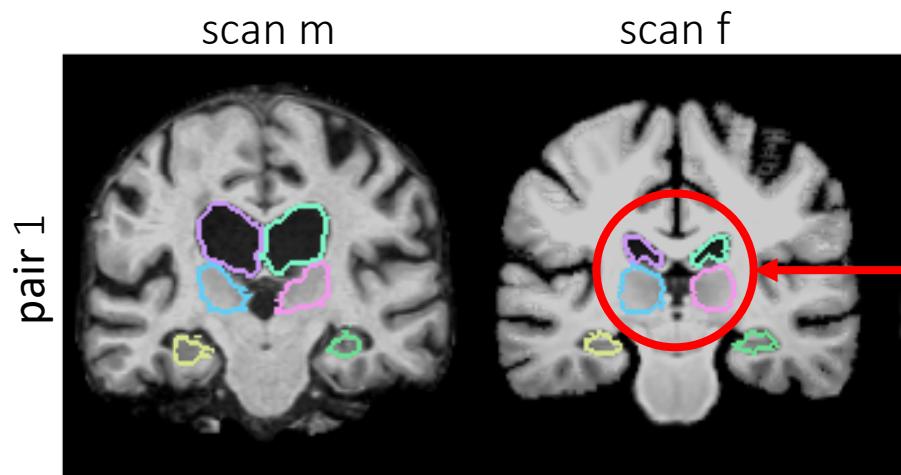
# Runtime for a new 3D image pair

---



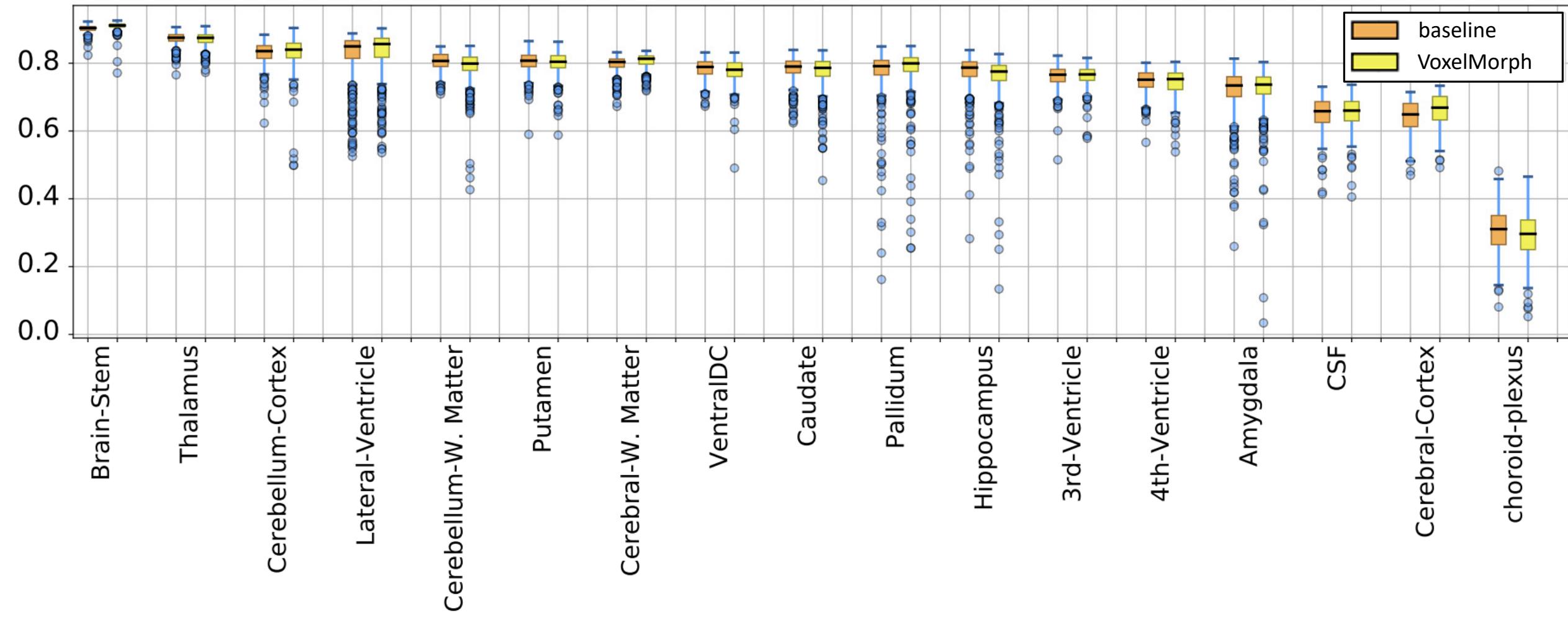
# Anatomical volume overlap

---



\*algorithms only see images, no segmentation maps

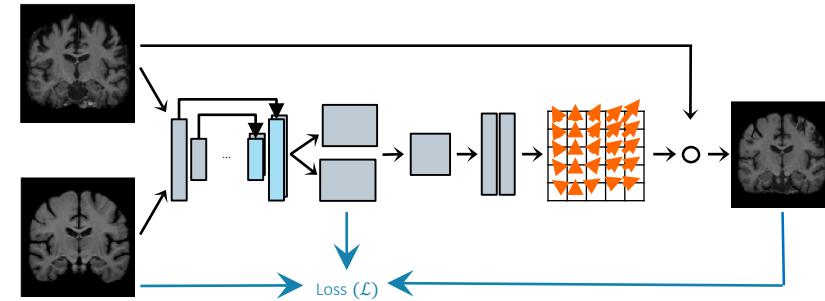
# Accuracy via volume overlap (Dice)



# Outline

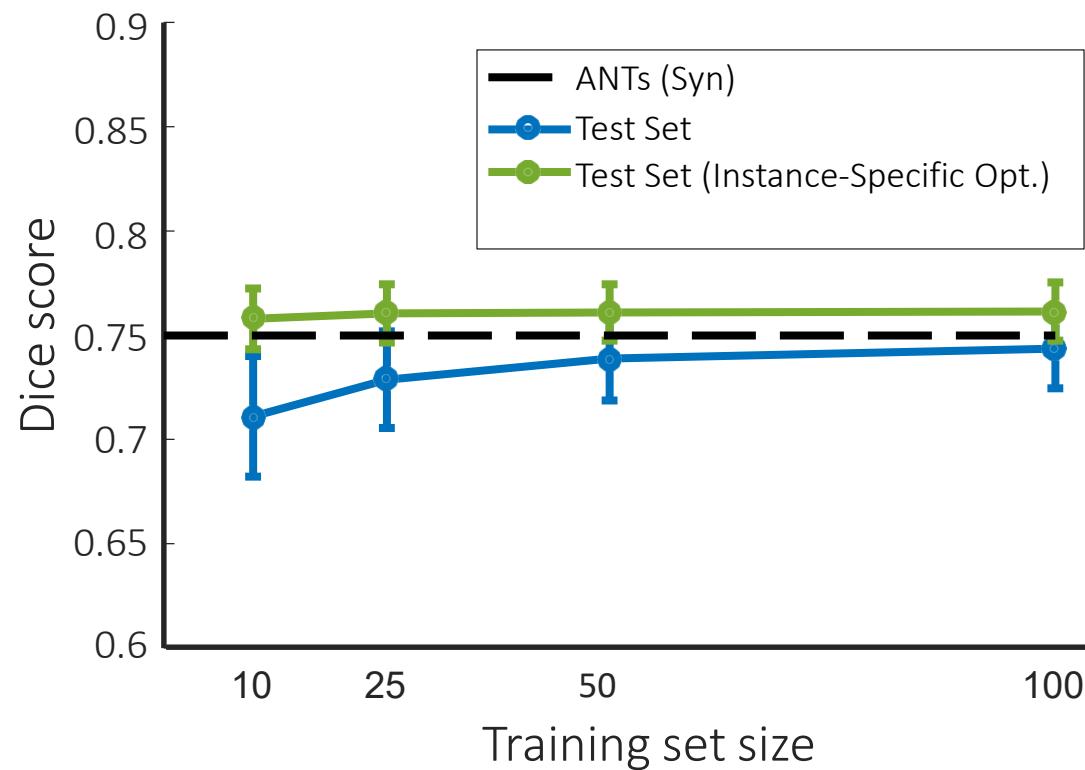
---

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

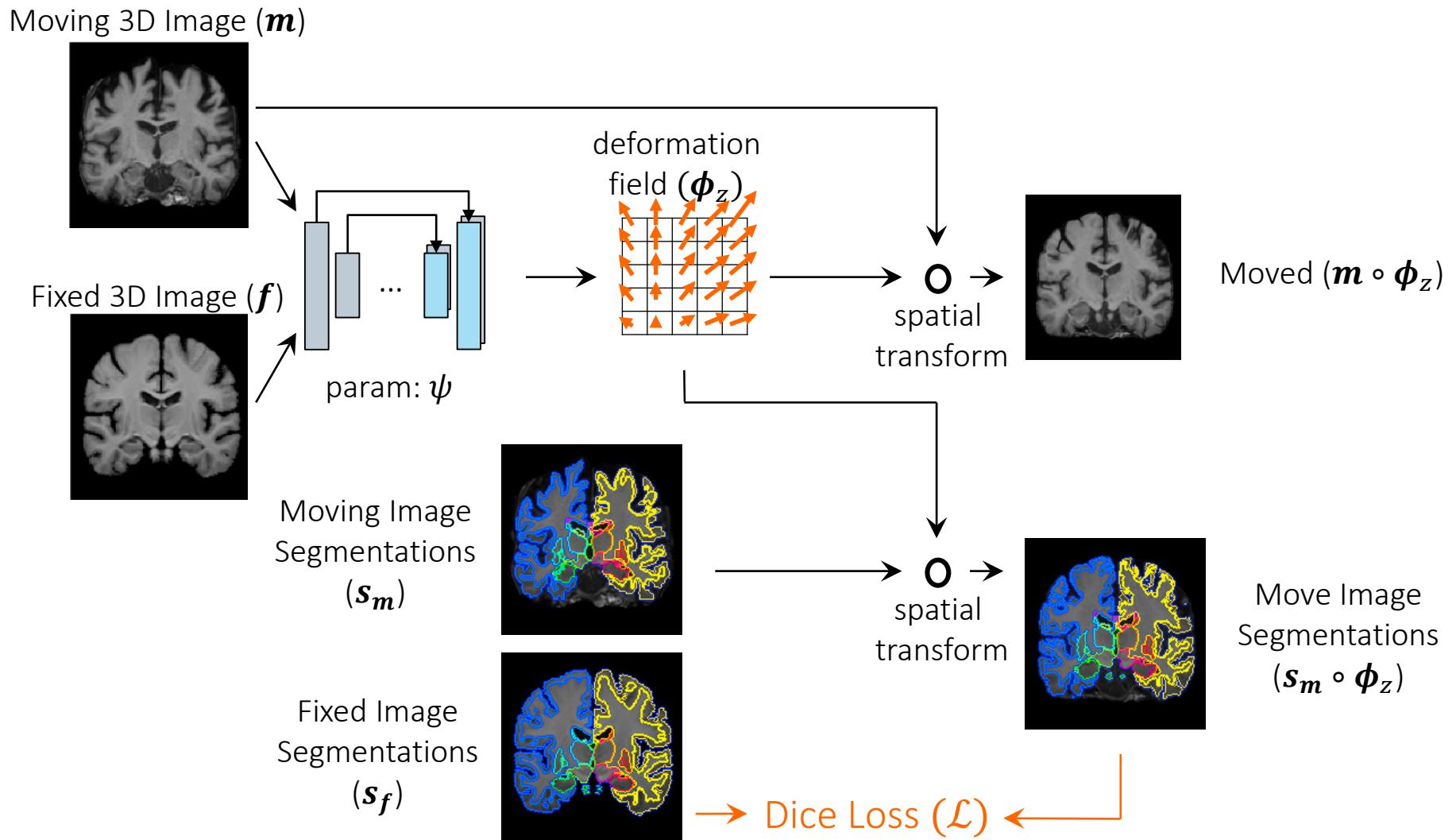


# Amortized analysis: training with limited data

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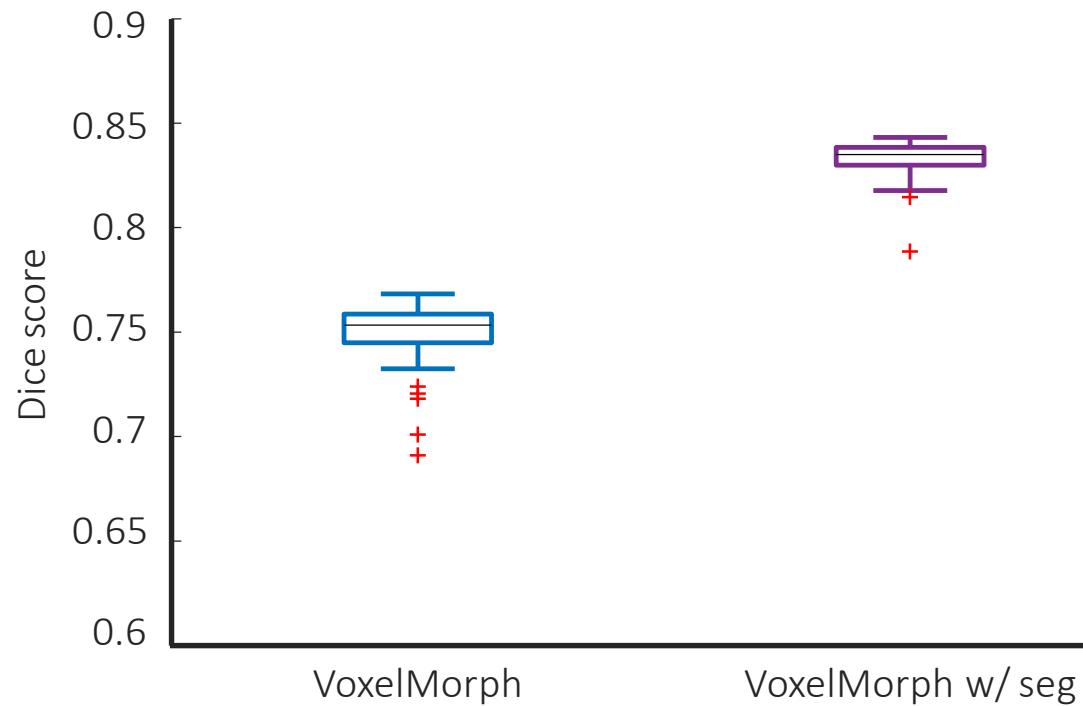


# Segmentation Maps available at training



# Test time performance

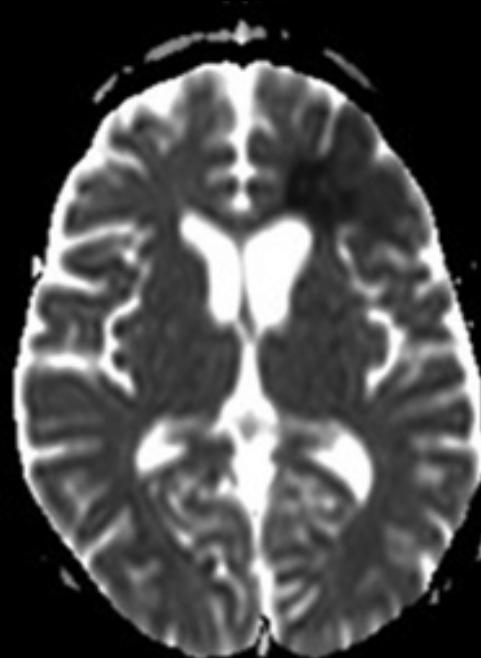
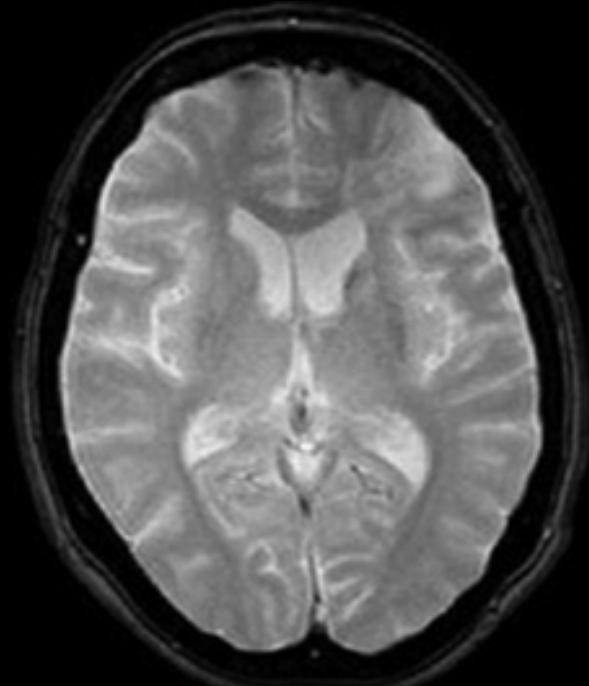
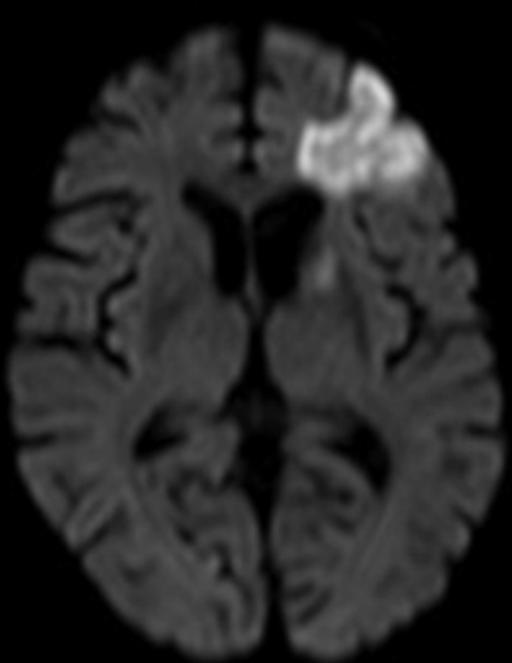
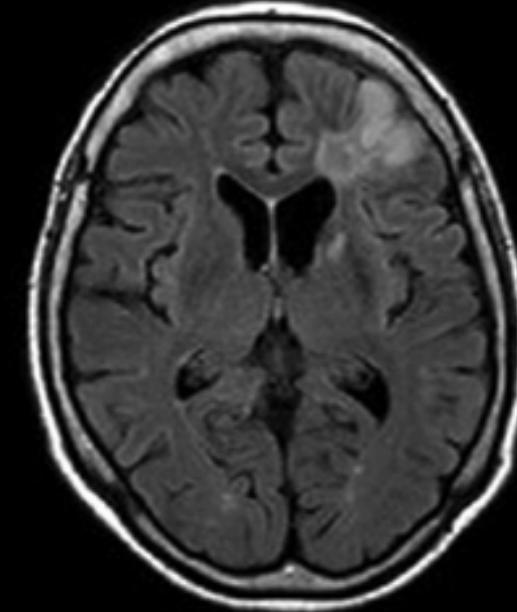
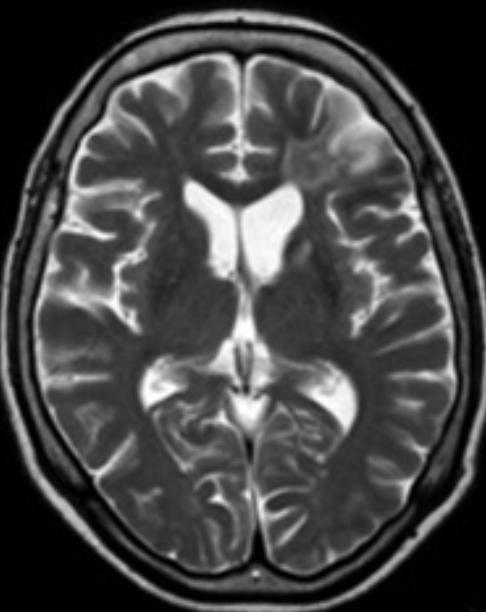
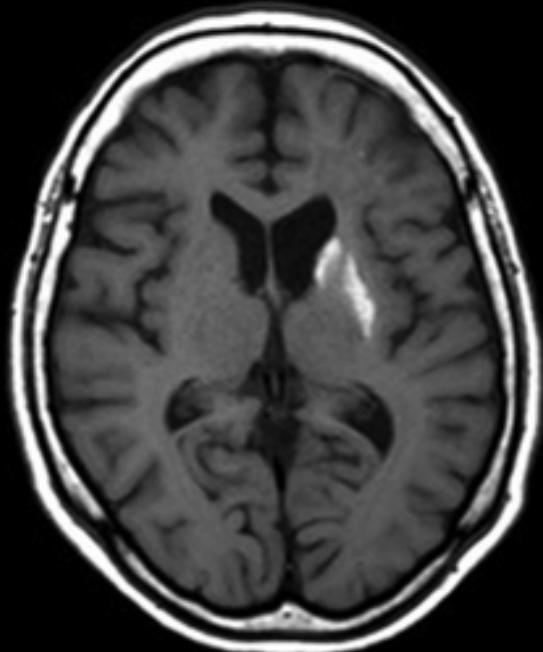
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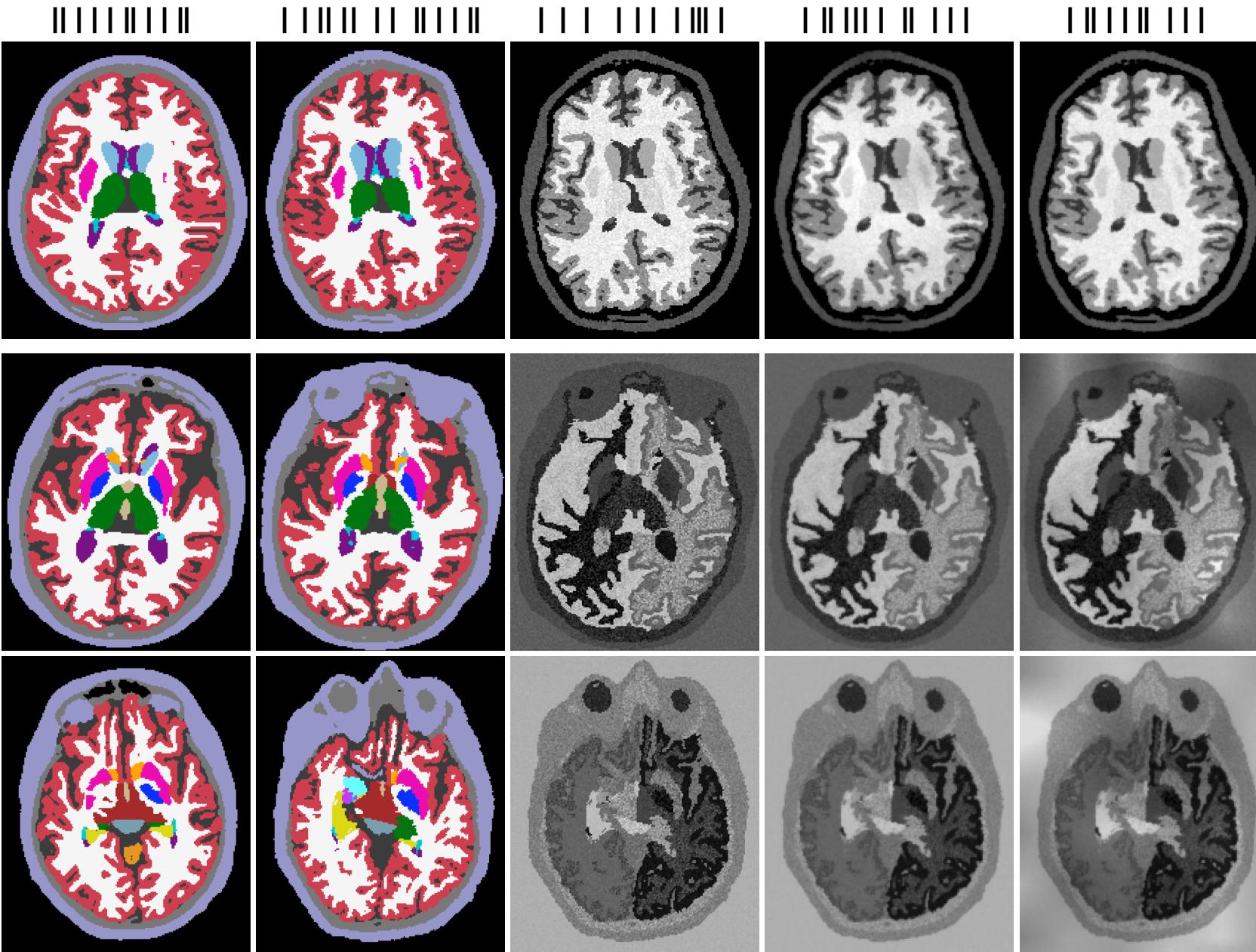


# SynthMorph (do we need real data?)

---

Hoffmann et al in submission





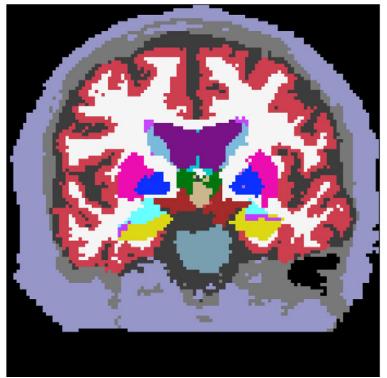
<https://github.com/BBillot/lab2im>

Billot MIDL 2020  
Billot MICCAI 2020

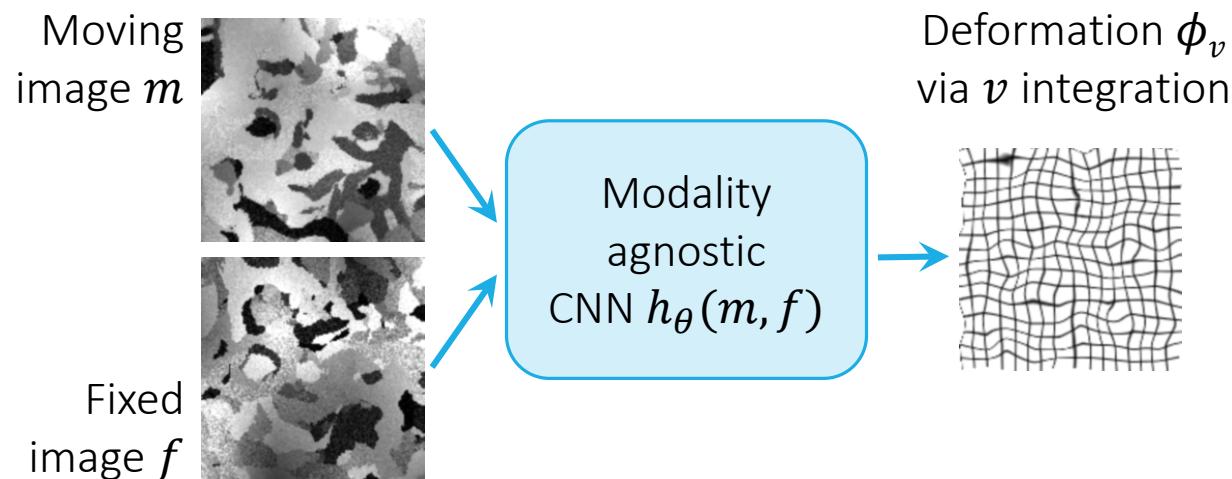
# Do we need anatomical images to train?

---

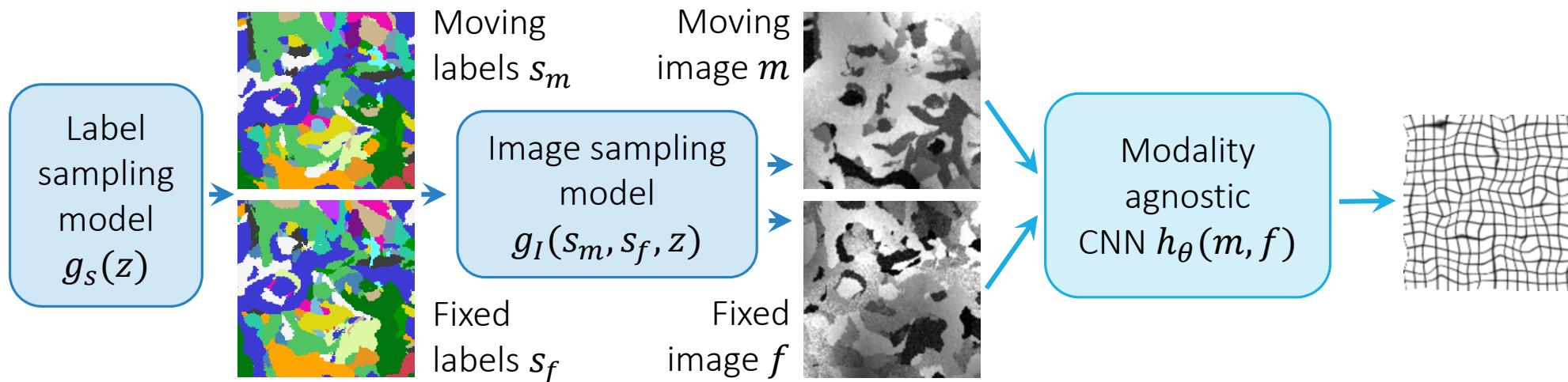
Brains



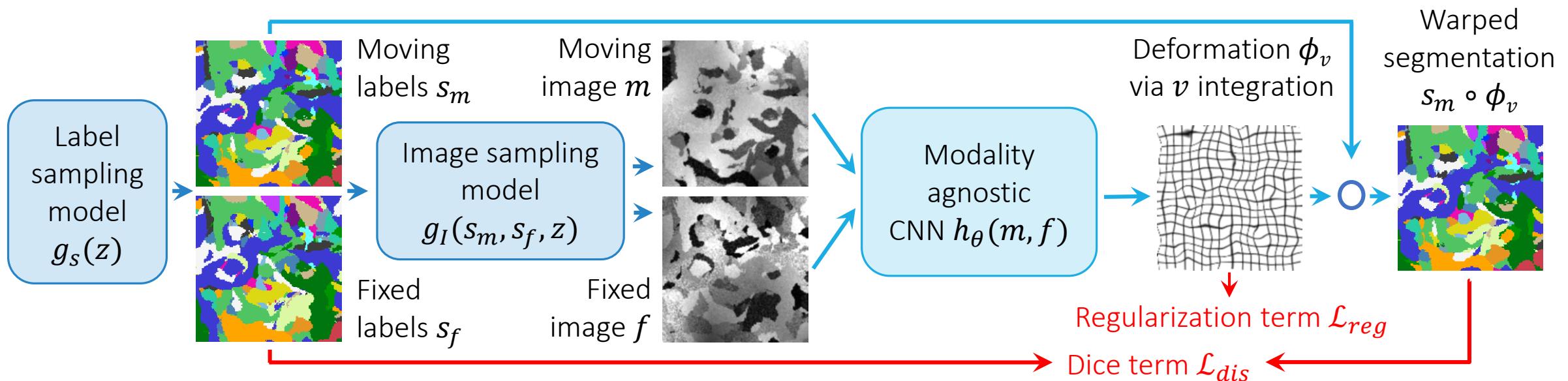
# Do we need anatomical images to train?



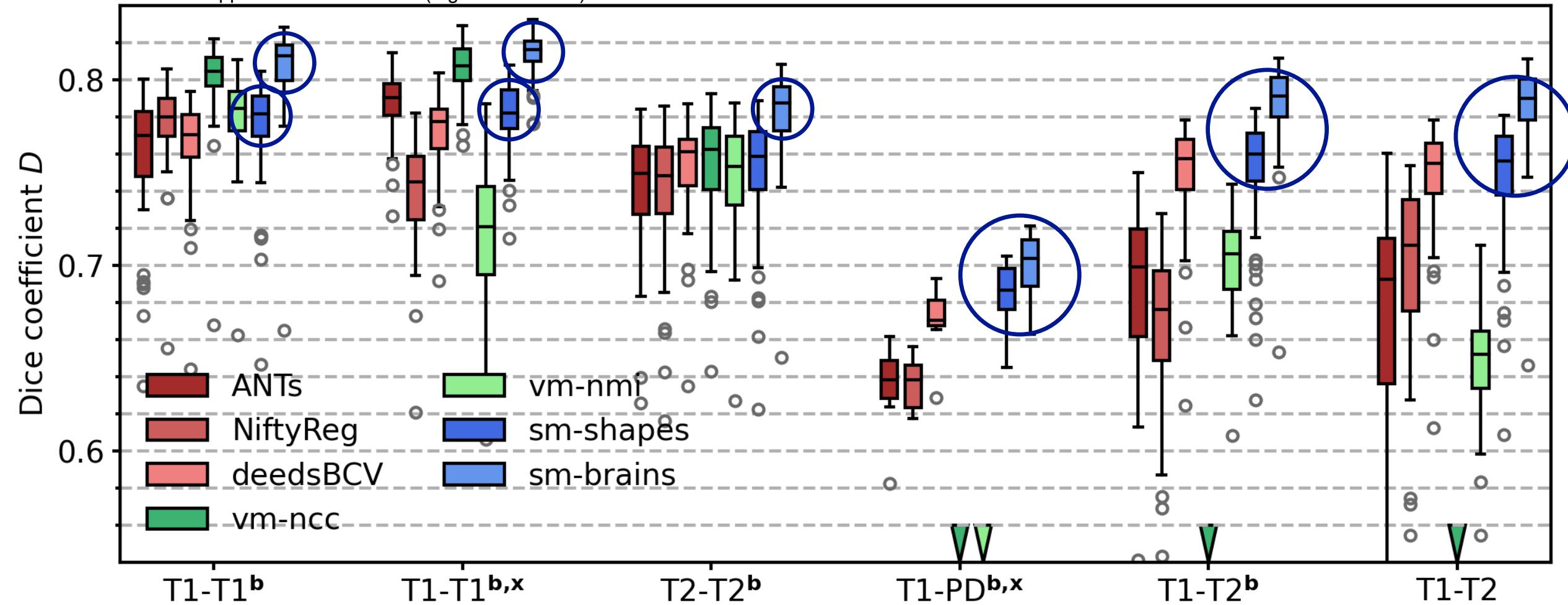
# Do we need anatomical images to train?

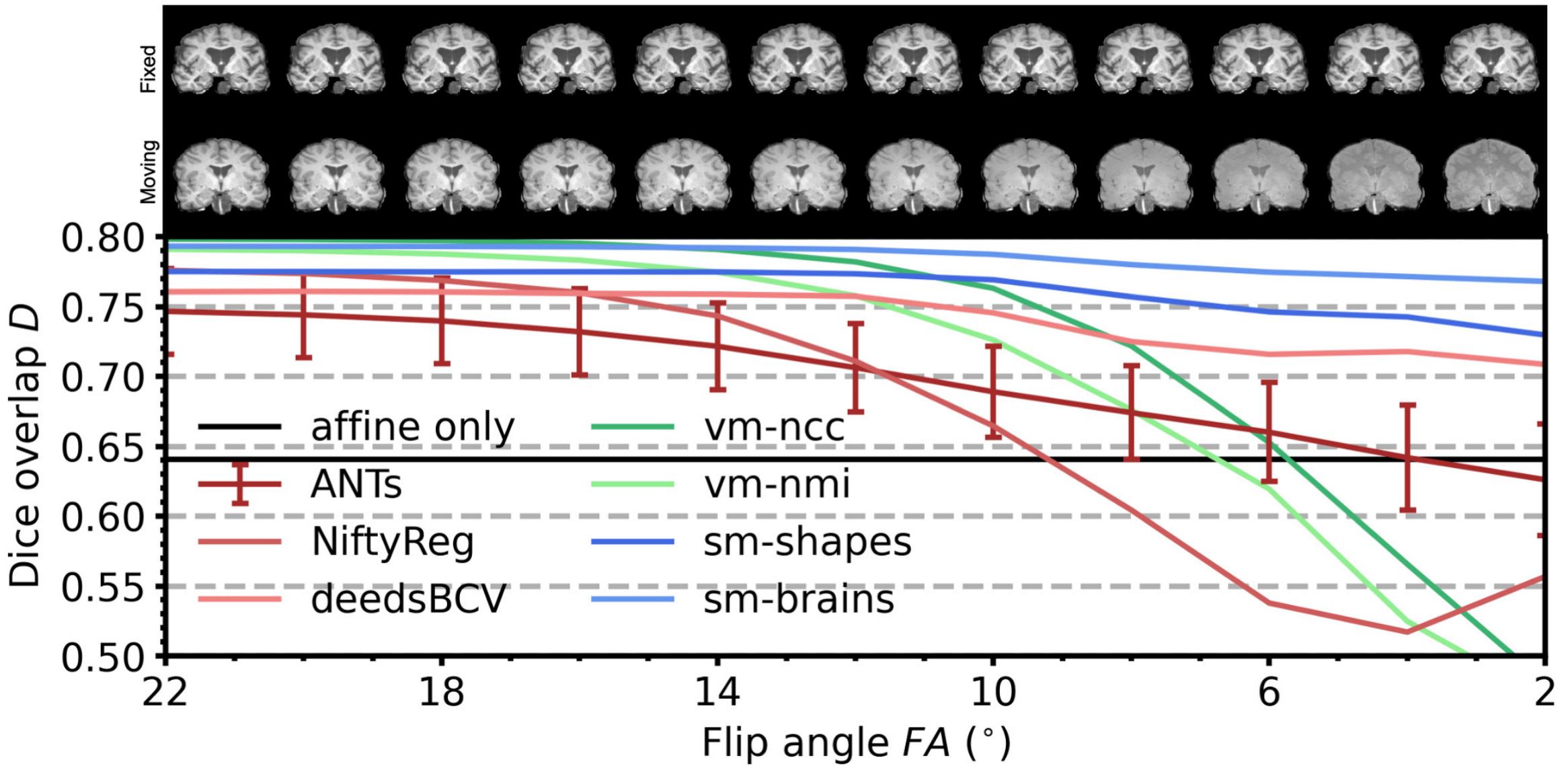


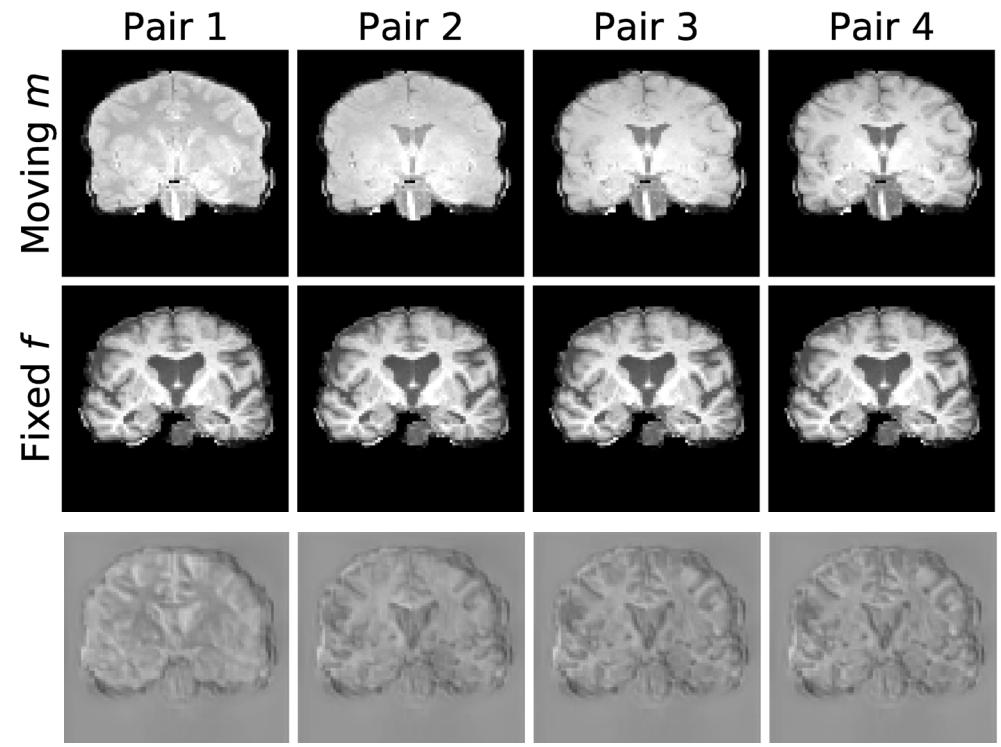
# Do we need anatomical images to train?



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







Pair 1      Pair 2      Pair 3      Pair 4

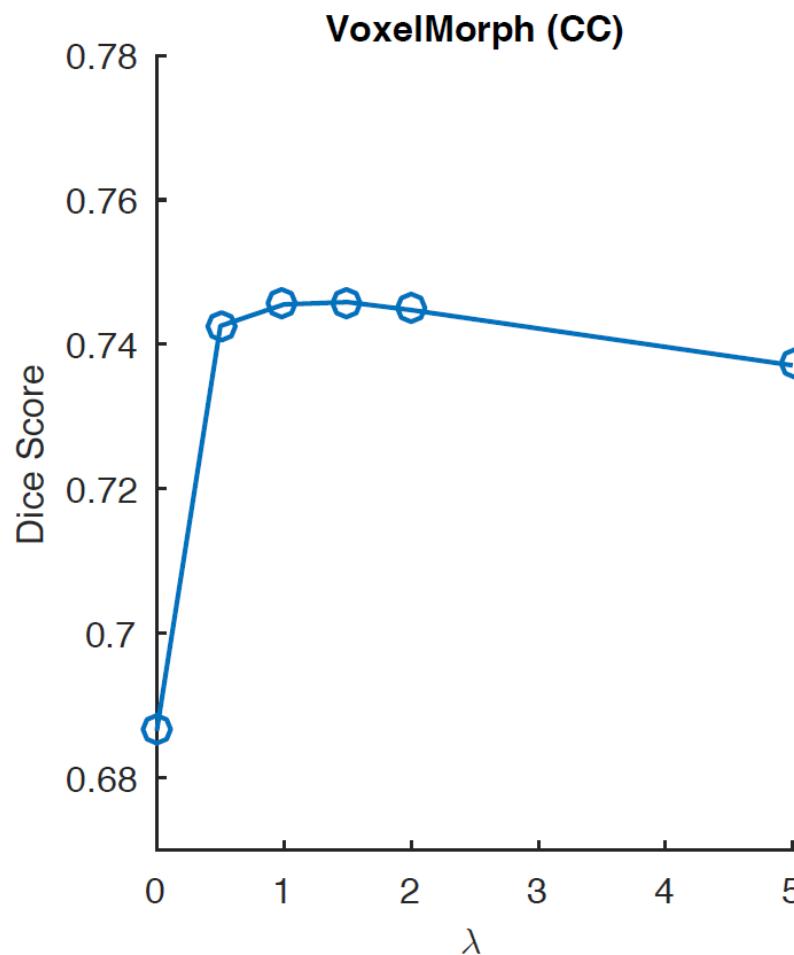
VoxelMorph - NMI

# HyperMorph: Amortized parameter learning

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

# Regularization Analysis (hyperparameters)

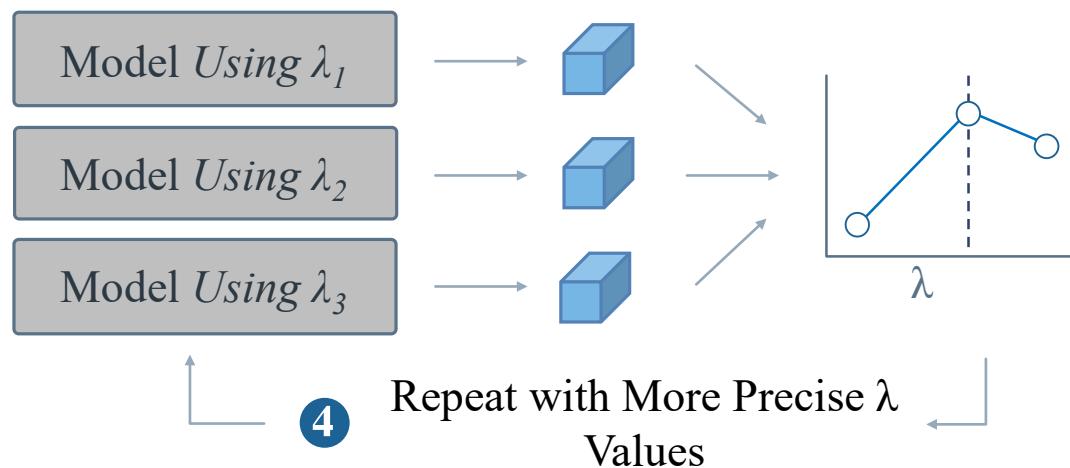


$$\mathcal{L} = \underbrace{\|m \circ \phi - f\|}_{\text{images match}} + \lambda \underbrace{\text{Reg}(\phi)}_{\text{smooth field}}$$

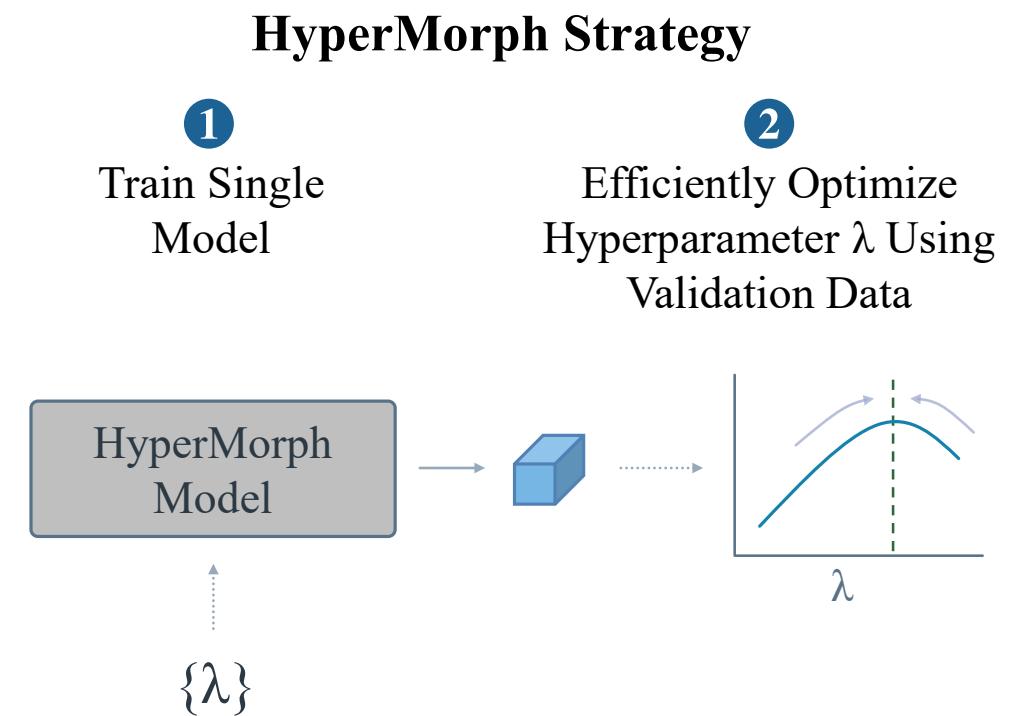
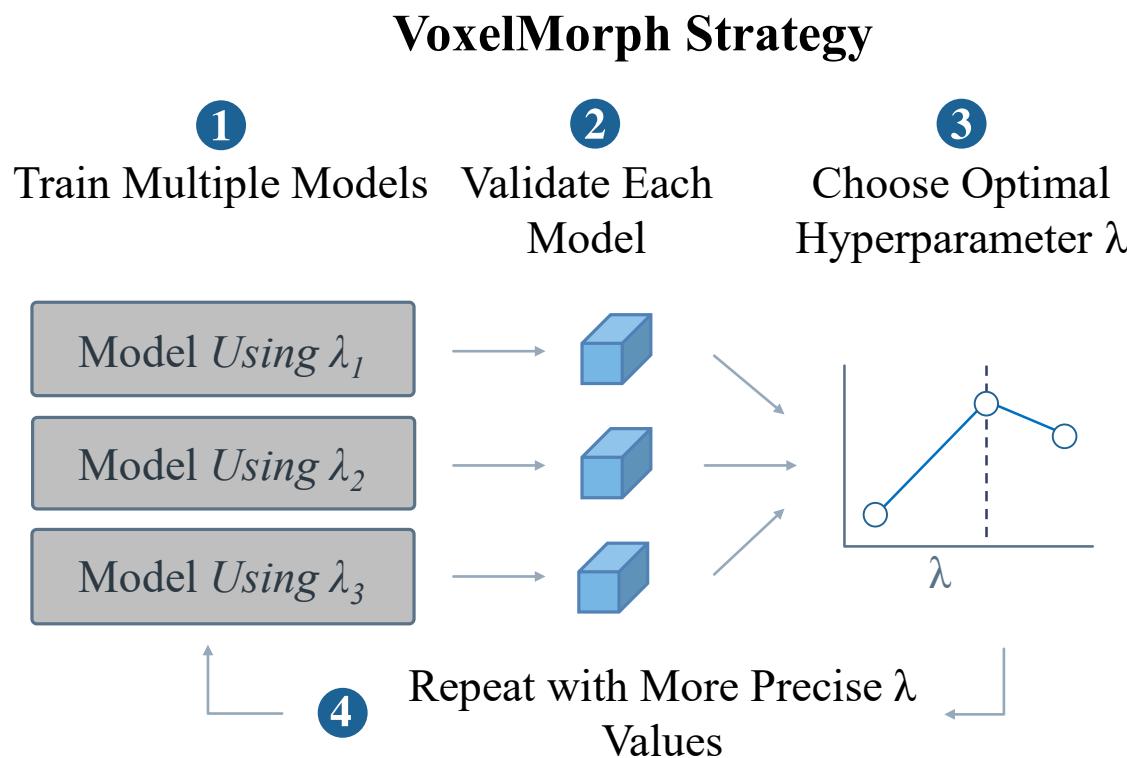
# HyperMorph

## VoxelMorph Strategy

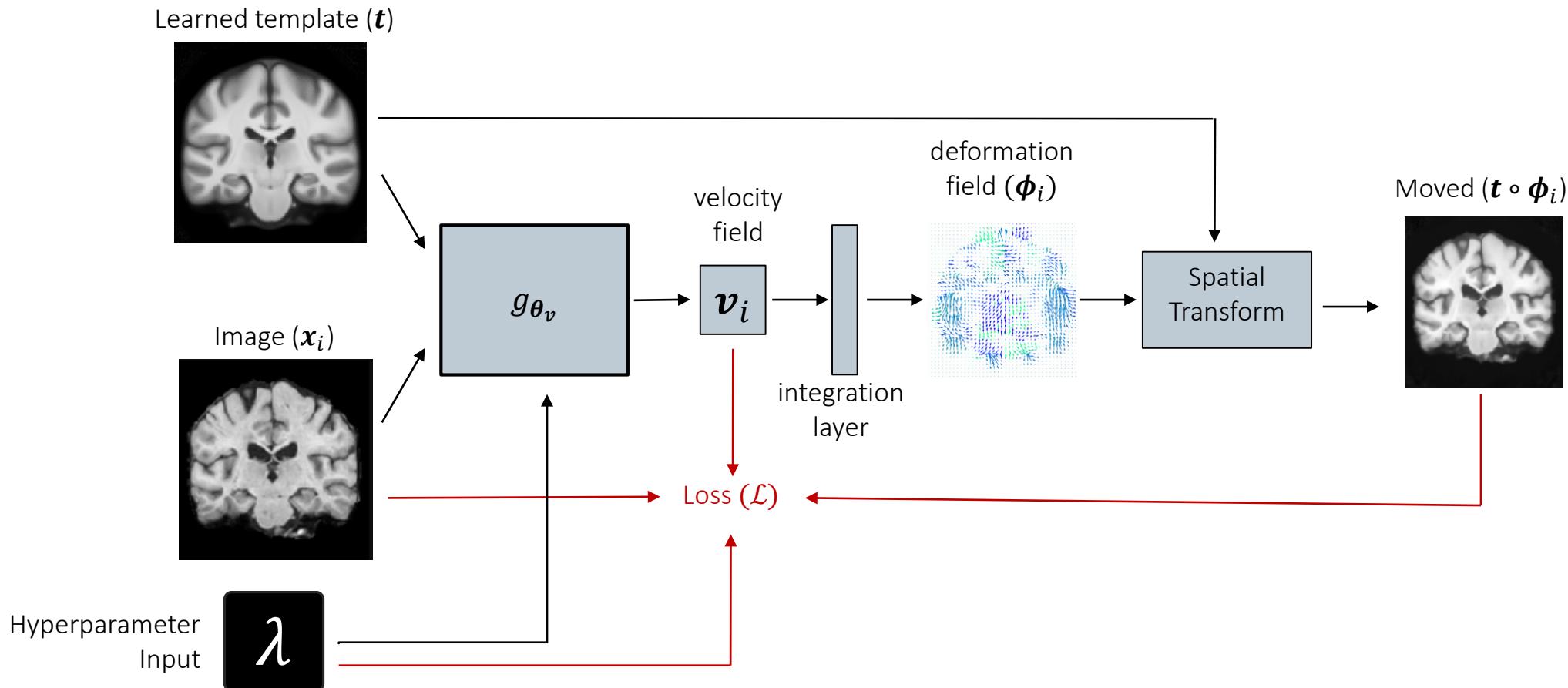
- 1 Train Multiple Models
- 2 Validate Each Model
- 3 Choose Optimal Hyperparameter  $\lambda$



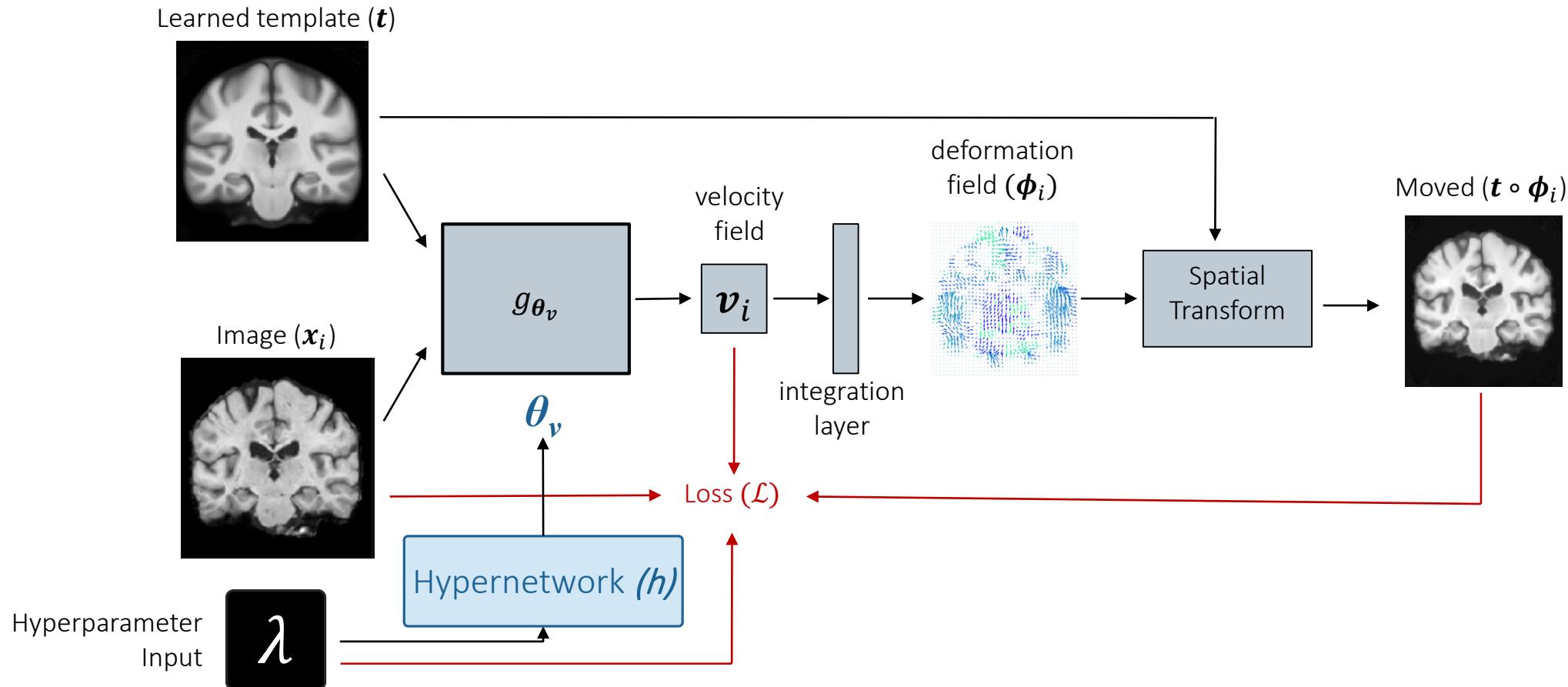
# HyperMorph



# HyperMorph

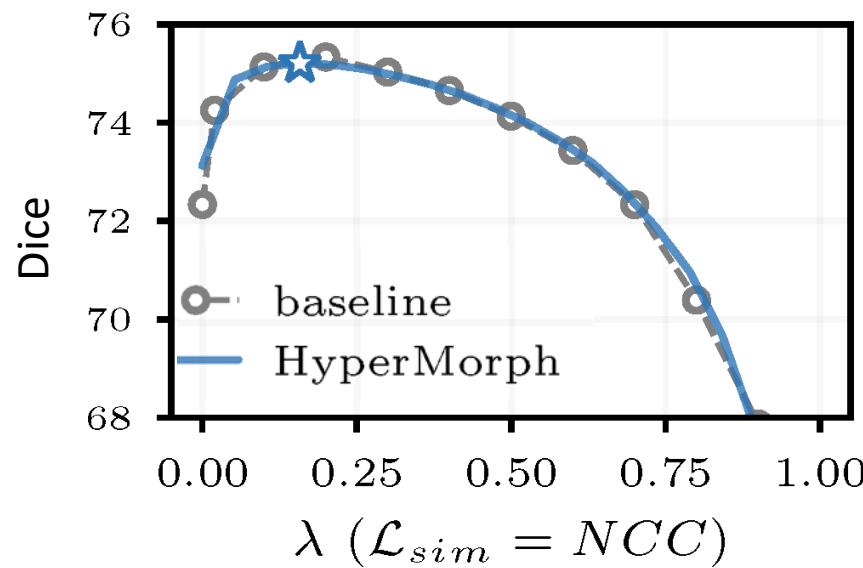


# HyperMorph



# Baseline Comparison

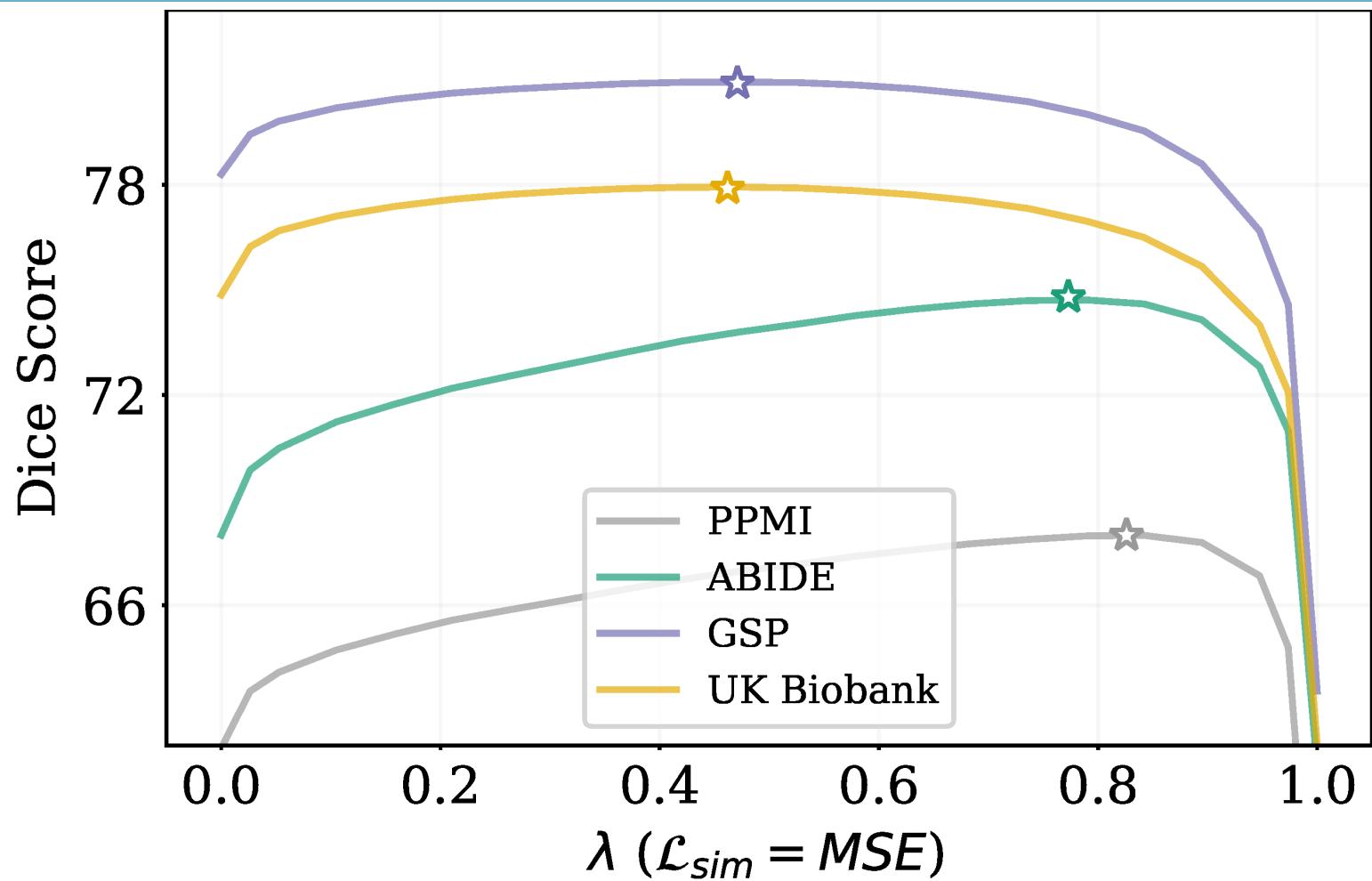
---



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

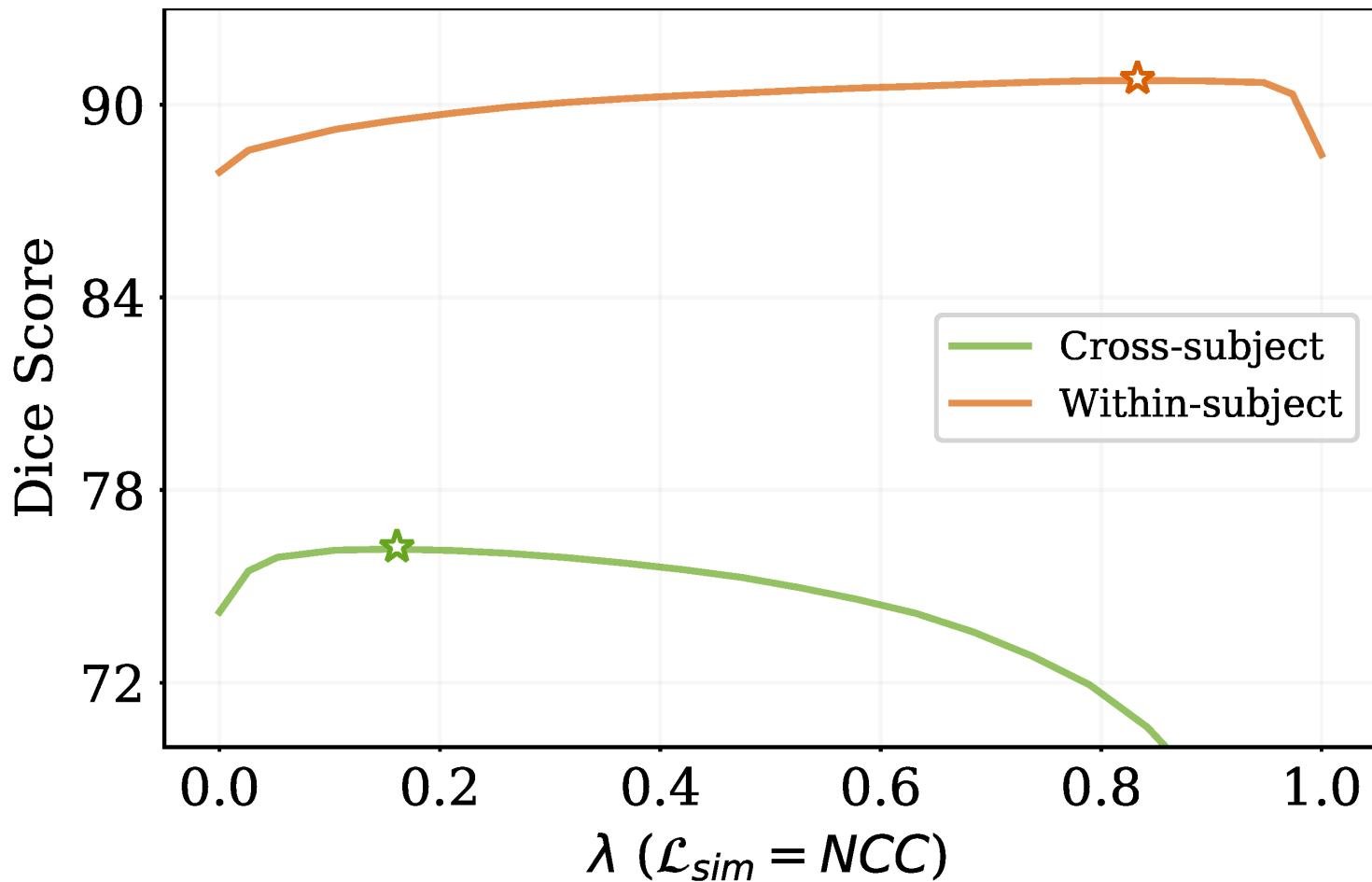


# Optimal Hyperparameters vary by dataset



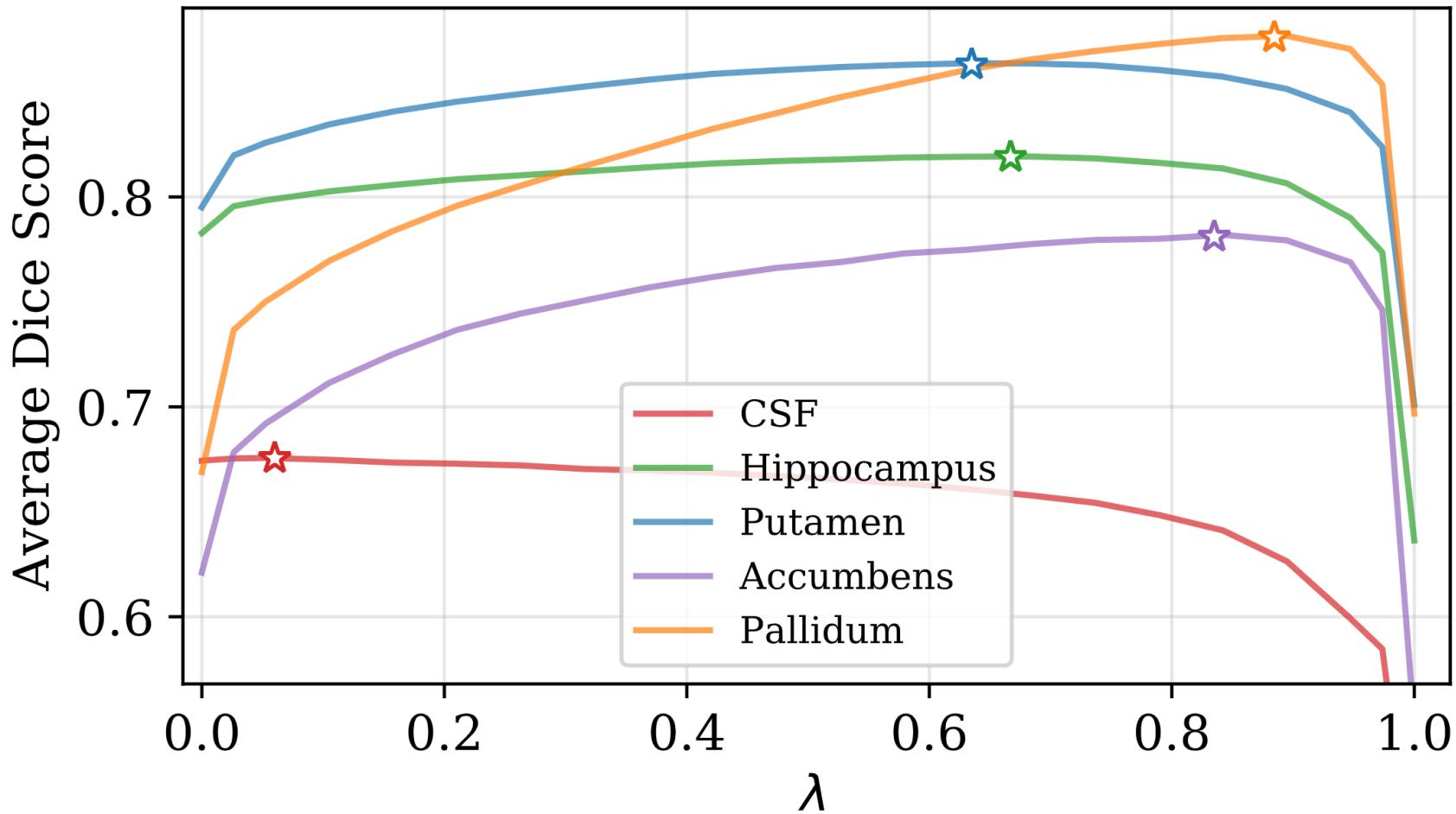
# Optimal Hyperparameters vary by task

---



... even by anatomical region!

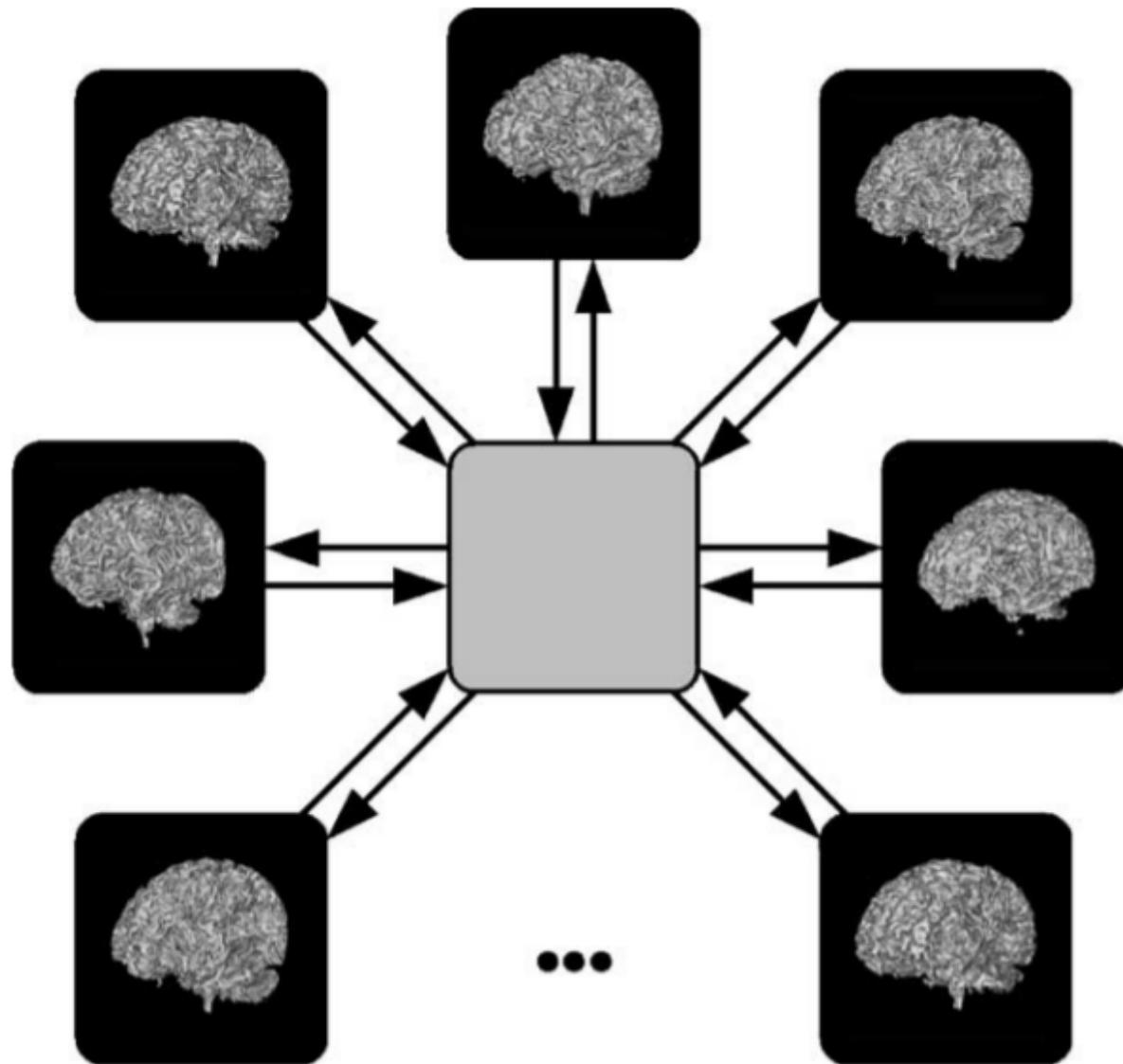
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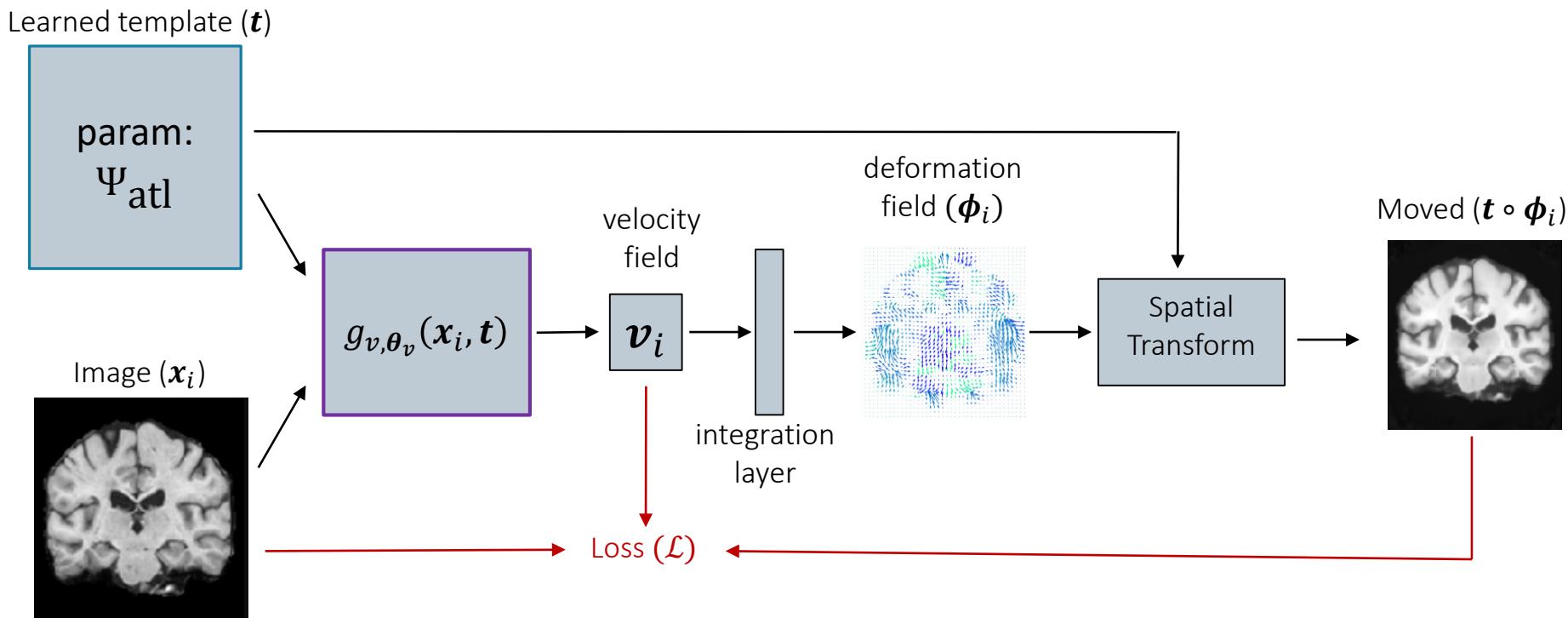
# Template construction

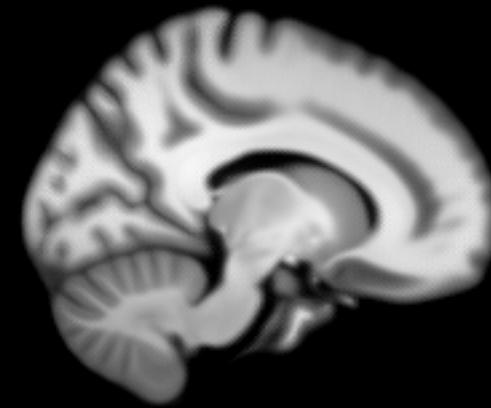
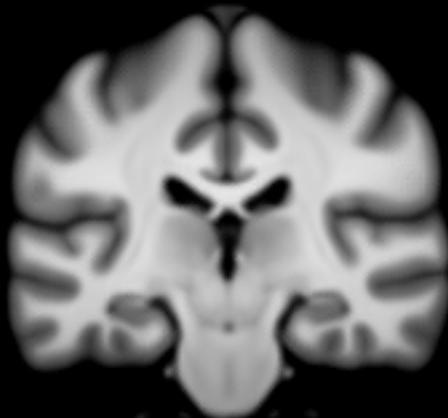
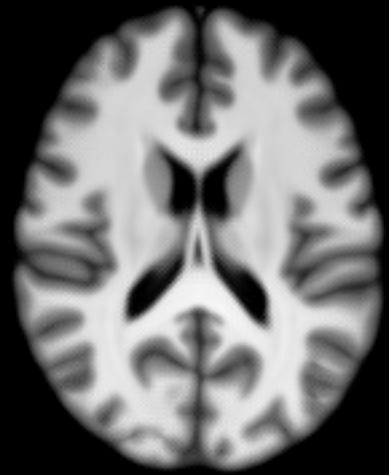
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Dalca, Rakic, Guttag, Sabuncu, NeurIPS 2019

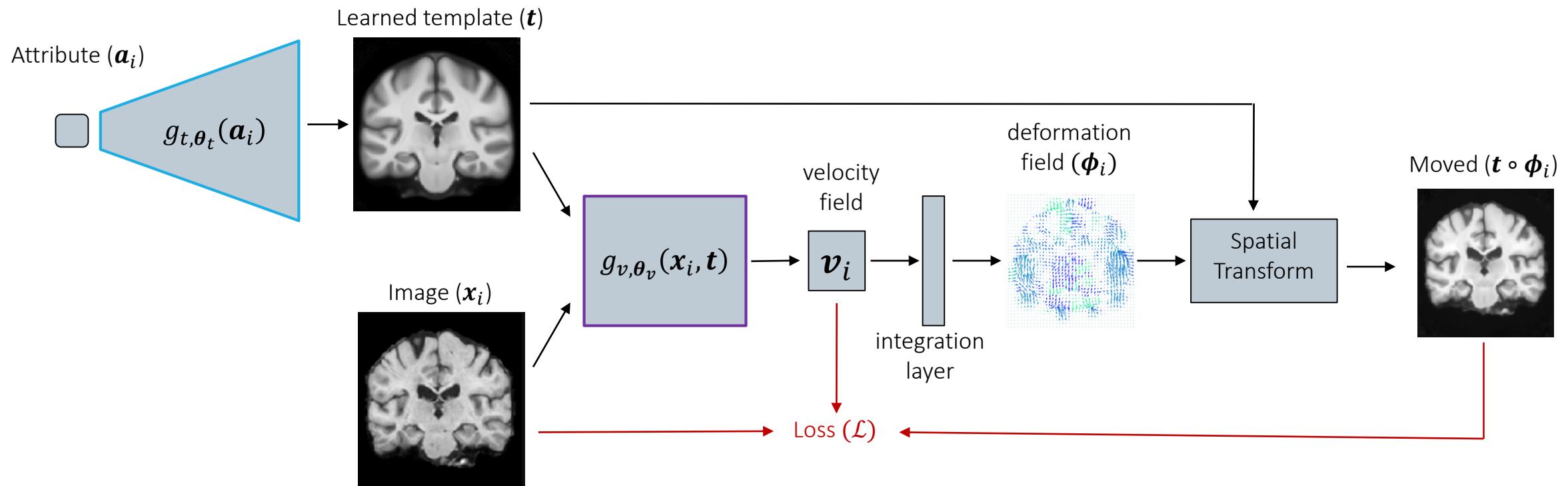


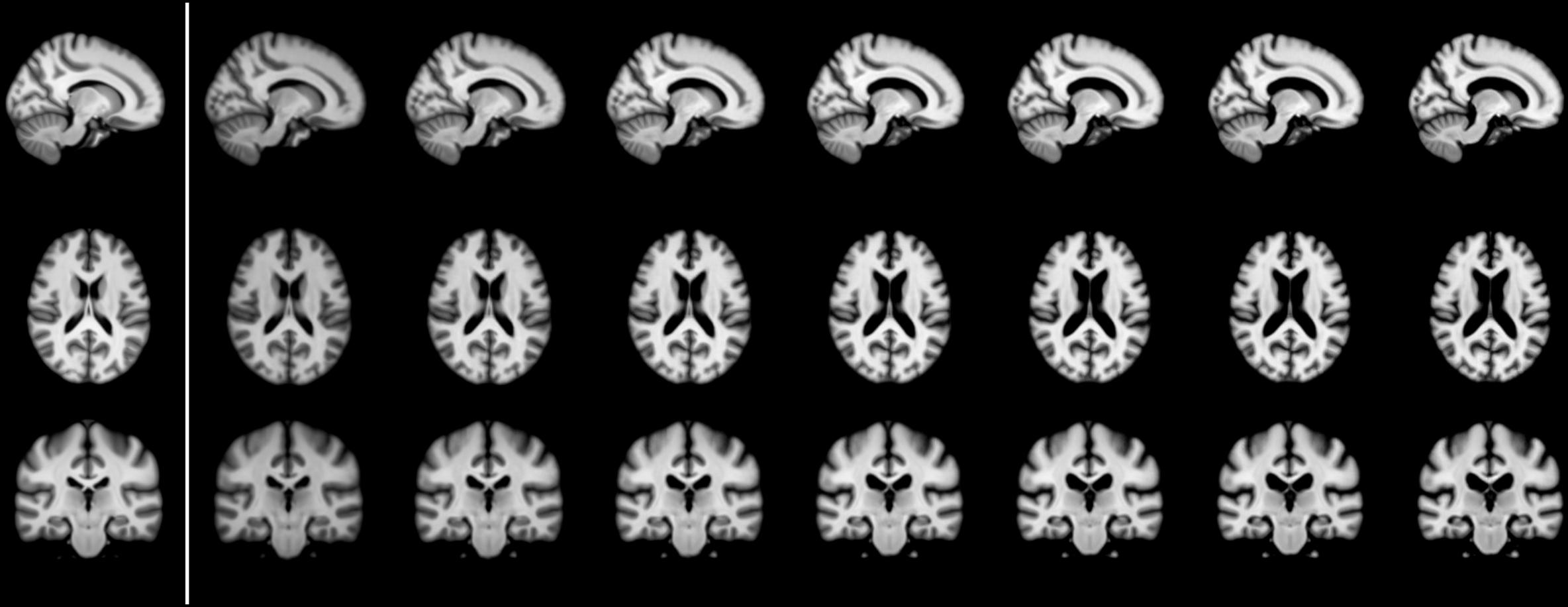
# Template Construction





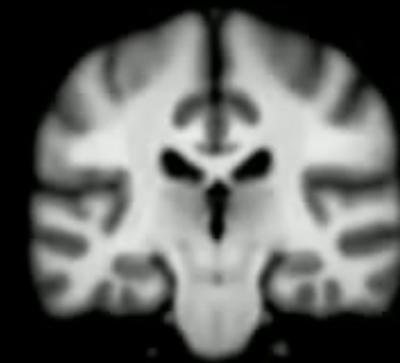
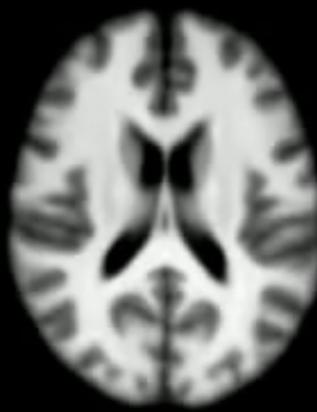
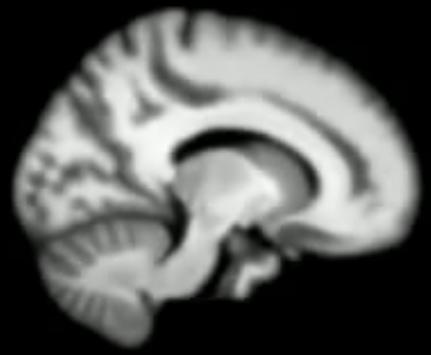
# Conditional template construction

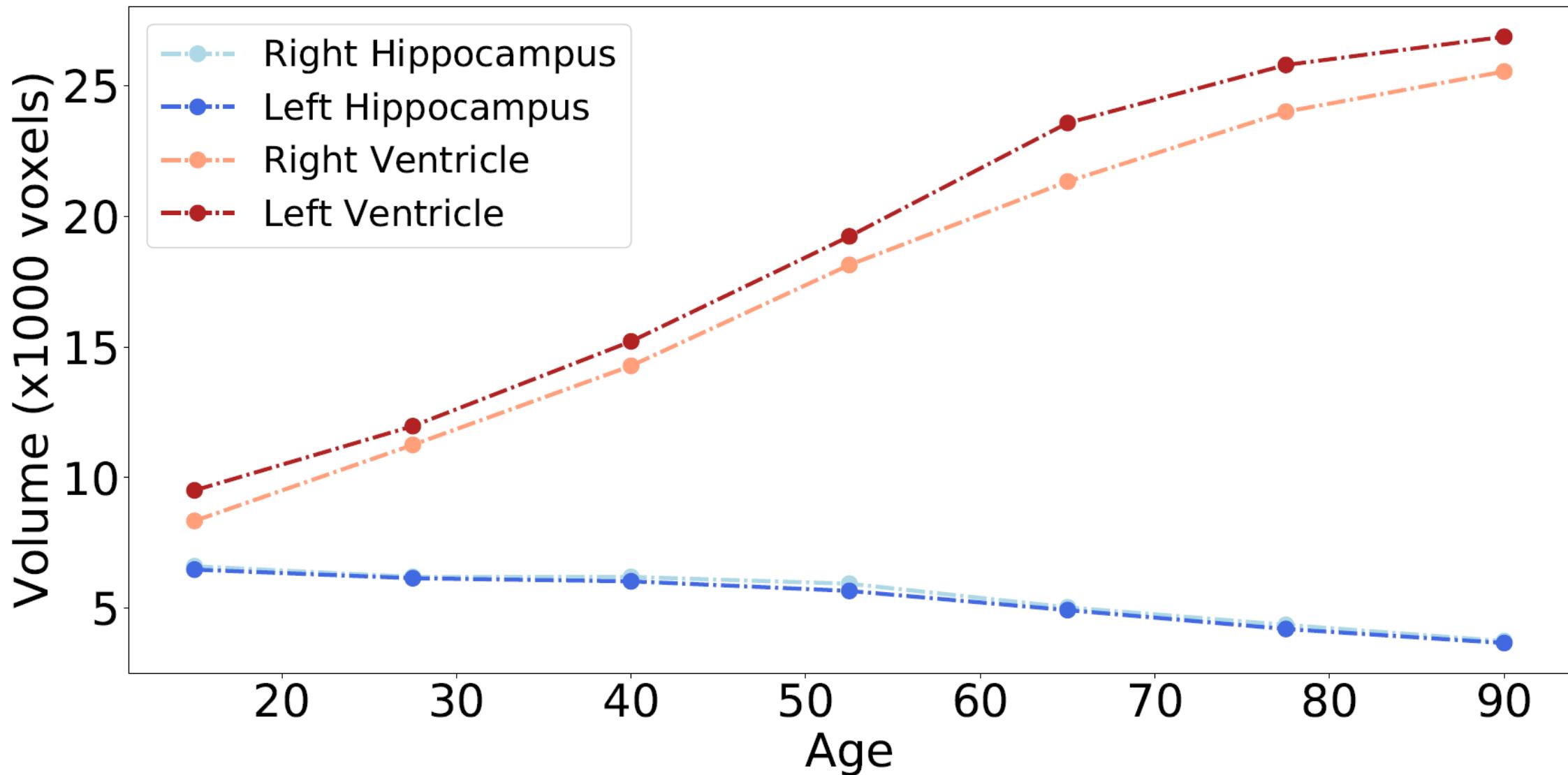


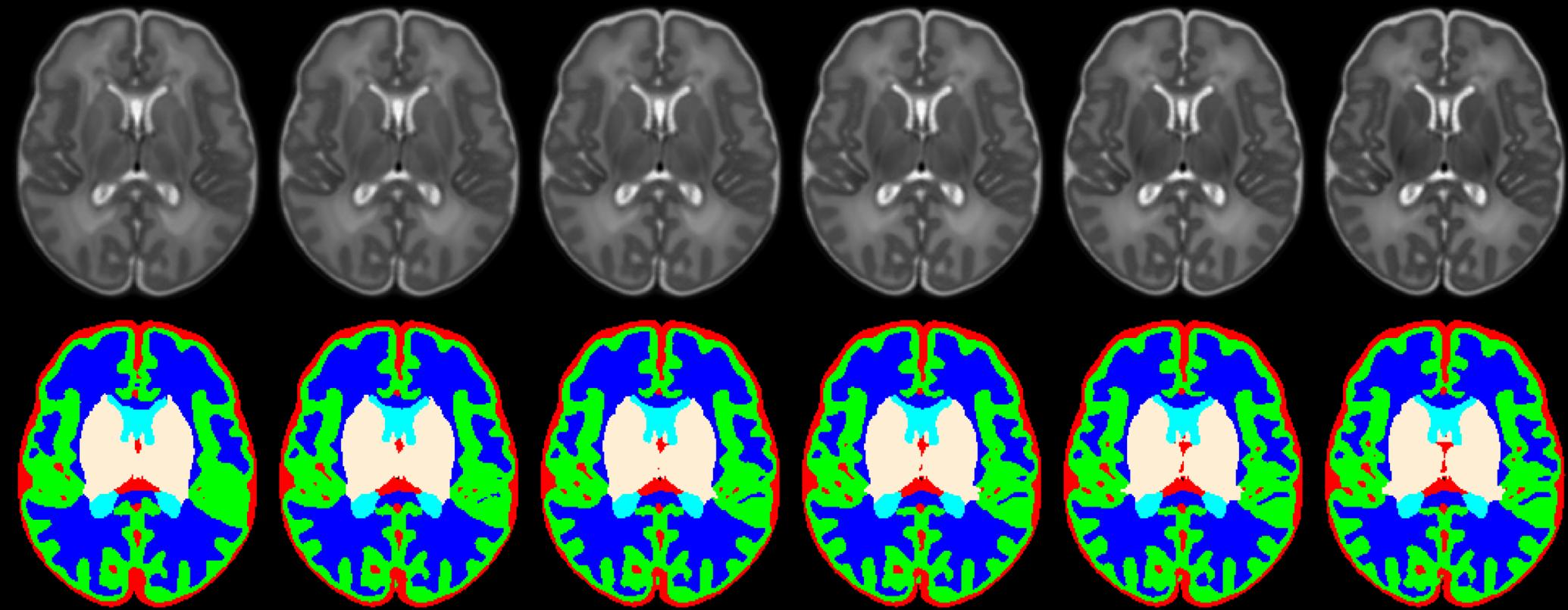


15 ← → 90

age: 15.0







29 weeks

32

35

38

41

44

# Acknowledgements

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Guha Balakrishnan (MIT CSAIL DDIG)

Benjamin Billot (UCL CMIC)

Bruce Fischl (HMS/MGH LCN)

John Guttag (MIT CSAIL DDIG)

Malte Hoffmann (MGH LCN)

Andrew Hoopes (MGH LCN)

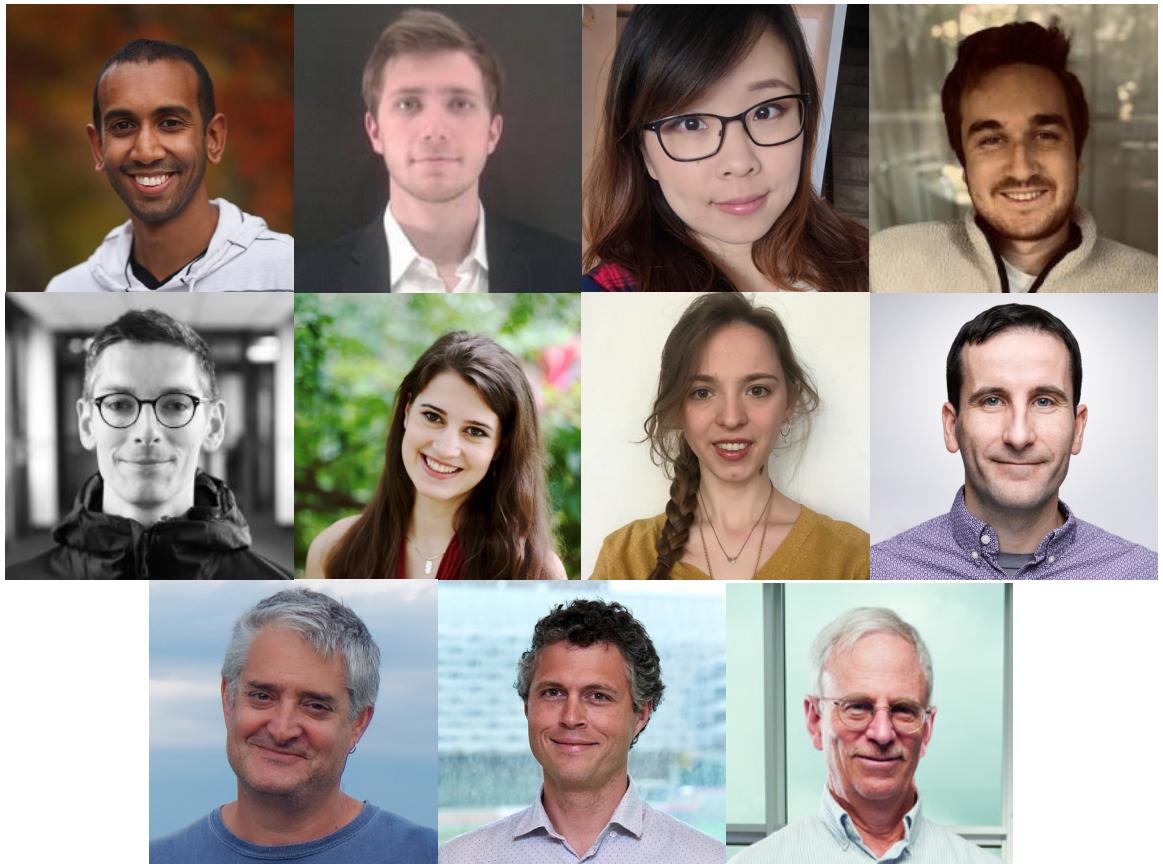
Eugenio Iglesias (MIT CSAIL, MGH HMS, UCL CMIC)

Kathleen Lewis (MIT CSAIL DDIG)

Marianne Rakic (MIT CSAIL DDIG, ETH)

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

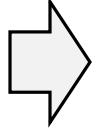


- Very **fast** for new image pair
- State-of-the-art **accuracy**
- **Diffeomorphic** deformations
- **Uncertainty** estimation

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

# voxelmorph

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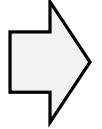
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- 
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- Limited training data → use VM as initialization
- Segmentation at training → better test Dice performance
- No atlas → construct atlas automatically
- Synthesis → invariant representations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

# voxelmorph

---

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