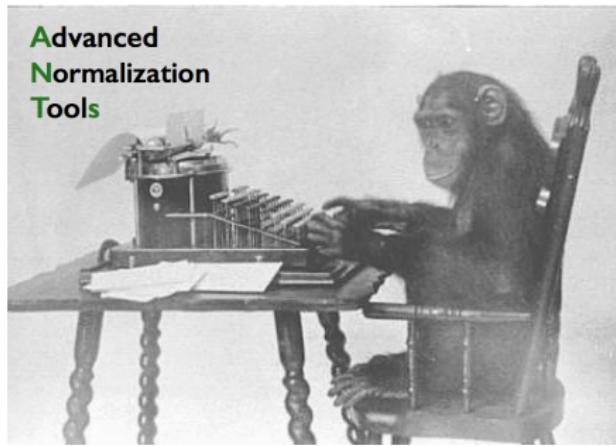


# “Dr. Tustison (UVA) presentation”

Nick Tustison

University of Virginia

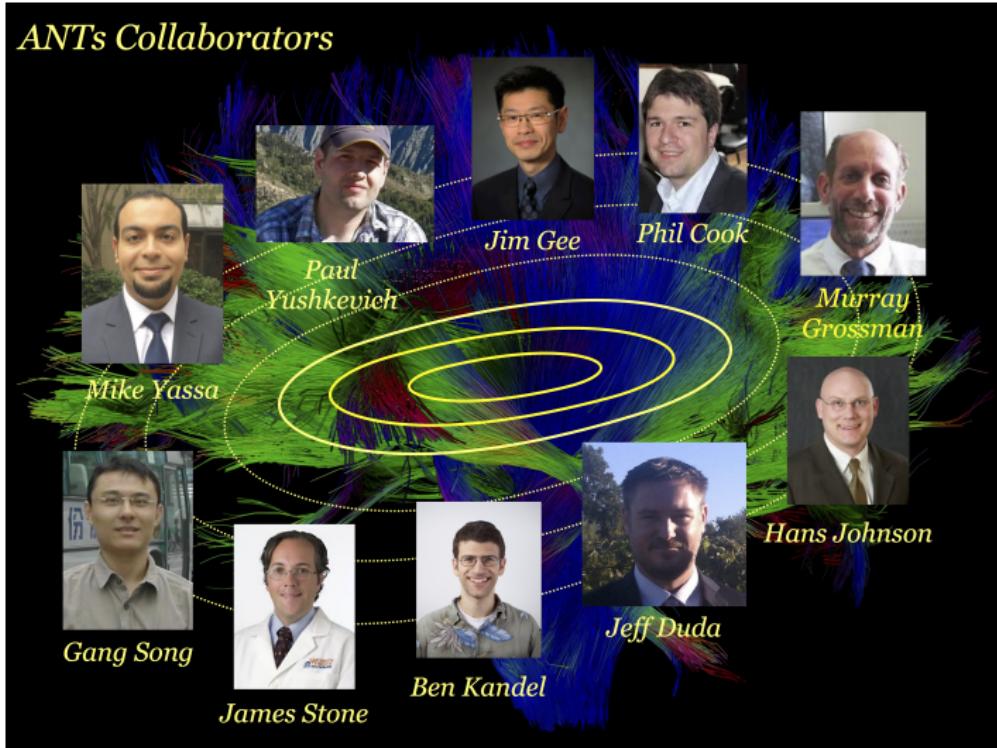


# Developers and collaborators

# Founders: Brian and Nick



## ANTs Collaborators



+ neurodebian, slicer, brainsfit, nipype, itk and more . . .

Why would you care?

# Software for medical image analysis

- FSL
- SPM
- FreeSurfer
- MIPAV
- AFNI
- Slicer, Elastix, SimpleITK, ANTs  $\longleftrightarrow$  Insight Toolkit
- Many more at [idoimaging.com](http://idoimaging.com)

# International competitions

- Klein 2009: MRI brain registration
- EMPIRE 2010: CT lung registration
- Multi-Atlas Label Challenge 2012: MRI brain registration and segmentation
- SATA Challenge 2013: MRI cardiac and canine hind leg registration
- BRATS 2013: Multi-modal MRI brain segmentation
- STACOM 2014 MoCo Challenge: MRI cardiac motion estimation

## Major ANTs utilities

# Donoho?

*“Papers are just advertisements for the science.”*

# Beyond original SyN

frontiers in  
**NEUROINFORMATICS**

ORIGINAL RESEARCH ARTICLE

published: 28 April 2014  
doi: 10.3389/fninf.2014.00044



## The Insight ToolKit image registration framework

**Brian B. Avants<sup>1\*</sup>, Nicholas J. Tustison<sup>2</sup>, Michael Stauffer<sup>1</sup>, Gang Song<sup>1</sup>, Baohua Wu<sup>1</sup> and James C. Gee<sup>1</sup>**

<sup>1</sup> Penn Image Computing and Science Laboratory, Department of Radiology, University of Pennsylvania, Philadelphia, PA, USA

<sup>2</sup> Department of Radiology and Medical Imaging, University of Virginia, Charlottesville, VA, USA

frontiers in  
**NEUROINFORMATICS**

METHODS ARTICLE  
published: 23 December 2013  
doi: 10.3389/fninf.2013.00039



## Explicit B-spline regularization in diffeomorphic image registration

**Nicholas J. Tustison<sup>1\*</sup> and Brian B. Avants<sup>2</sup>**

# antsRegistration

```
$ antsRegistration --help
```

## COMMAND:

### antsRegistration

This program is a user-level registration application. It uses **ITKv4-only** classes. The user can specify any number of command-line options. The program consists of a transform; an image metric; and iterative optimization parameters. The transform consists of a series of rigid, affine, and smooth deformations. The metric measures the similarity between two images. The optimizer iterates between the transform and the metric until convergence. The output is a registered image and a transformation matrix. Note that dimensionality is not specified as an option; it is determined by the input images. The output is a registered image and a transformation matrix. Note that dimensionality is not specified as an option; it is determined by the input images.

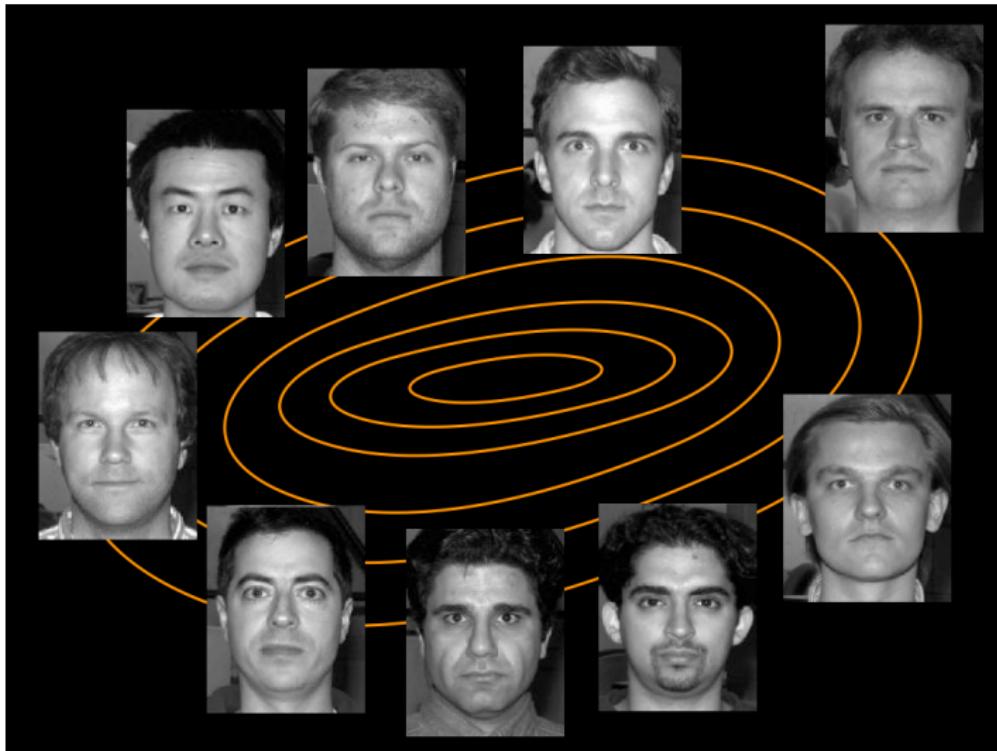
## OPTIONS:

### --version

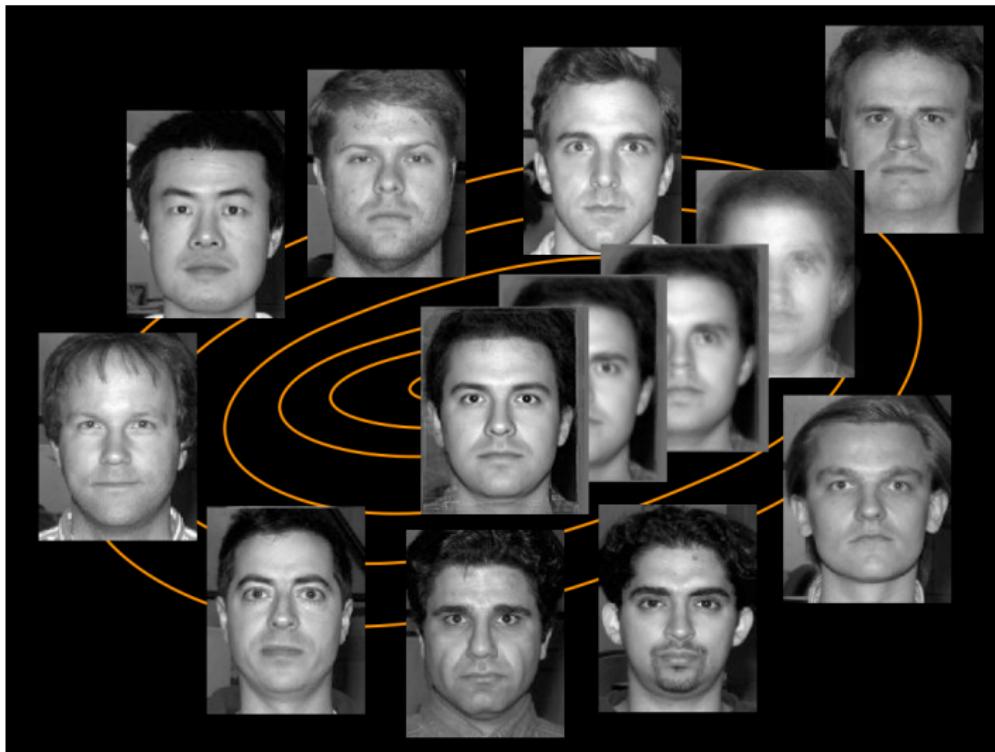
Get Version Information.

-d --dimensionality 2/3

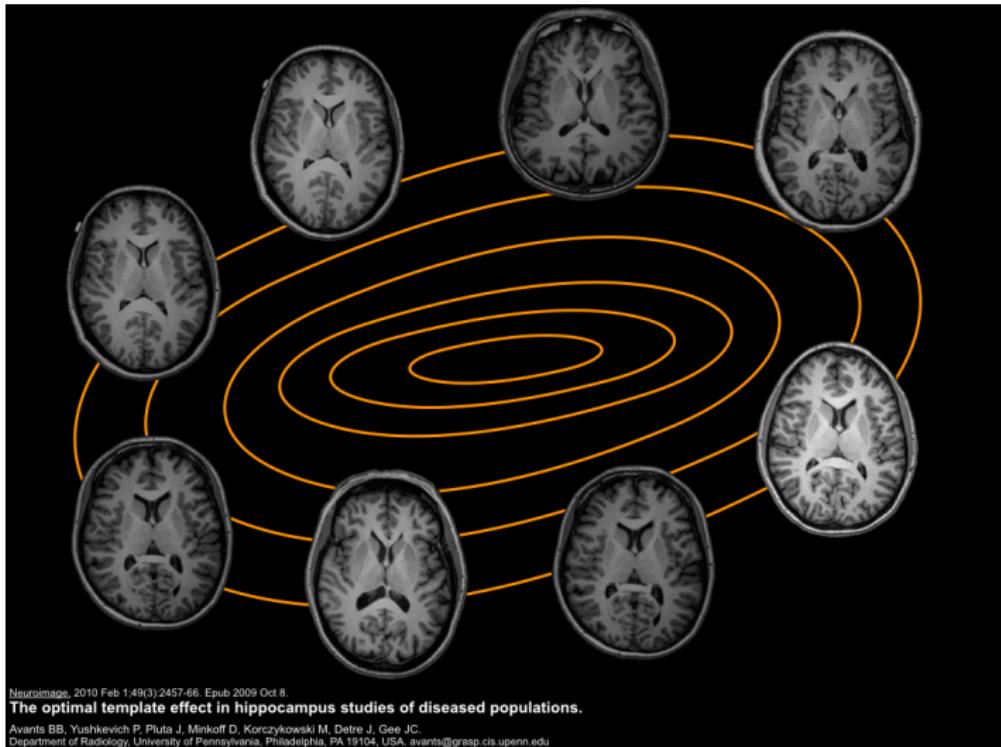
# Template building: creating the average Joe



# “Attractiveness” → mental processing?



# What about brains?



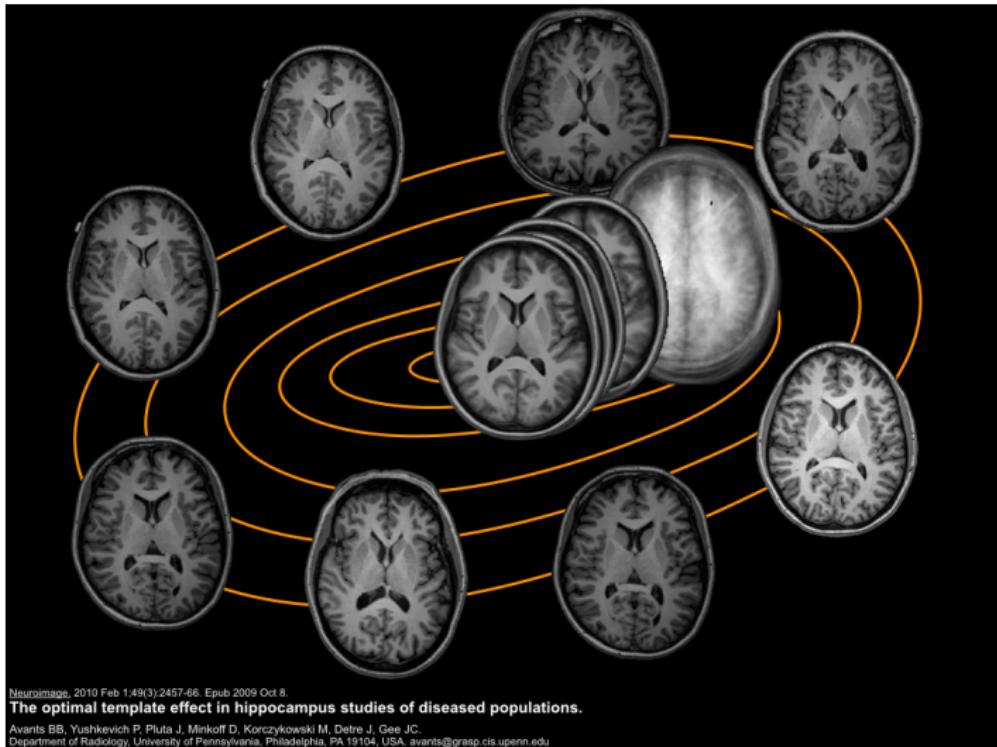
Neuroimage, 2010 Feb 149(3):2457-66. Epub 2009 Oct 8.

## The optimal template effect in hippocampus studies of diseased populations.

Avants BB, Yushkevich P, Pluta J, Minkoff D, Korczykowski M, Detre J, Gee JC.

Department of Radiology, University of Pennsylvania, Philadelphia, PA 19104, USA, avants@grasp.cis.upenn.edu

# Templates facilitate computation



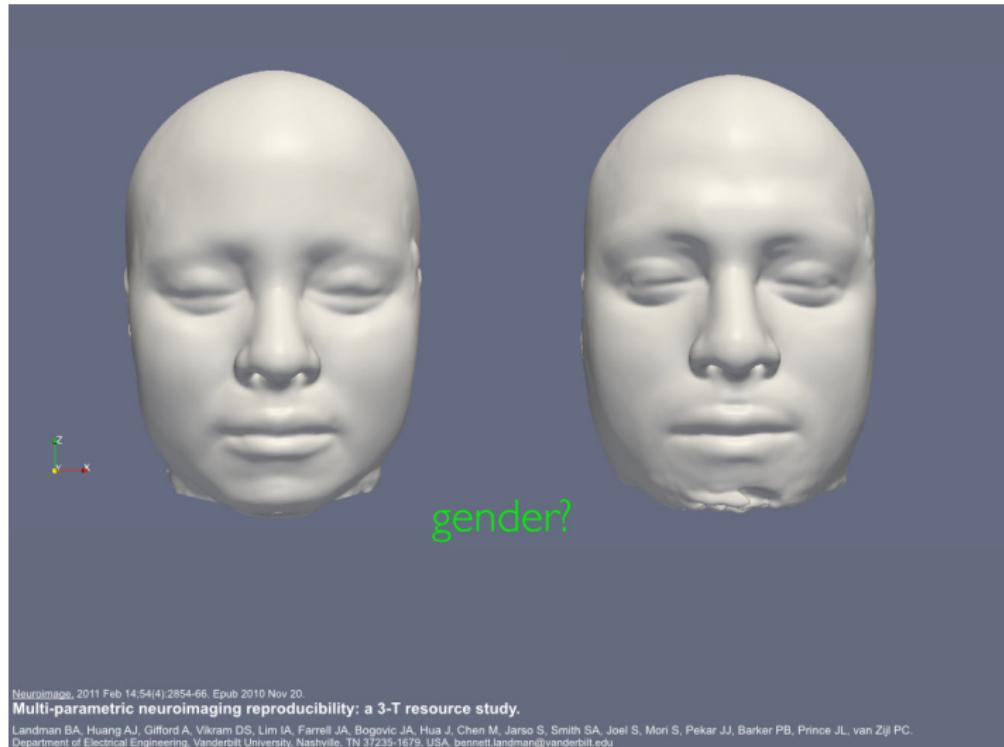
Neuroimage, 2010 Feb 149(3):2457-66. Epub 2009 Oct 8.

## The optimal template effect in hippocampus studies of diseased populations.

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Department of Radiology, University of Pennsylvania, Philadelphia, PA 19104, USA, avants@grasp.cis.upenn.edu

# Gender discernibility?



Neuroimage, 2011 Feb 14;54(4):2854-66. Epub 2010 Nov 20.

## Multi-parametric neuroimaging reproducibility: a 3-T resource study.

Landman BA, Huang AJ, Gifford A, Vikram DS, Lim IA, Farrell JA, Bogovic JA, Hua J, Chen M, Jarso S, Smith SA, Joel S, Mori S, Pekar JJ, Barker PB, Prince JL, van Zijl PC.  
Department of Electrical Engineering, Vanderbilt University, Nashville, TN 37235-1679, USA. bennett.landman@vanderbilt.edu

## antsMultivariateTemplateConstruction.sh

```
$ antsMultivariateTemplateConstruction.sh
```

### Usage:

```
antsMultivariateTemplateConstruction.sh -d ImageDimension -o [
```

Compulsory arguments (minimal command line requires SGE cluster)

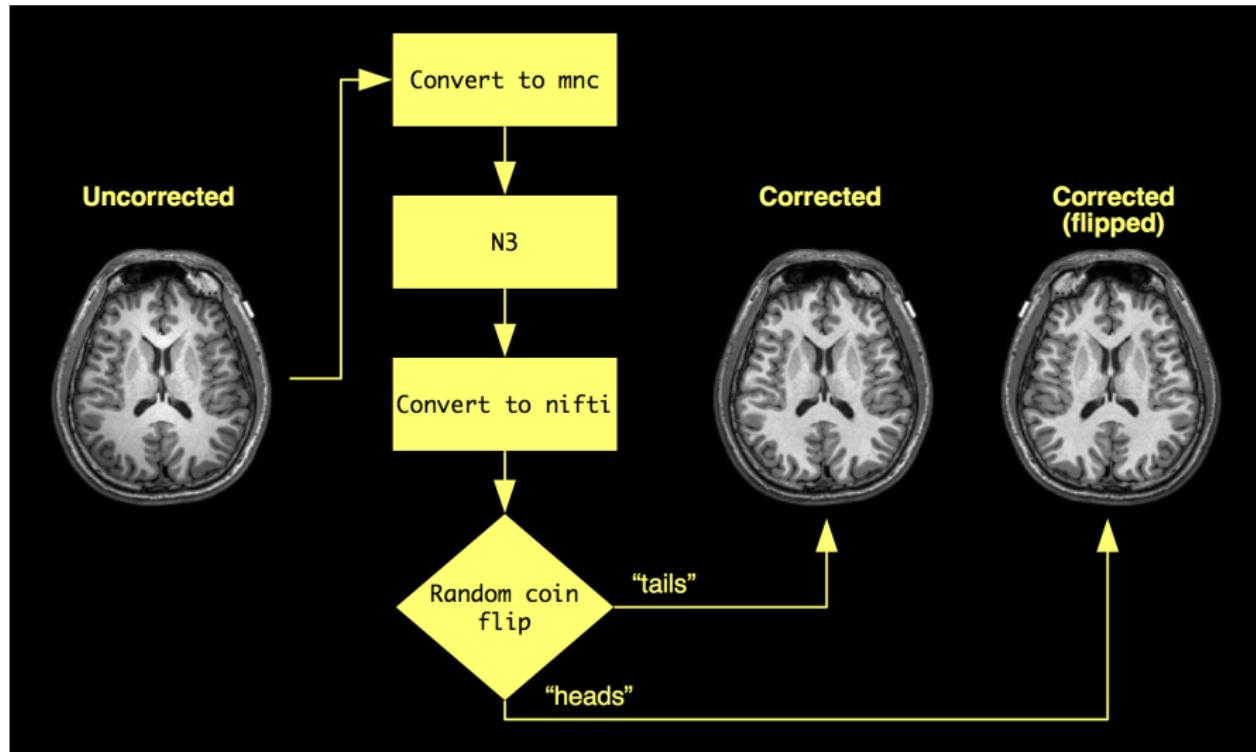
-d: ImageDimension: 2 or 3 (for 2 or 3 dimensional registration)

ImageDimension: 4 (for template generation of time-series data)

-o: OUTPREFIX; A prefix that is prepended to all output files

<images> List of images in the current directory, eg \*\_t1.nii  
of the command. Optionally, one can specify a .csv file where each line is the location of the input image. One can also

# N3 adoption issues



# N4BiasFieldCorrection

```
$ N4BiasFieldCorrection --help
```

## COMMAND:

### N4BiasFieldCorrection

N4 is a variant of the popular N3 (nonparameteric nonrigid retrospective bias correction algorithm. Based on the corruption of the low frequency bias field can be modeled by a Gaussian, the basic algorithm iterates between deconvolving the intensity histogram of the intensities, and then spatially smoothing this estimate of the bias field itself. The modifications from and the original N3 algorithm are described in the following paper, N4ITK: Improved N3 Bias Correction, IEEE Transactions on Medical Imaging, 29(6):1310-1320, June 2010.

## OPTIONS:

Nick Tustison (University of Virginia)

# Atropos: flexible code base

“20+ years of development. *Show me the code!*”

## Initialization

- Gaussian
- Non-parametric
  - histogram Parzen windows
  - manifold Parzen windows

## Likelihood models

- Gaussian
- Non-parametric
  - histogram Parzen windows
  - manifold Parzen windows

# Atropos

## Prior models

- Markov random field
- Prior label images
- Prior probability images

## Miscellaneous

- Label geodesic/Euclidean propagation
- Outlier handling
- localized adaptive intensity handling

# Atropos

```
$ Atropos --help
```

## COMMAND:

### Atropos

A finite mixture modeling (FMM) segmentation approach specifying prior constraints. These prior constraints of a prior label image, prior probability images (or MRF prior to enforce spatial smoothing of the labels) FAST and SPM. Reference: Avants BB, Tustison NJ, Wu source multivariate framework for n-tissue segmentation public data. Neuroinformatics. 2011 Dec;9(4):381-400.

## OPTIONS:

**-d, --image-dimensionality 2/3/4**

This option forces the image to be treated as a specific dimensionality. If not specified, Atropos tries to infer the dimensionality from the input images.

# DenoiseImage — contribution from Jose Manjon

```
$ DenoiseImage --help
```

## COMMAND:

`DenoiseImage`

`Denoise` an image using a spatially adaptive filter  
Manjon, P. Coupe, Luis Marti-Bonmati, D. L. Collins,  
Non-Local Means Denoising of MR Images With Spatial  
Journal of Magnetic Resonance Imaging, 31:192-203, J

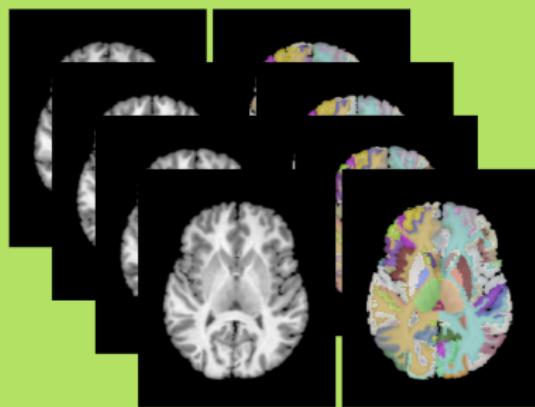
## OPTIONS:

`-d, --image-dimensionality 2/3/4`

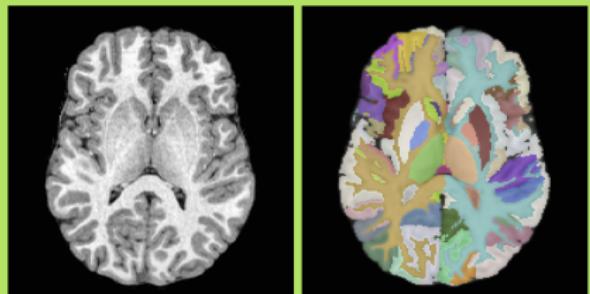
This option forces the image to be treated as a specific dimensionality. If not specified, the program tries to infer the dimensionality of the image.

# Multi-atlas segmentation

## Joint label fusion



Atlases  
(grayscale + segmentation)



Target image

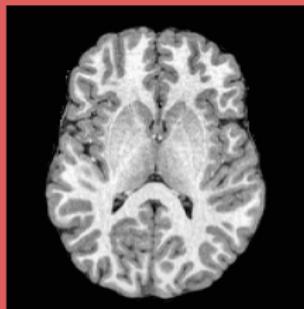
Target segmentation

# New work: joint intensity fusion

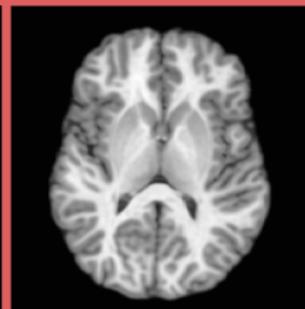
## Joint intensity fusion



Atlases  
(grayscale only)



Target image



Target fusion image

# Possible uses

- “Correct” images
  - motion correction
  - “remove” lesions
- Project atlas set intensity signature
- Use in “corrective learning”

# antsJointFusion — contribution from Hongzhi Wang (with some added features)

```
$ antsJointFusion --help
```

COMMAND:

`antsJointFusion`

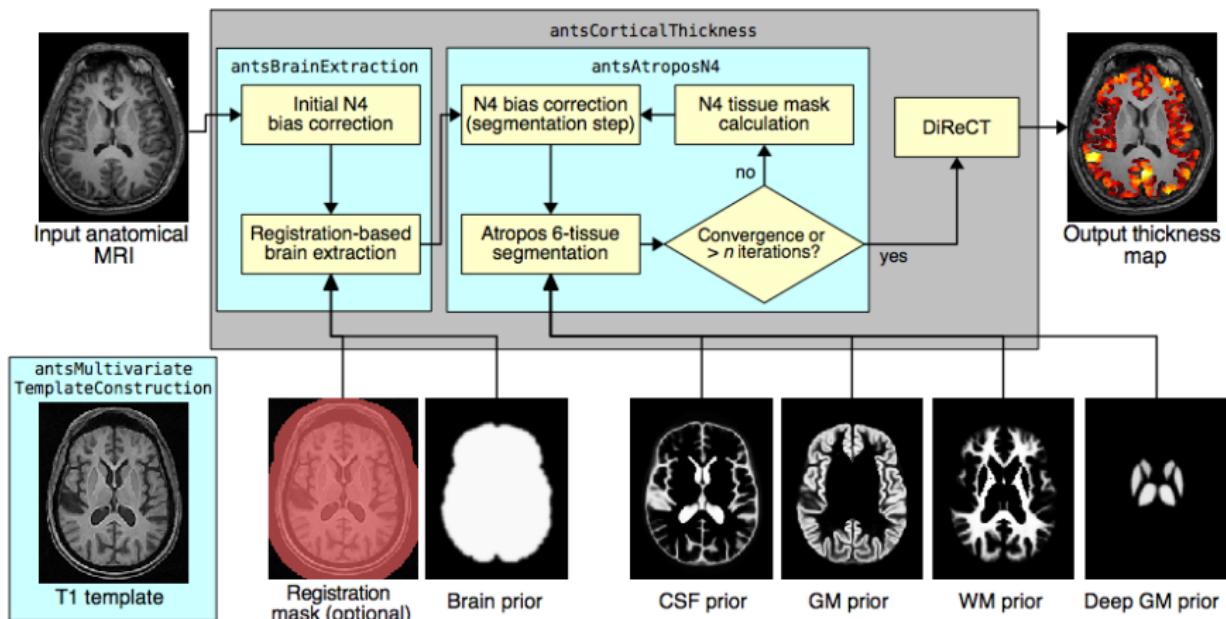
`antsJointFusion` is an image fusion algorithm developed by Paul Avants and Brian Yushkevich which won segmentation challenges at MICCAI 2012. The original label fusion framework was extended to account for multi-atlas label fusion by Hongzhi Wang and Paul Yushkevich. This implementation is based on Paul's original code and Brian's ANTsR implementation. References include 1) H. Wang, P. A. Yushkevich, Multi-atlas label fusion IEEE Trans. on Pattern Analysis and Machine Intelligence, 35(4):611-623, 2013. and 2) H. Wang and P. A. Yushkevich, "Joint label fusion and corrective learning--an application to multi-atlas segmentation," Neuroinformatics, 11(1), 2013.

## Putting it all together—the ANTs cortical thickness pipeline

# Cortical thickness studies

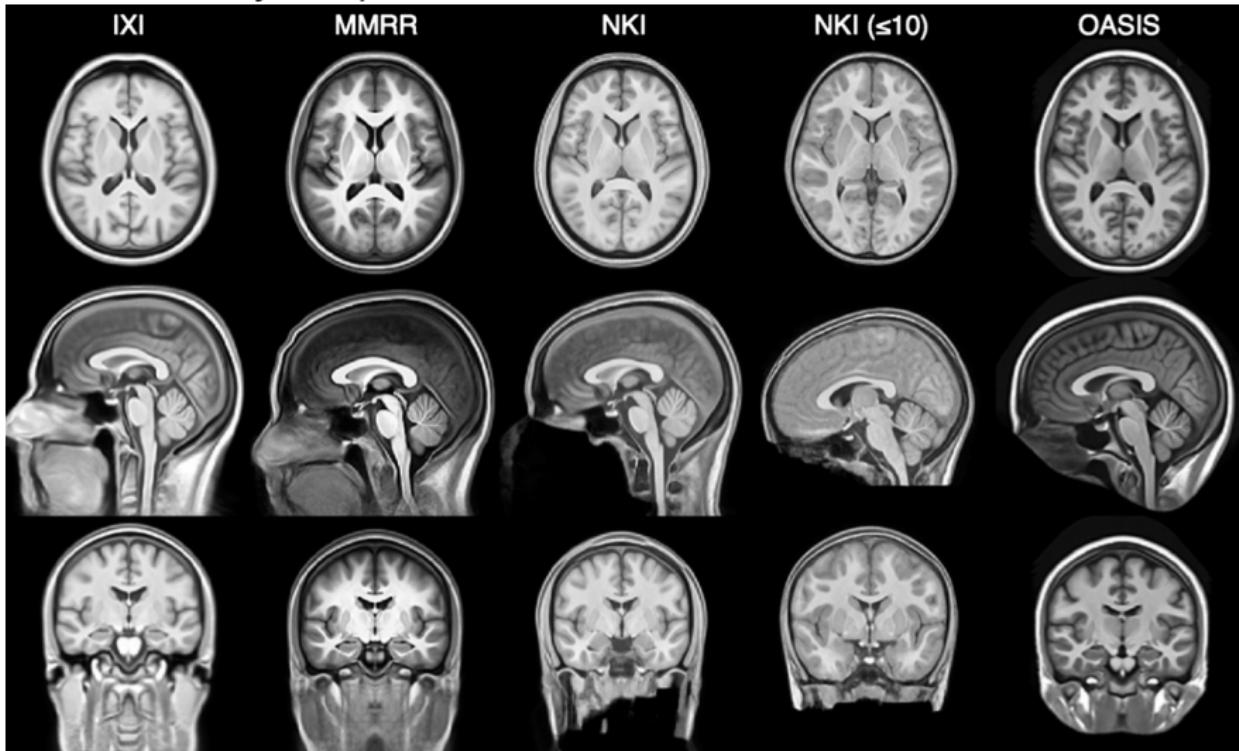
Column1	Column2
Tetris-playing ability	chronic pancreatitis
Huntington's disease	obsessive-compulsive disorder
schizophrenia	ADHD
bipolar disorder	obesity
Alzheimer's disease	heritable depression
frontotemporal dementia	elderly depression
Parkinson's disease	age
Williams syndrome	gender
multiple sclerosis	handedness
autism	intelligence
migraines	athletic ability
chronic smoking	meditative practices
alcoholism	musical ability
cocaine addiction	tendency toward criminality

# The ANTs structural brain mapping workflow

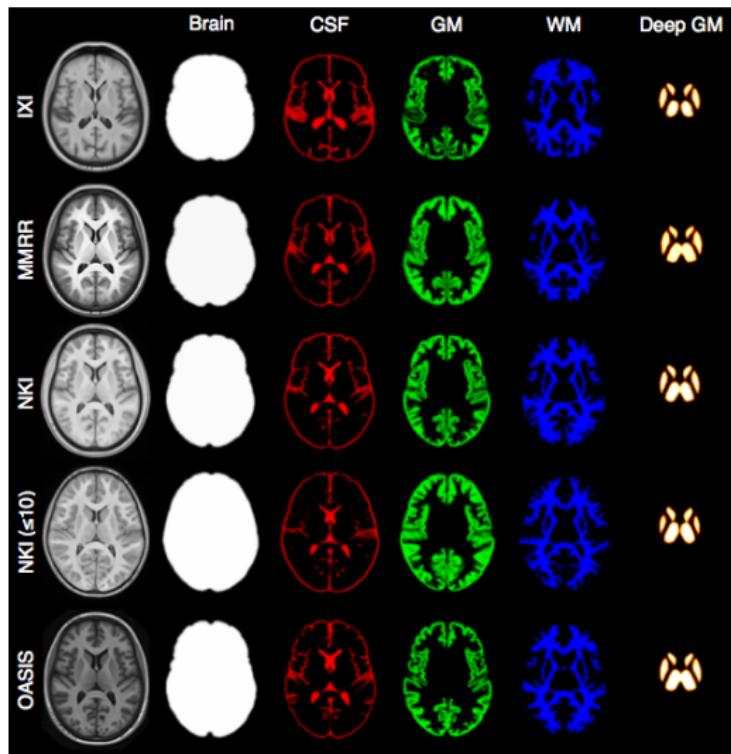


# Template building

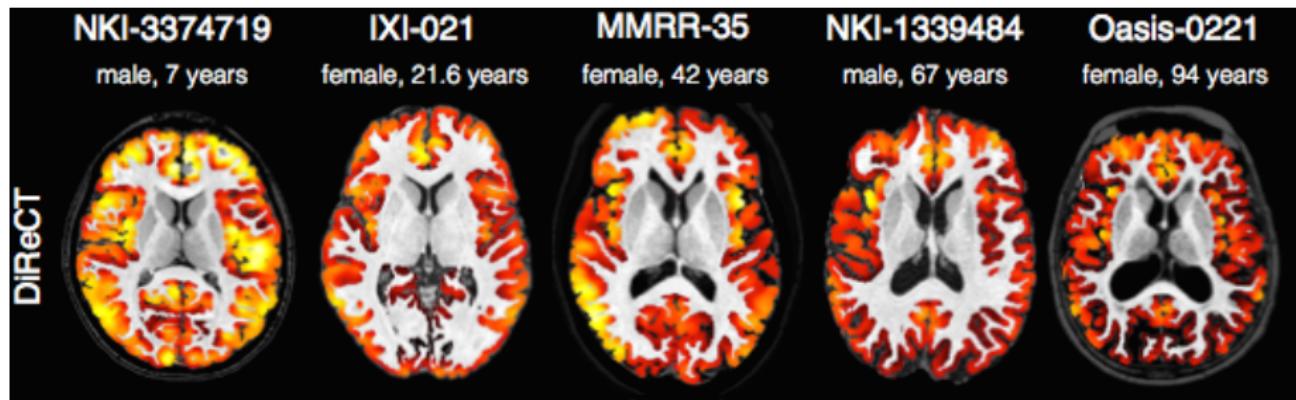
*Tailor data to your specific cohort*



# Template priors



# Cortical thickness maps



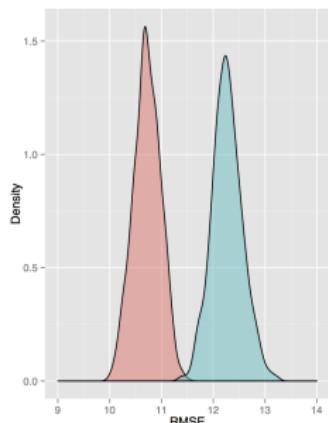
In contrast to FreeSurfer which warps coupled surface meshes to segment the gray matter, *ANTs* diffeomorphically registers the white matter to the combined gray/white matters while simultaneously estimating thickness.

*But without ground truth, how does one evaluate the pipeline?*

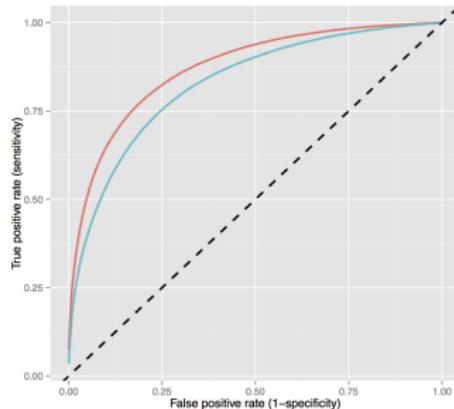
# Predict age and gender

$$AGE \sim VOLUME + GENDER + \sum_{i=1}^{62} T(DKT_i)$$

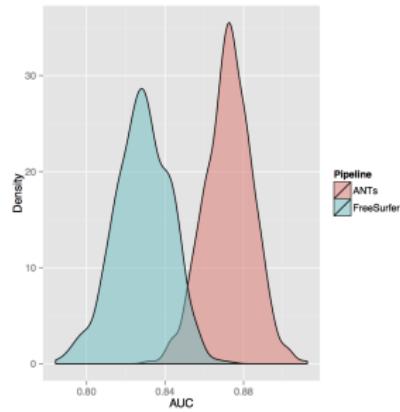
# Prediction from cortical thickness data



Age



Gender



# Age prediction per site

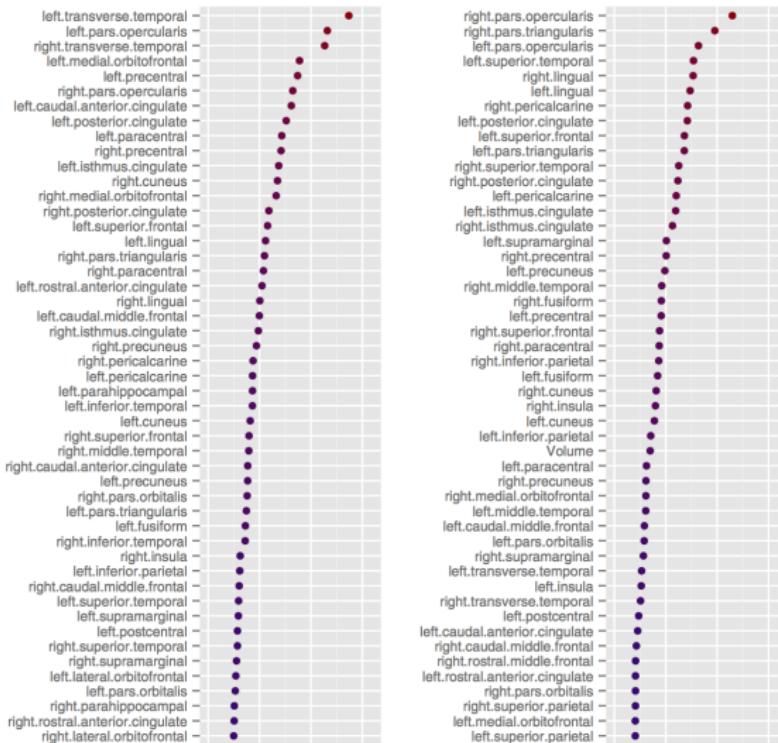
**Table 3**

Mean RMSE for age prediction in years.

	Linear model	Random forest
ANTs (combined)	10.7	10.2
FreeSurfer (combined)	12.3	11.9
ANTs (IXI)	9.3	8.6
FreeSurfer (IXI)	12.3	11.7
ANTs (NKI)	NA <sup>a</sup>	10.9
FreeSurfer (NKI)	NA <sup>a</sup>	13.3
ANTs (OASIS)	15.0	12.4
FreeSurfer (OASIS)	15.0	11.4

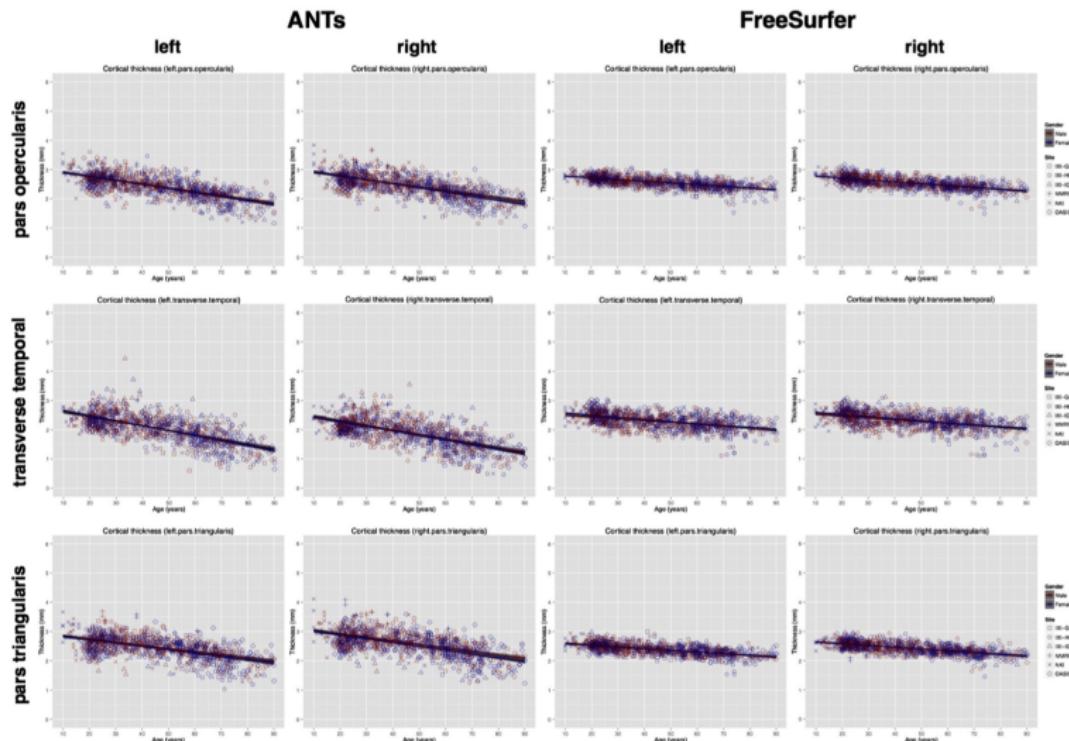
<sup>a</sup> Fitting error.

# Regional importance comparison



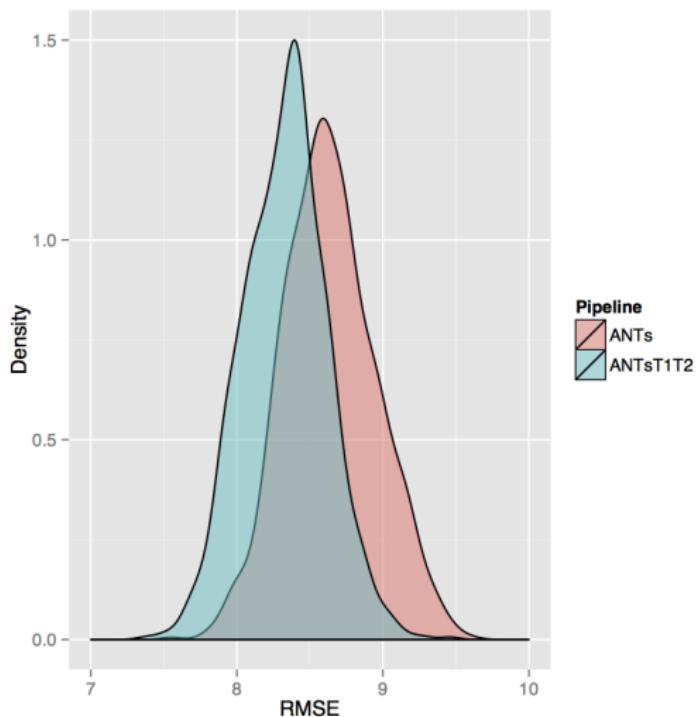
ANTs (left) vs. FreeSurfer (right)

# Regional measurements

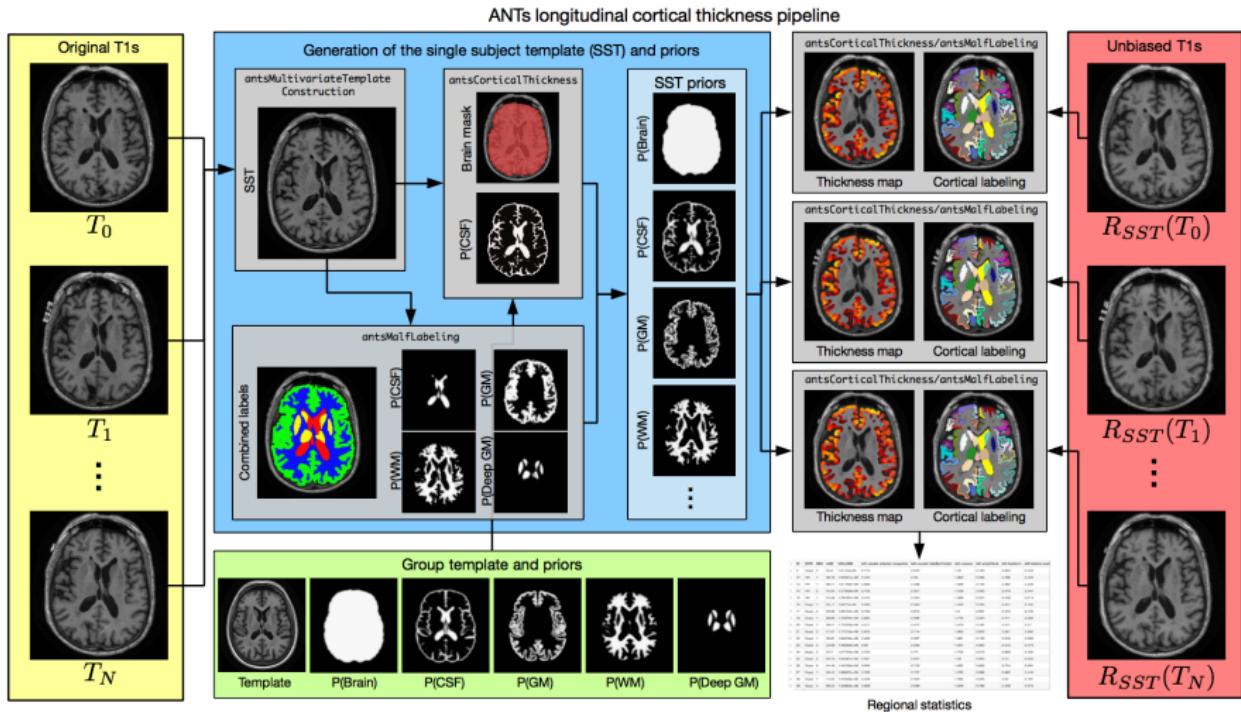


But, wait, there's more!

# ANTs tools are multivariate



# Longitudinal processing



# Current work and Advanced Normalization Tools in R (ANTsR)

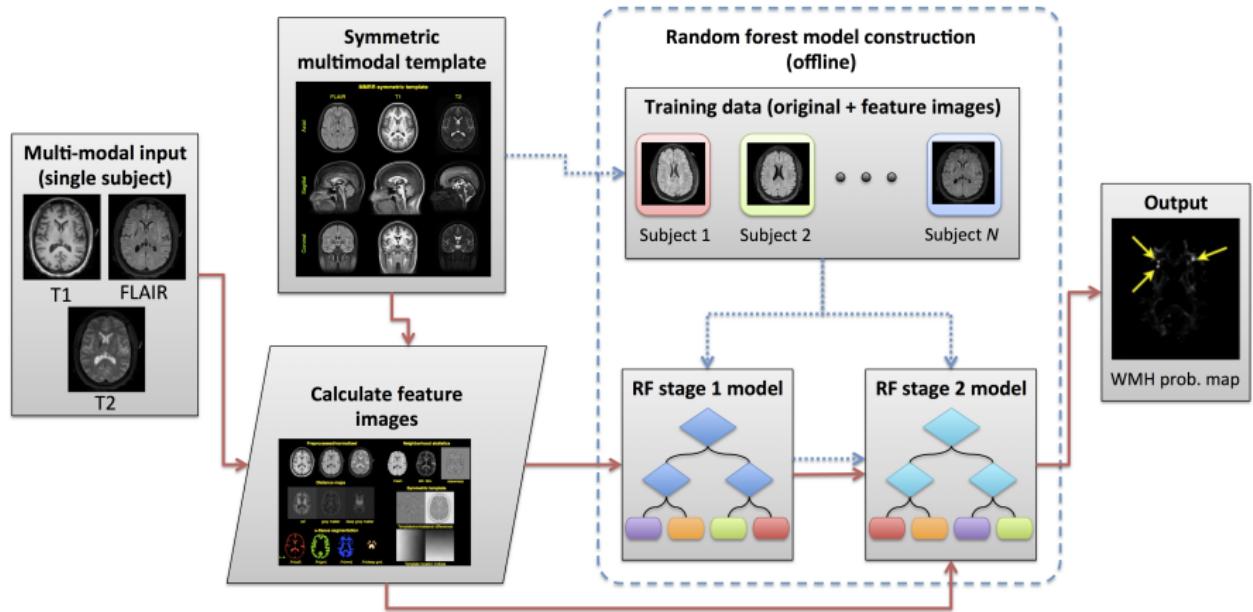
# Multimodal Brain Tumor Segmentation (BRATS 2013)

## Patient

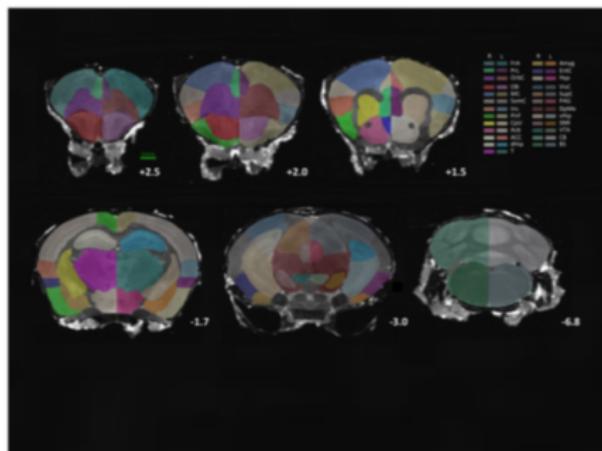
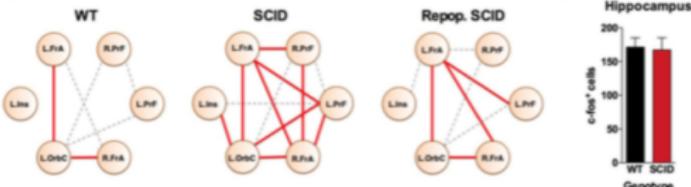
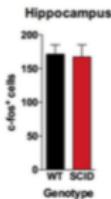
Position	User	Dice			Positive Predictive Value			Sensitivity			Kappa	Complete tumor Rank	Tumor core Rank	Enhancing tumor Rank
		complete	core	enhancing	complete	core	enhancing	complete	core	enhancing				
1	Nick Tustison	0.87 (1)	0.78 (1)	0.74 (1)	0.85 (2)	0.74 (4)	0.69 (4)	0.89 (2)	0.88 (1)	0.83 (1)	0.99 (1)	1.67	2.00	1.89
2	Raphael Meier	0.82 (5)	0.73 (2)	0.69 (3)	0.76 (6)	0.78 (2)	0.71 (1)	0.92 (1)	0.72 (4)	0.73 (3)	0.99 (4)	4.00	2.67	3.00
3	Syed Reza	0.83 (4)	0.72 (3)	0.72 (2)	0.82 (3)	0.81 (1)	0.70 (3)	0.86 (5)	0.69 (6)	0.76 (2)	0.99 (3)	4.00	3.33	3.22
4	Liang Zhao	0.84 (3)	0.70 (4)	0.65 (5)	0.80 (4)	0.67 (5)	0.65 (6)	0.89 (3)	0.79 (3)	0.70 (4)	0.99 (5)	3.33	4.00	4.11
5	Nicolas Cordier	0.84 (2)	0.68 (5)	0.65 (6)	0.88 (1)	0.63 (6)	0.68 (5)	0.81 (6)	0.82 (2)	0.66 (6)	0.99 (2)	3.00	4.33	4.33
6	Joana Festa	0.72 (6)	0.66 (6)	0.67 (4)	0.77 (5)	0.77 (3)	0.70 (2)	0.72 (7)	0.60 (7)	0.70 (5)	0.98 (6)	6.00	5.33	5.00
7	Senan Doyle	0.71 (7)	0.46 (7)	0.52 (7)	0.66 (7)	0.38 (7)	0.58 (7)	0.87 (4)	0.70 (5)	0.55 (7)	0.98 (7)	6.00	6.33	6.44

Tustison, et al., Optimal symmetric multimodal templates and concatenated random forests for supervised brain tumor segmentation (simplified) with ANTsR, *Neuroinformatics*.

# White matter hyperintensities in TBI



# Social behavior and immunity dysfunction in mice

**a****b****c**

## Other ANTsR work

- Pediatric template of brain perfusion
- Automated segmentation of chronic stroke lesions using LINDA: Lesion identification with neighborhood data analysis
- Eigenanatomy
- Corrective learning for segmentation refinement