Active Learning for Glioblastoma Segmentation

Jens Petersen
Medical Image Computing (E132)



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GERMAN CANCER RESEARCH CENTER
IN THE HELMHOLTZ ASSOCIATION

50 Years – Research for
A Life Without Cancer



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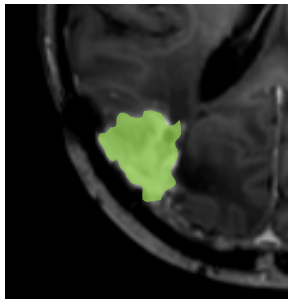
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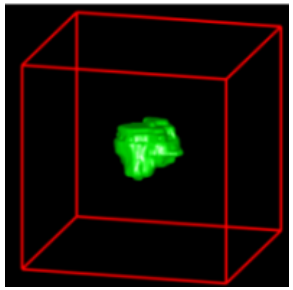
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Why Segmentation?

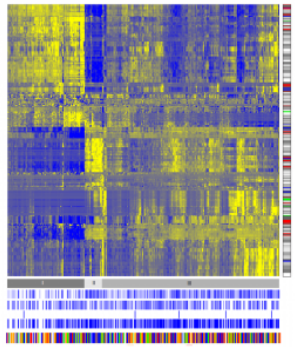
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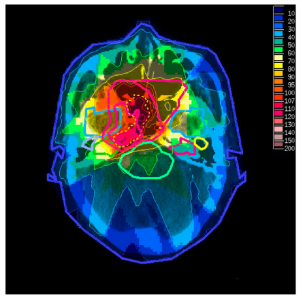
Tumor Volumetry



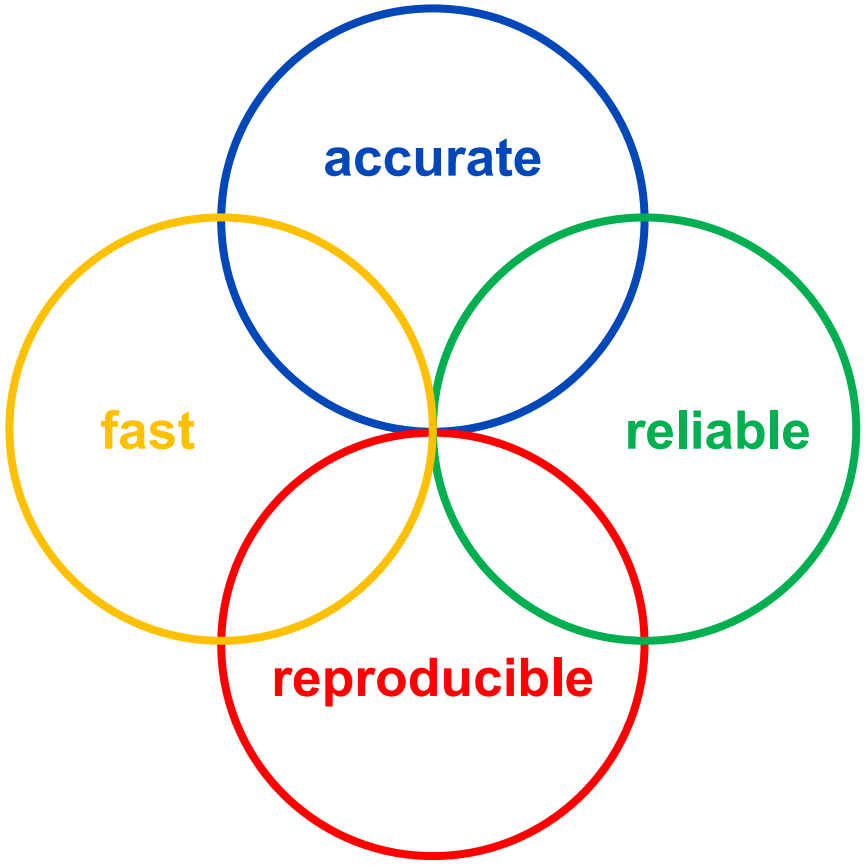
Radiomics



Radiotherapy



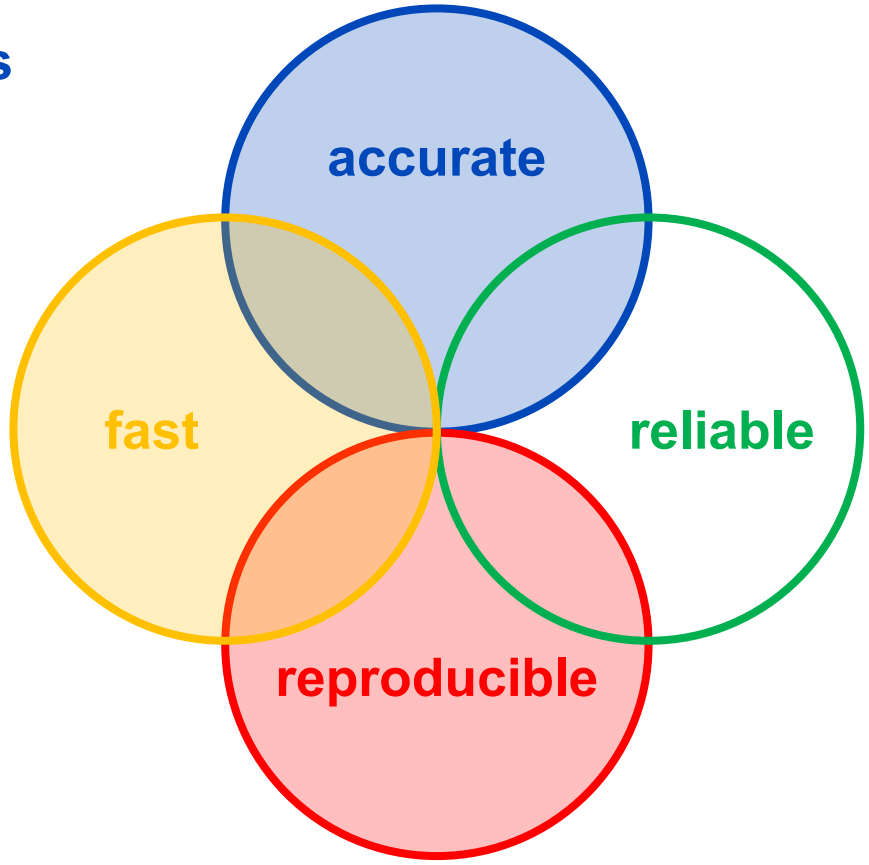
Tradeoffs



Tradeoffs

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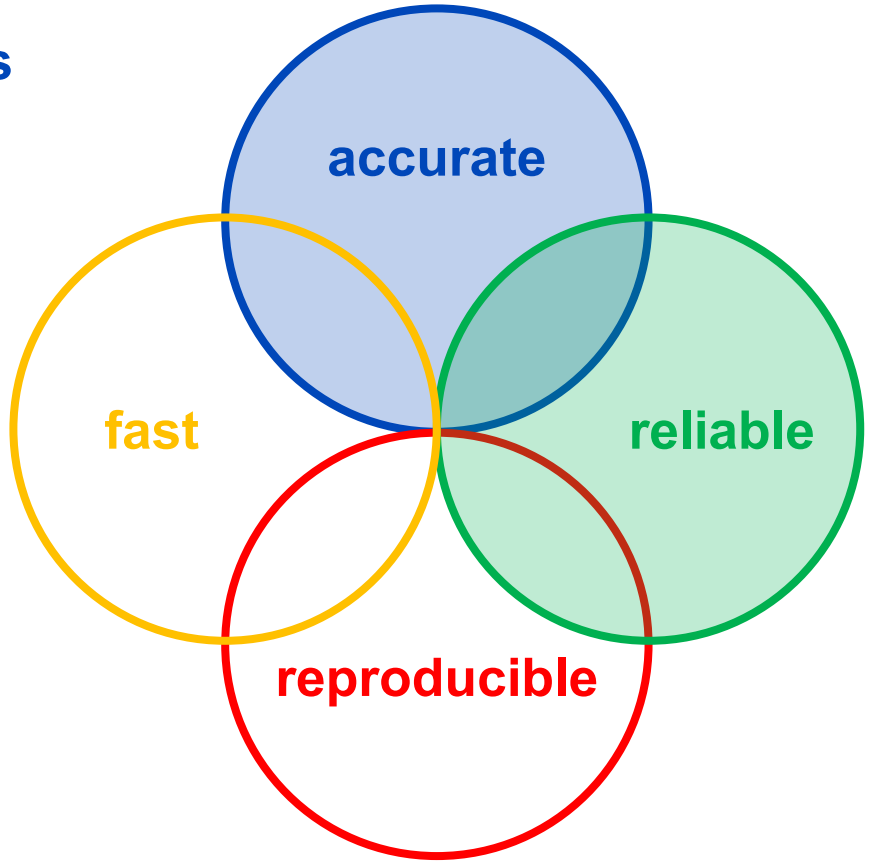
Automatic methods
CNNs
Random Forests
etc…



Tradeoffs

Automatic methods
CNNs
Random Forests
etc…

Manual segmentation
Contouring
Region Growing
etc…

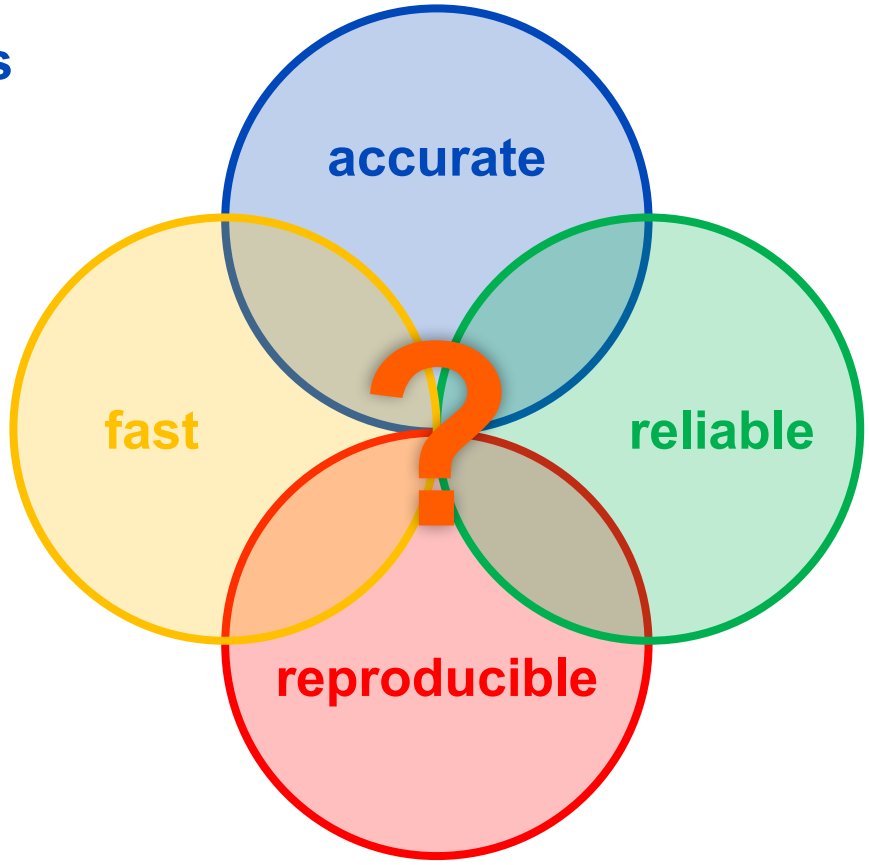


Tradeoffs

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Automatic methods
CNNs
Random Forests
etc…

Manual segmentation
Contouring
Region Growing
etc…



Overview

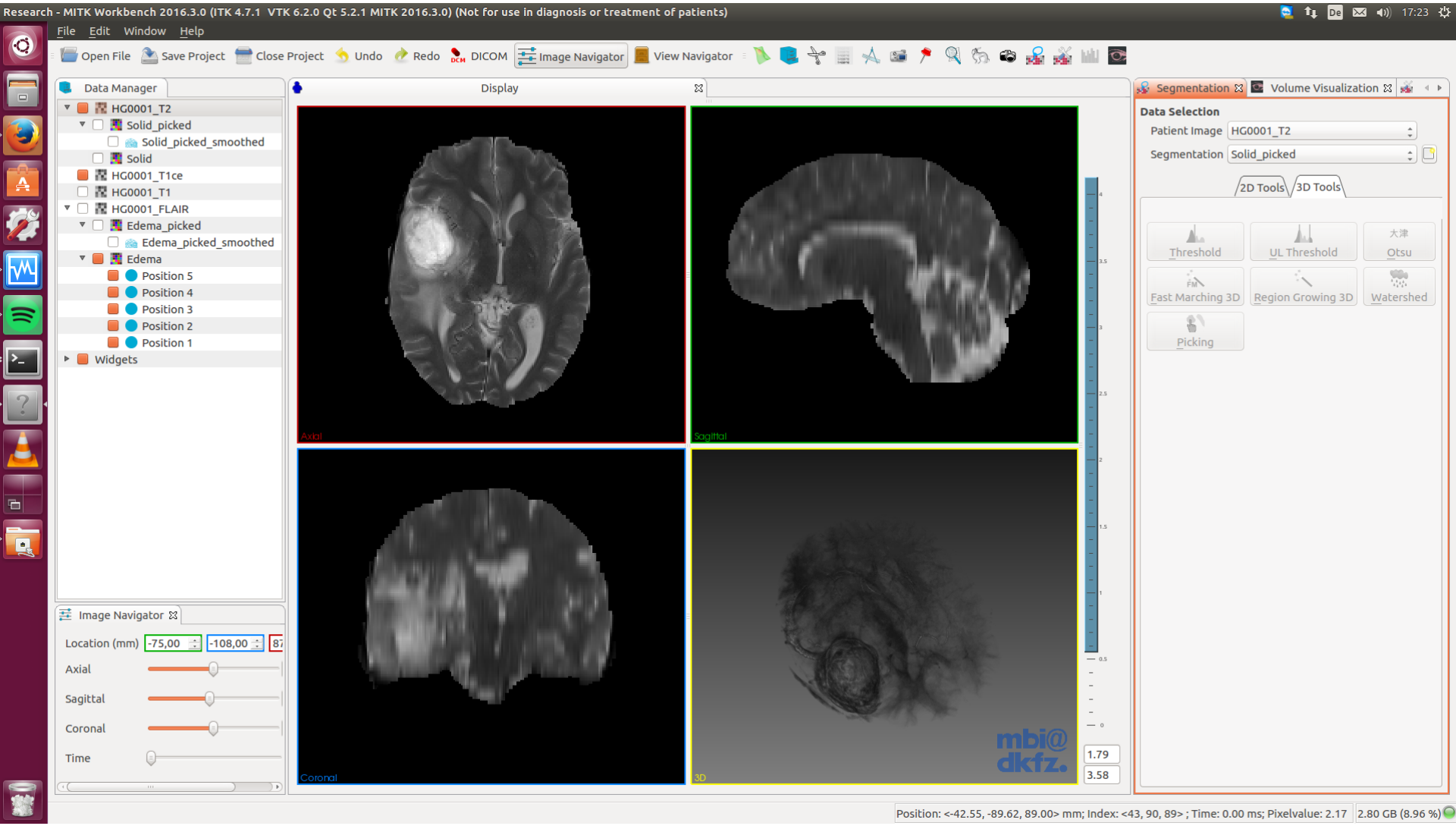
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Interactive segmentation

Neural Networks

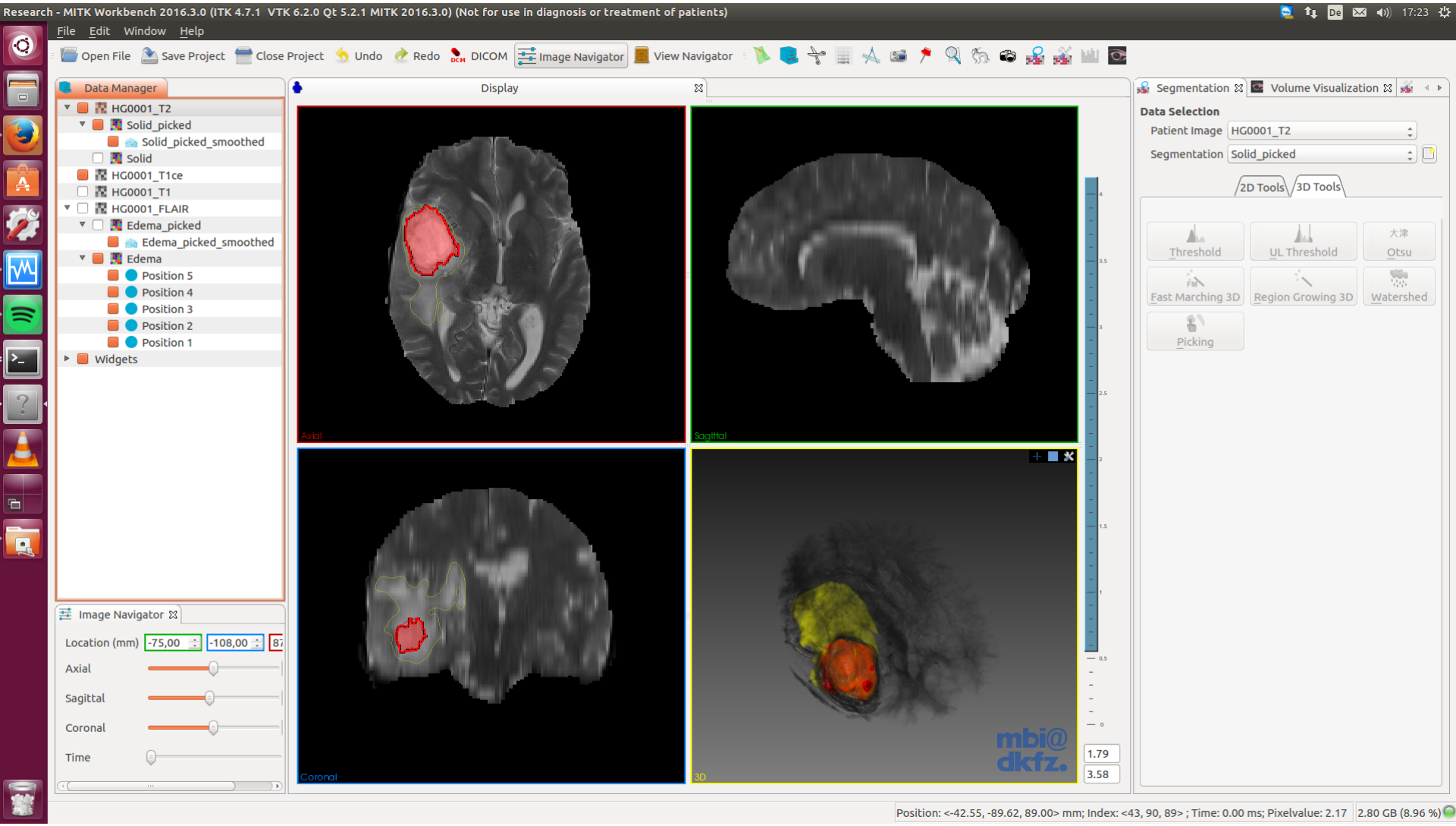
Active Learning

MITK


Research - MITK Workbench 2016.3.0 (ITK 4.7.1 VTK 6.2.0 Qt 5.2.1 MITK 2016.3.0) (Not for use in diagnosis or treatment of patients)
File Edit Window Help
Open File
Save Project
Close Project
Undo
Redo
DICOM
Image Navigator
View Navigator
Data Manager
HG0001_T2
Solid_picked
Solid_picked_smoothed
Solid
HG0001_T1ce
HG0001_T1
HG0001_FLAIR
Edema_picked
Edema_picked_smoothed
Edema
Position 5
Position 4
Position 3
Position 2
Position 1
Widgets
Display
Axial
Sagittal
Coronal
3D
mbi@dkfz.
Image Navigator
Location (mm)
-75,00
-108,00
Axial
Sagittal
Coronal
Time
Segmentation
Volume Visualization
Data Selection
Patient Image
HG0001_T2
Segmentation
Solid_picked
2D Tools
3D Tools
Threshold
UL Threshold
Otsu
Fast Marching 3D
Region Growing 3D
Watershed
Picking
1.79
3.58
Position: <-42.55, -89.62, 89.00> mm; Index: <43, 90, 89> ; Time: 0.00 ms; Pixelvalue: 2.17
2.80 GB (8.96 %)

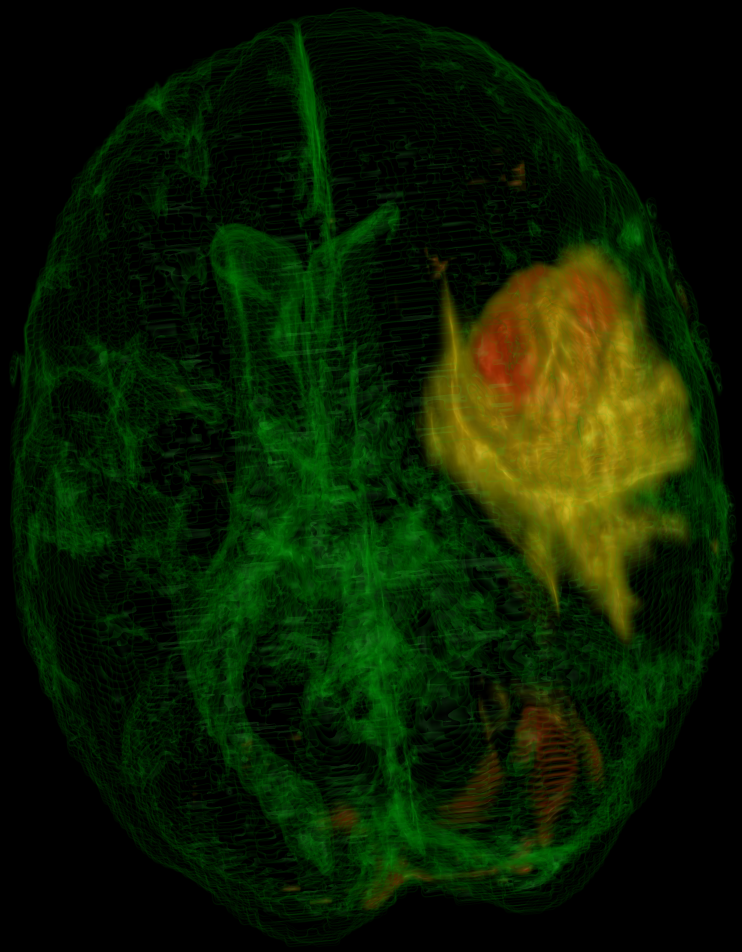
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TurtleSeg

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TurtleSeg

Interactive 3D Image Segmentation Software

http://www.turtleseg.org

ilastik

MRI Volumetry of a Longitudinal Brain Tumor Examination

Overview

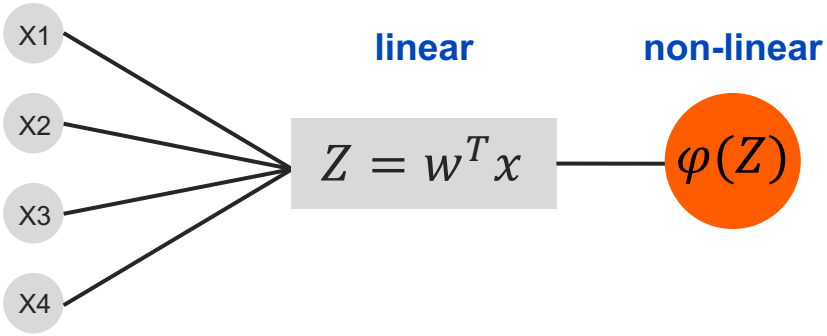
Interactive segmentation

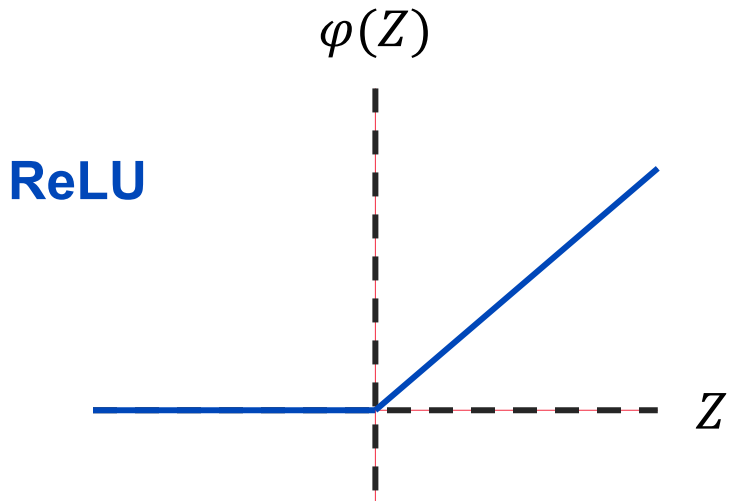
Neural Networks

Active Learning

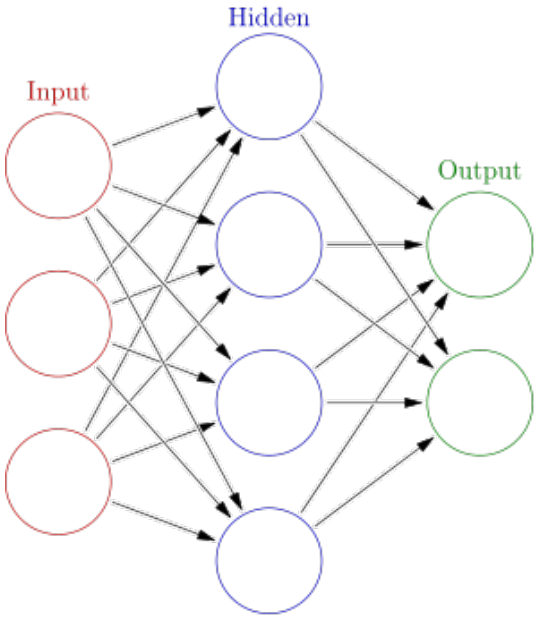
Artificial Neural Networks – Introduction

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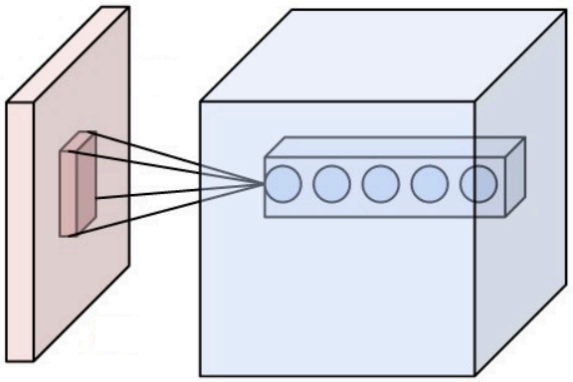




Convolutional Neural Networks

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1. Convolutional Layer

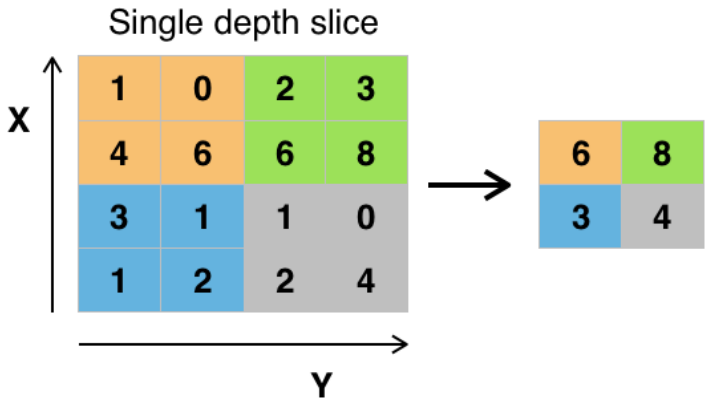


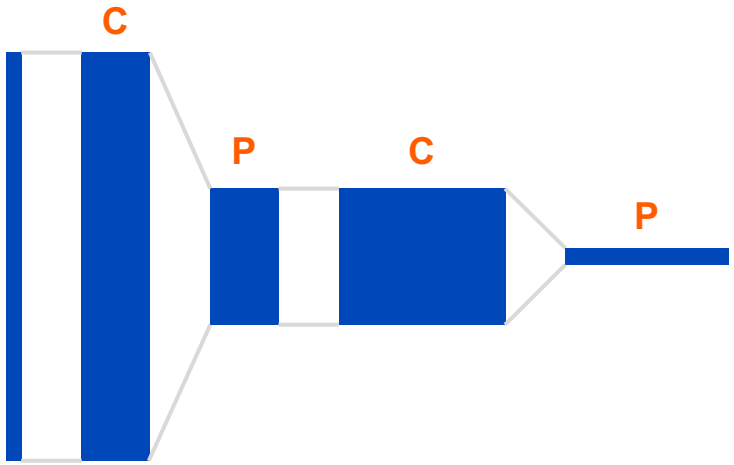
Receptive field

Weight sharing

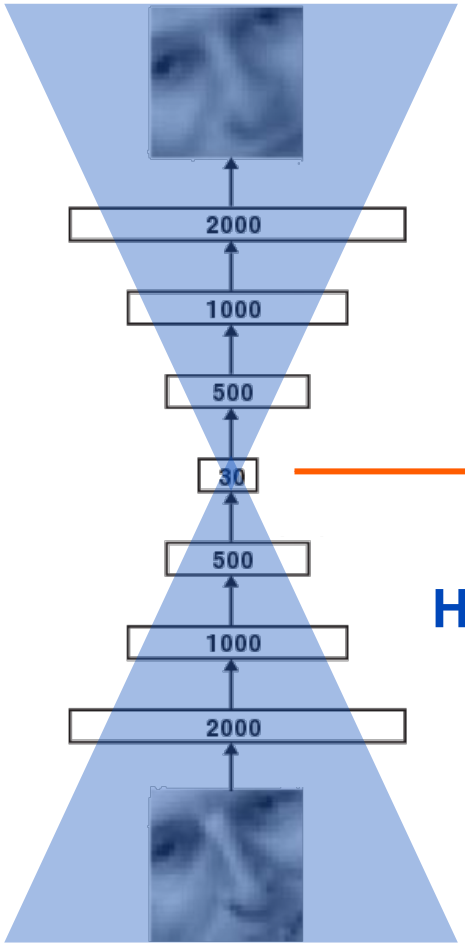
Multiple filters per layer

2. (Max-) Pooling Layer





Autoencoder



Reconstruction

2 Eyes, 1 Nose, 0.5 Mouth, Position

Hierarchical Information Compression

Shapes

Edges etc…

Pixels

Hinton, G. E. and Salakhutdinov, R. R.: *Reducing the Dimensionality of Data with Neural Networks,* Science 313, 2006

Overview

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Interactive segmentation

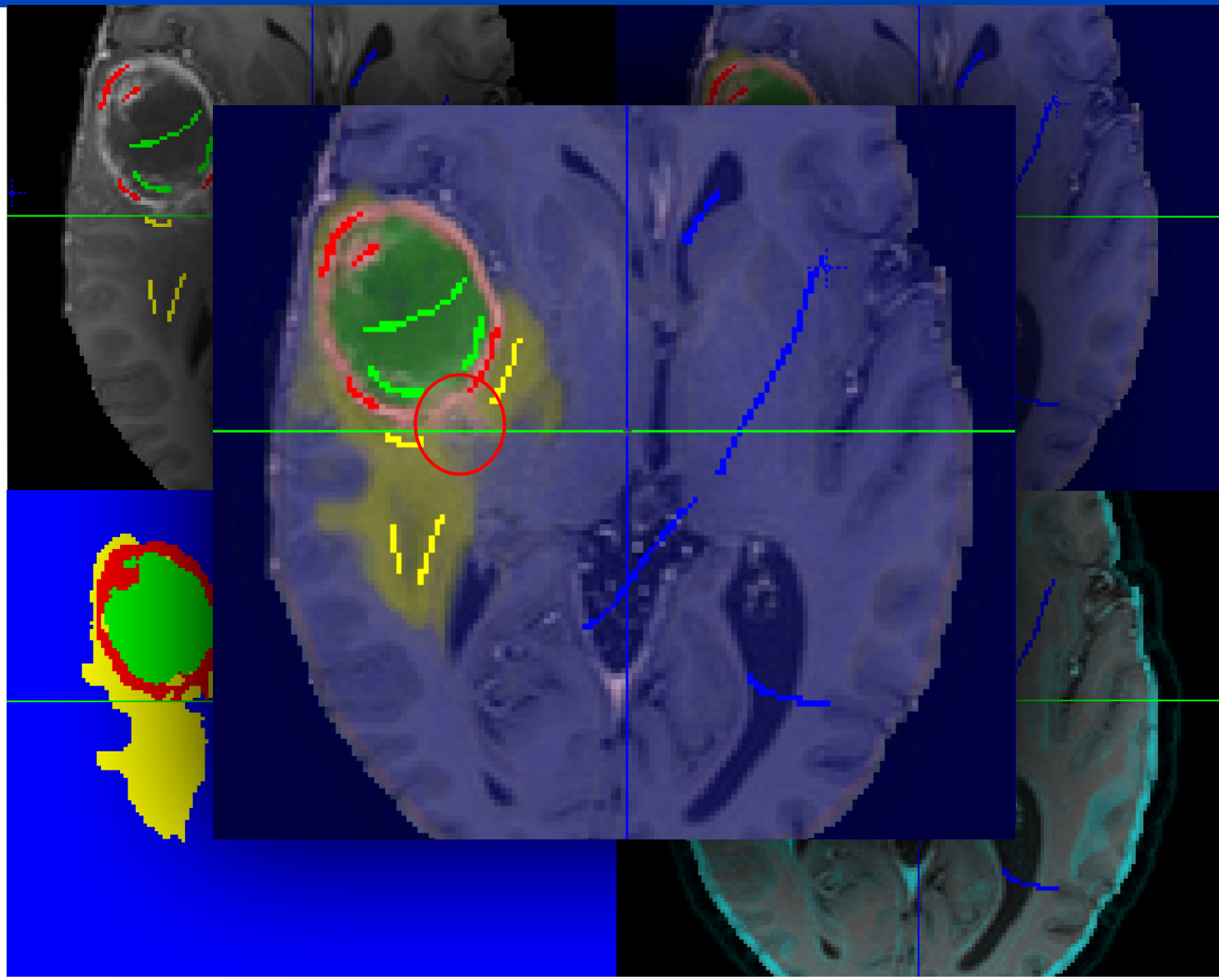
Neural Networks

Active Learning

Pixel Classification with User Guidance

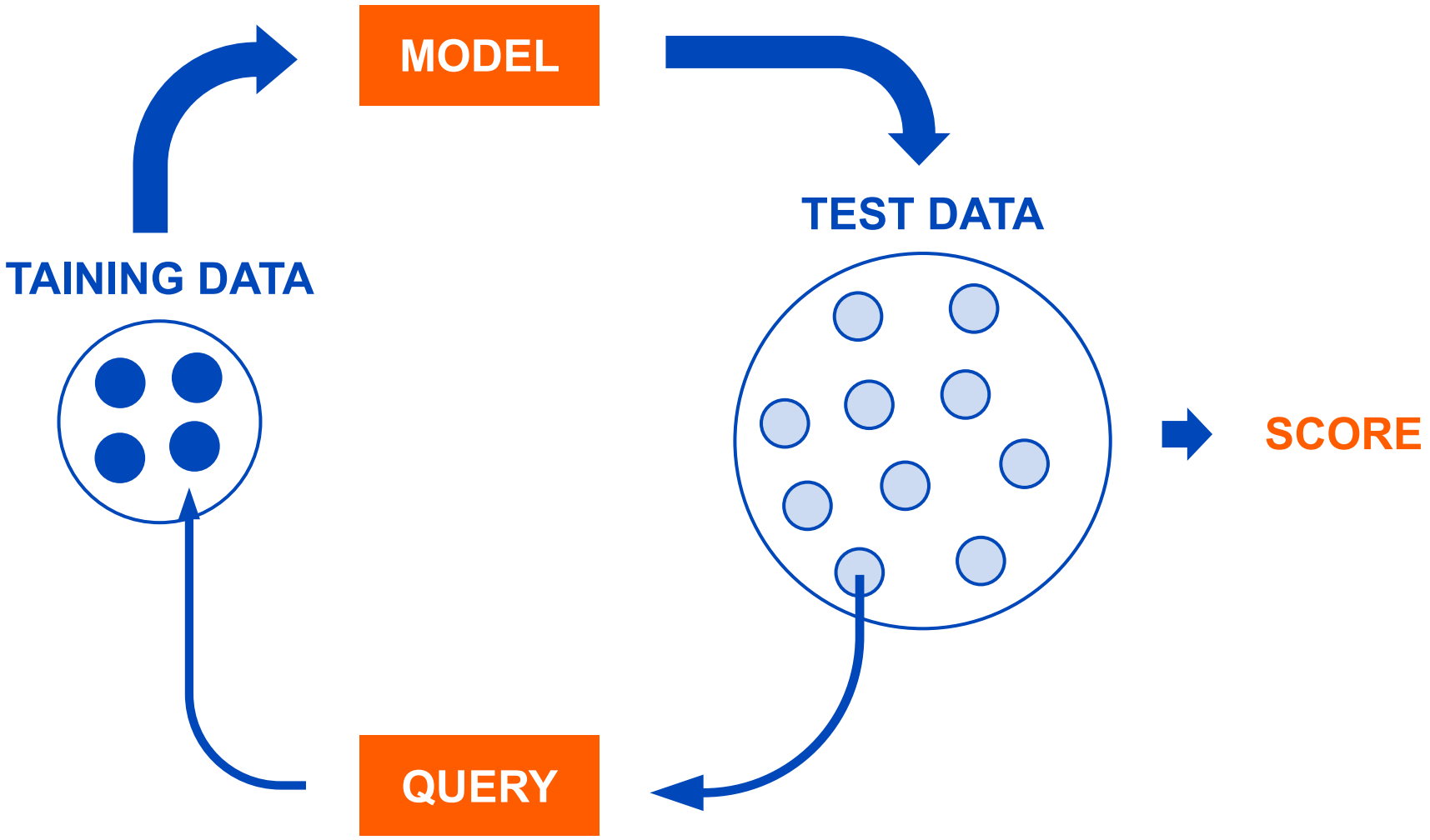
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- enhancing tumor
- non-enhancing tumor
- edema
- other



Active Learning Principle

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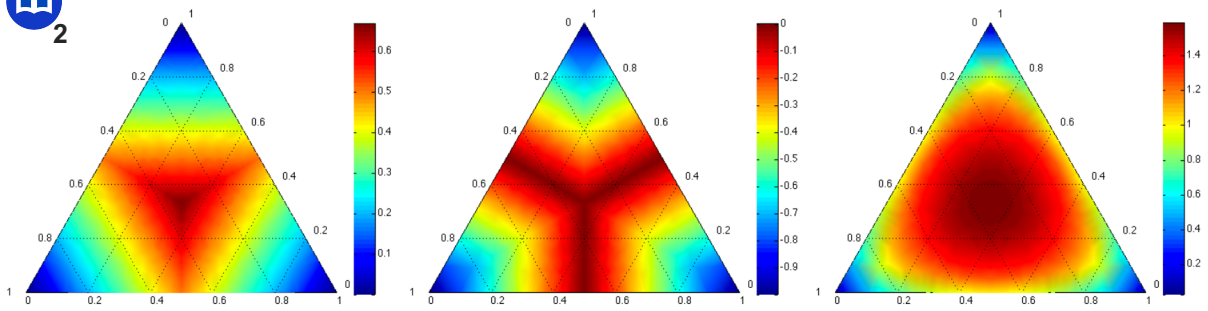
How to select Query Data

Uncertainty Sampling

Expected Model Change

Query by Committee

3 class problem



Confidence Margin Entropy

Lewis, D. and Gale, W.: *A sequential algorithm for training text classifiers*, Proceedings of the 17th ACM SIGIR Conference, 1994

[2] Settles, B.: *Active Learning Literature Survey*, Computer Sciences Technical Report 1648, University of Wisconsin – Madison, 2010, accessed 4.3.16

How to select Query Data

Uncertainty Sampling

Expected Model Change

Query by Committee



Applicable in almost all gradient based optimizations

Computationally expensive

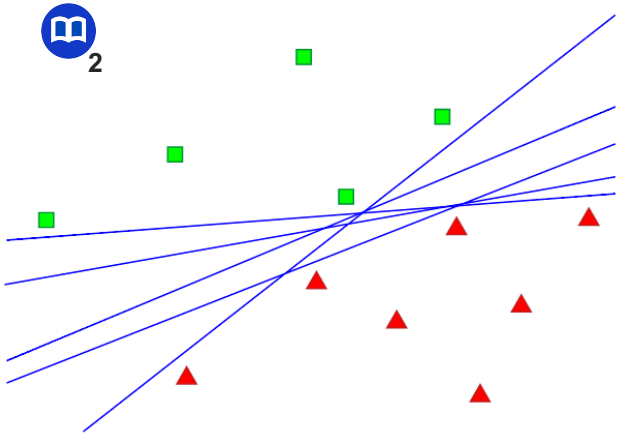
Settles, B., Craven, M. and Ray, S.: *Multiple-instance Active Learning*, Advances in NIPS, 2008

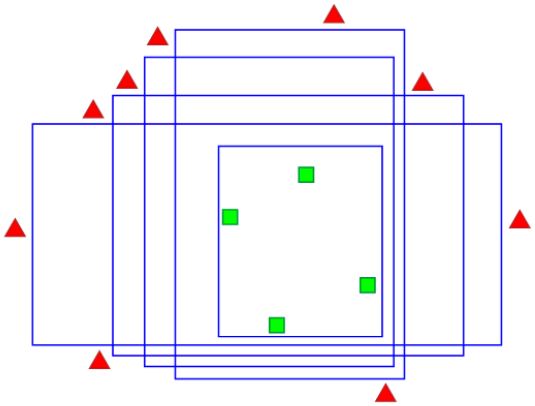
How to select Query Data

Uncertainty Sampling

Expected Model Change

Query by Committee





1. **Multiple models that describe known data**
2. **Measure of disagreement**

Reduce version space

Seung, H. S., Opper, M. and Sompolinsky, H.: *Query by committee*, Proceedings of the ACM Workshop on Computational Learning Theory, 1992, pp. 287-294

Settles, B.: *Active Learning Literature Survey*, Computer Sciences Technical Report 1648, University of Wisconsin – Madison, 2010, accessed 4.3.16

Key Contributions

New Query Strategies

- „Superpixels“
- Cluster representation

Pre-Training

- Clustering
- Learned features
- Low-dimensional representations

Software

- Ready-to-use
- Generalizable



Thank you for your attention!

Further information on www.dkfz.de

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The Foundation – EORTC 26101 Study

EORTC 26101 BOVAREC

437 Patients

First recurrence of GBM

Chemotherapy

Radiotherapy



Lomustine (CCNU)
alkylating agent
+
Bevacizumab (Avastin)
angiogenesis inhibitor

2

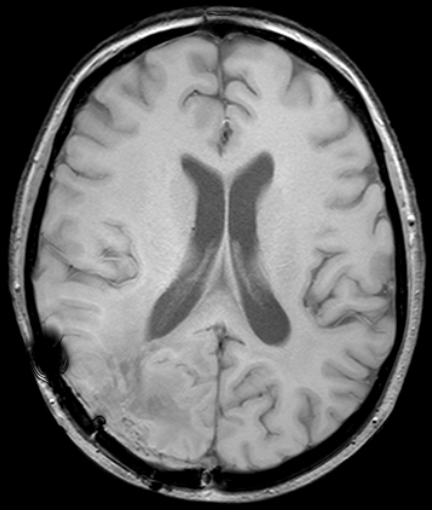
Lomustine (CCNU)
alkylating agent

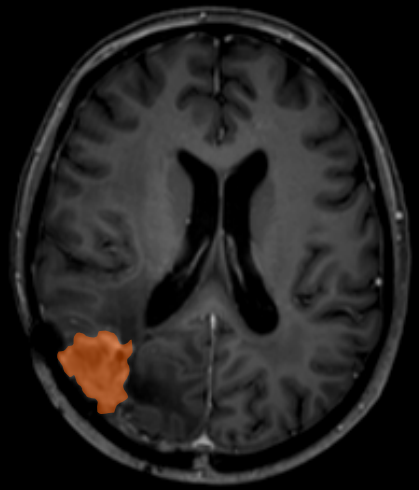
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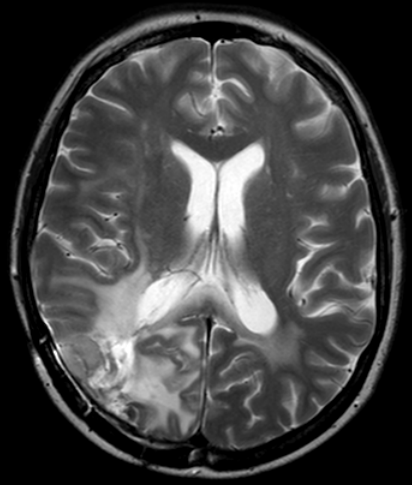
Wick, W. et al.: *LB-05. PHASE III TRIAL EXPLORING THE COMBINATION OF BEVACIZUMAB AND LOMUSTINE IN PATIENTS WITH FIRST RECURRENCE OF A GLIOBLASTOMA: THE EORTC 26101 TRIAL,* Neuro-Oncology 17(suppl. 5), 2015, pp. v1

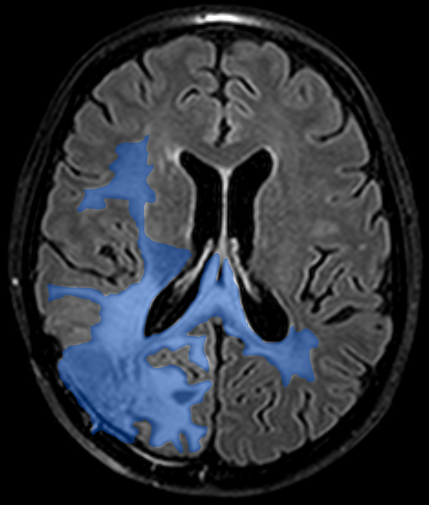
MRI Glioblastoma Segmentation

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Field Strength:

3T	52.5%
1.5T	46.0%
1T	1.5%

Vendors:

Siemens	73.9%
GE	16.1%
Philips	10.0%

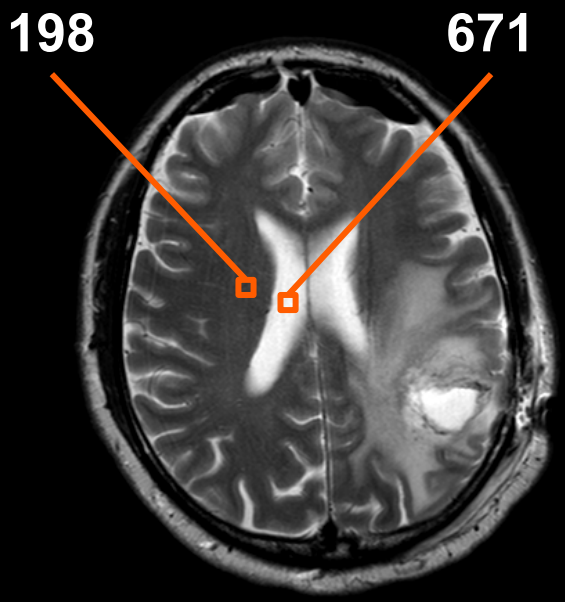
Common Flaws:

Missing sequences
Missing data

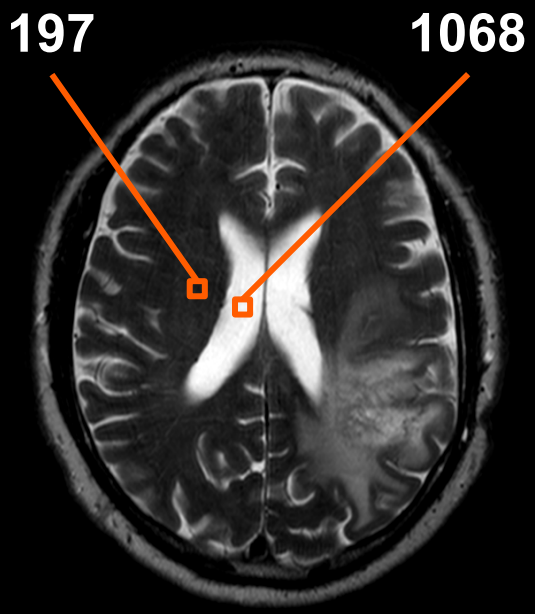
DWI PWI SWI T2* T2ce PD

MRI – Intensities are not comparable

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512 x 512
4mm spacing
[0, 874]

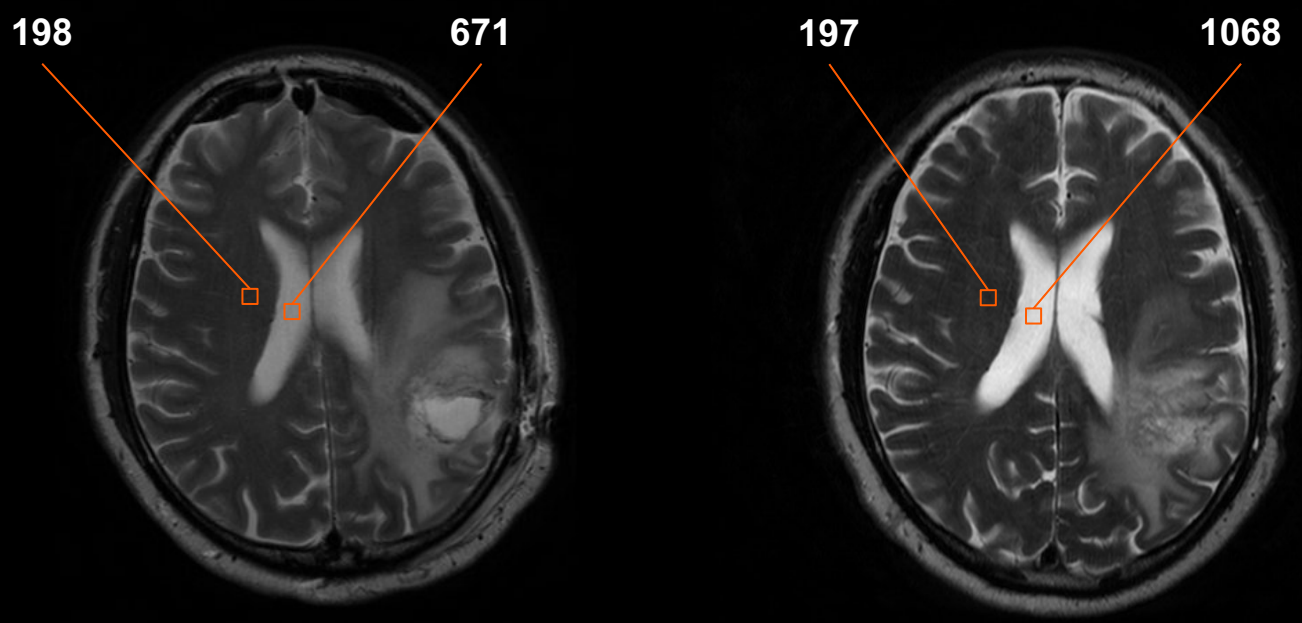


800 x 800
5mm spacing
[0, 1202]

Shinohara, R. T. et al.: *Statistical normalization techniques for magnetic resonance imaging,* NeuroImage: Clinical 6, 2014, pp. 9-19

MRI – Intensities are not comparable

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Can we model bias field and transfer functions to learn invariant representation?
Works well for noise correction.

Burger, H. et al.: *Image Denoising: Can plain neural networks compete with BM3D?,* Computer Vision and Pattern Recognition, Proceedings, 2012, pp. 2392-2399

Shinohara, R. T. et al.: *Statistical normalization techniques for magnetic resonance imaging,* NeuroImage: Clinical 6, 2014, pp. 9-19

Goal

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„Interactive Segmentation of very large image datasets with minimal effort“

Overview

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- Brain Tumor Segmentation Overview
- Artificial Neural Networks
- Active Learning
- Milestones

Overview

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Brain Tumor Segmentation – Overview

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Voxel			Volume
Handcrafted Features			Learned Features
Supervised			Unsupervised
Atlas			No Atlas
Interactive			Automatic

Random Forest

Neural Network

Overview

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- Active Learning
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Example: Separation of Style & Content



Gatys, L. A., Ecker, A. S. and Bethge, M.: *A Neural Algorithm of Artistic Style,* arXiv:1508.06576, 2015

Overview

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Overview

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- Milestones

Milestones



Implementation State of the Art

- Random Forest based pixel classification (extend Michael‘s & Jonas‘ work)
- GUI with active user guidance
- Single image volume
- Handcrafted & fixed features



Milestones

Implementation
State of the Art



Multi-Volume Segmentation

- **Focus on querying next volume**
- **Transfer learning**
- **Extend to other modalities (User defined features)**

Milestones

Implementation
State of the Art

Multi-Volume
Segmentation



Neural Network
Active Learning

- Autoencoder for large enough datasets
- Learn features
- Use low-dimensional similarity measure

Summary

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„Interactive Segmentation of Very Large Image Datasets with Minimal Effort“

Available

- Random Forest Classifier
- Autoencoder
- Active Learning Query Strategies
- Domain Adaptation Strategies

New

- Software with Active User Guidance
- Active Learning with Pre-Training
- Efficient Low-Dimensional Query
- Hierarchical Query



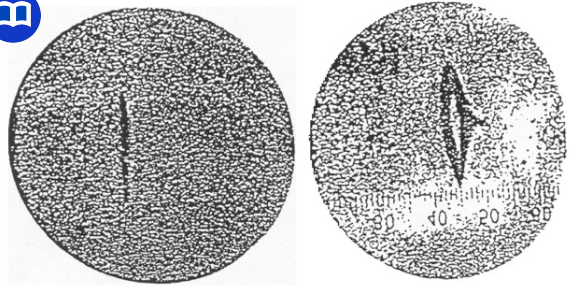
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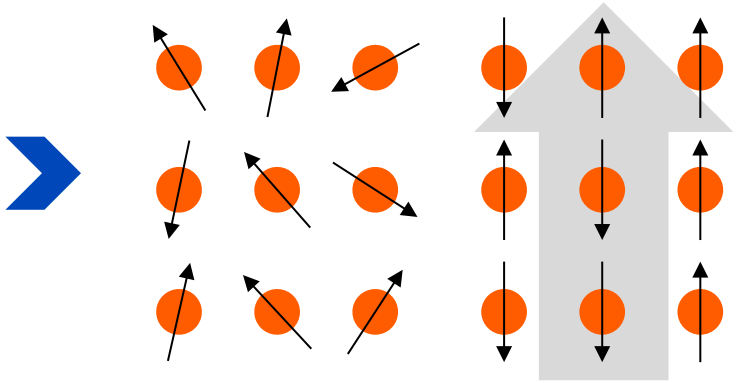
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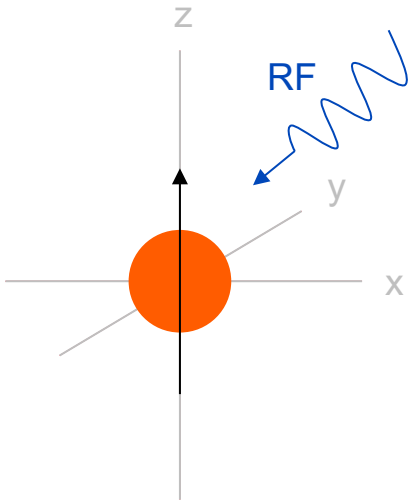
Quick MRI Review

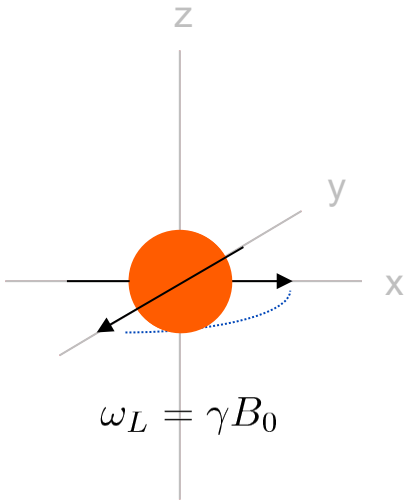




$$\frac{N_{\uparrow\uparrow}}{N_{\uparrow\downarrow}} = e^{\frac{\Delta E}{kT}}$$

1.00002
H_1 @ 3T, 300K





$$\omega_L = \gamma B_0$$

$$M_z(t) = M_z(0) \cdot \left(1 - c \cdot e^{-\frac{t}{T_1}}\right)$$

$$M_{xy}(t) = M_{xy}(0) \cdot e^{-\frac{t}{T_2}}$$

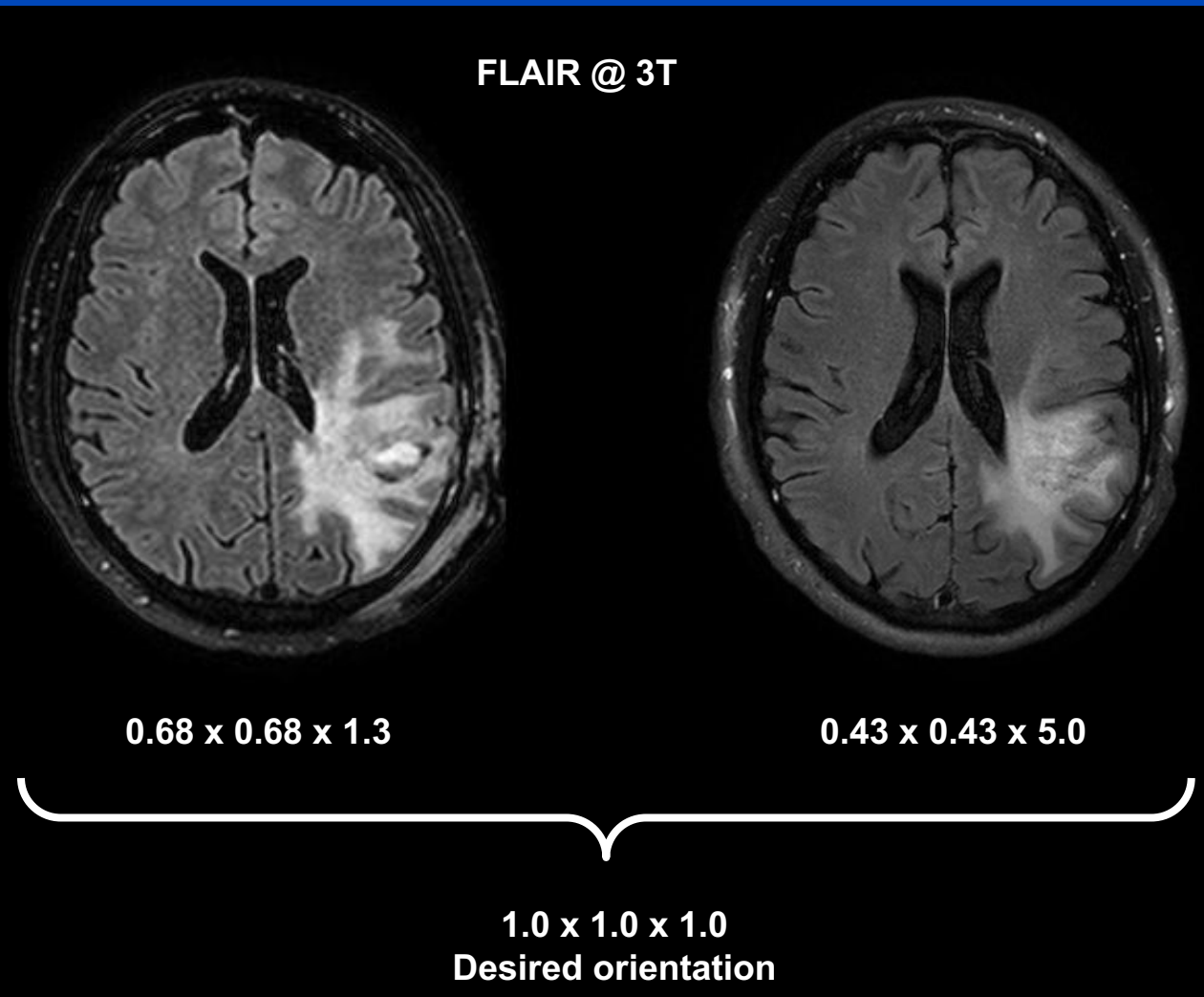
Lauterbur, P. C. and Mansfield, P.: *Nobel Prize in Physiology or Medicine 2003*

Gerlach, W. and Stern, O.: *Der experimentelle Nachweis der Richtungsquantelung im Magnetfeld*. Zeitschrift für Physik 9, 1922, pp. 349-352

Preprocessing

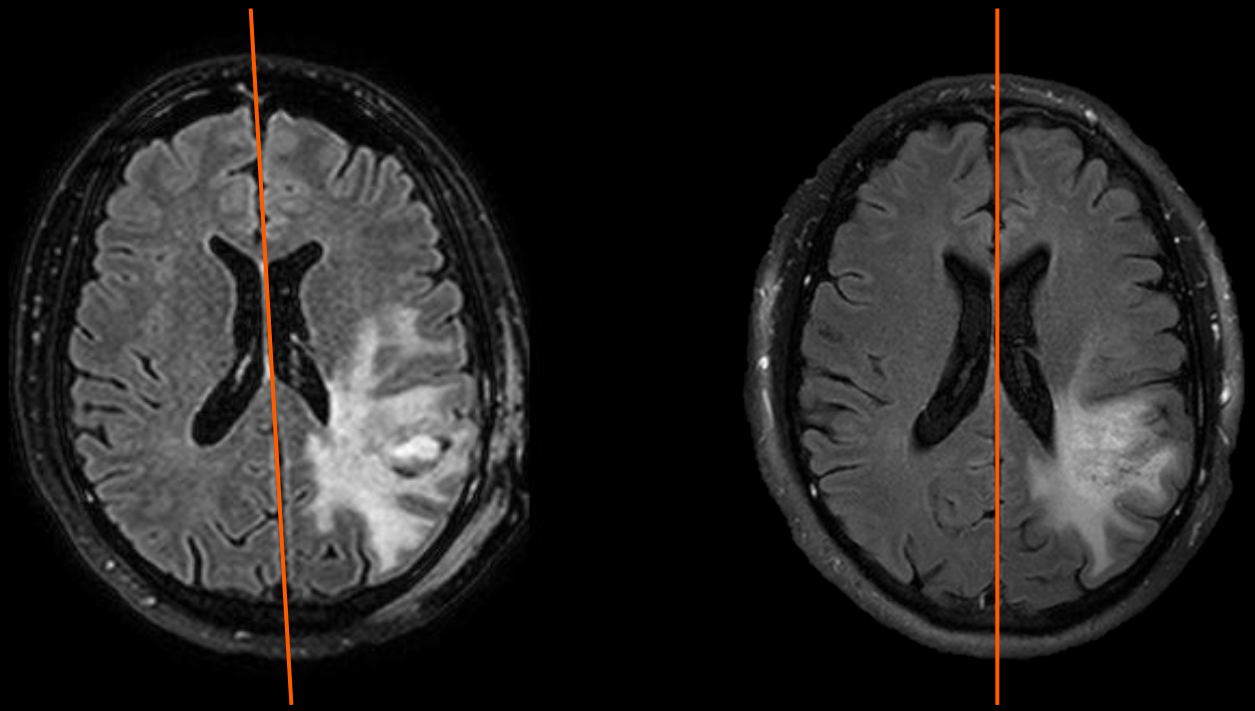
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Resampling
Registration
Brain Extraction
Bias Field Correction
Normalization



Preprocessing

- Resampling
- **Registration**
- Brain Extraction
- Bias Field Correction
- Normalization

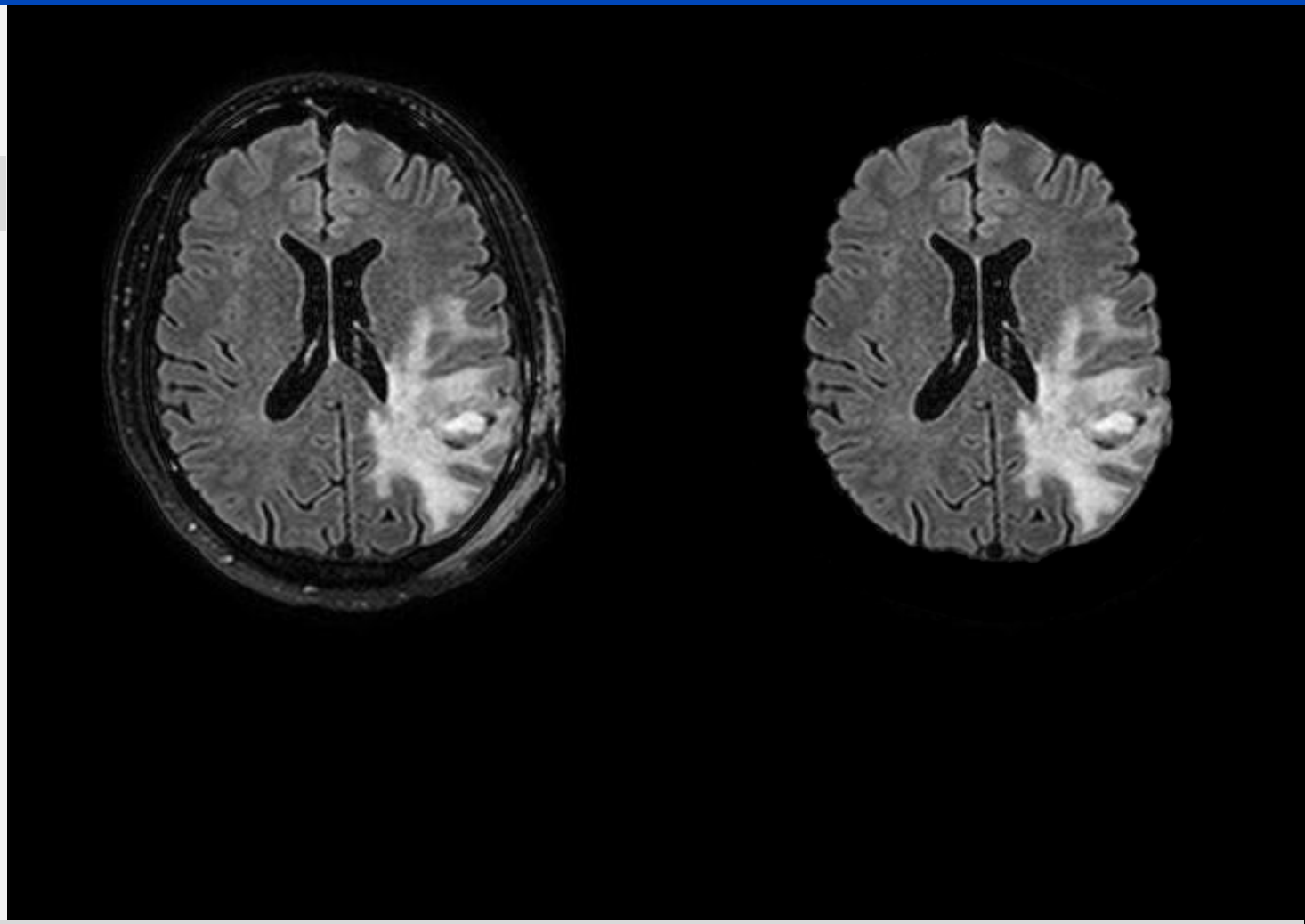


Rigid: 3T + 3R
Non-rigid: +3S (+arbitrary deformation)

Maximize Mutual Information
Combine with resampling

Preprocessing

- Resampling
- Registration
- **Brain Extraction**
- Bias Field Correction
- Normalization



ROBEX BEaST FSL-BET FREESURFER-HWA AFNI-3dSkullStrip BrainSuite-BSE ITK

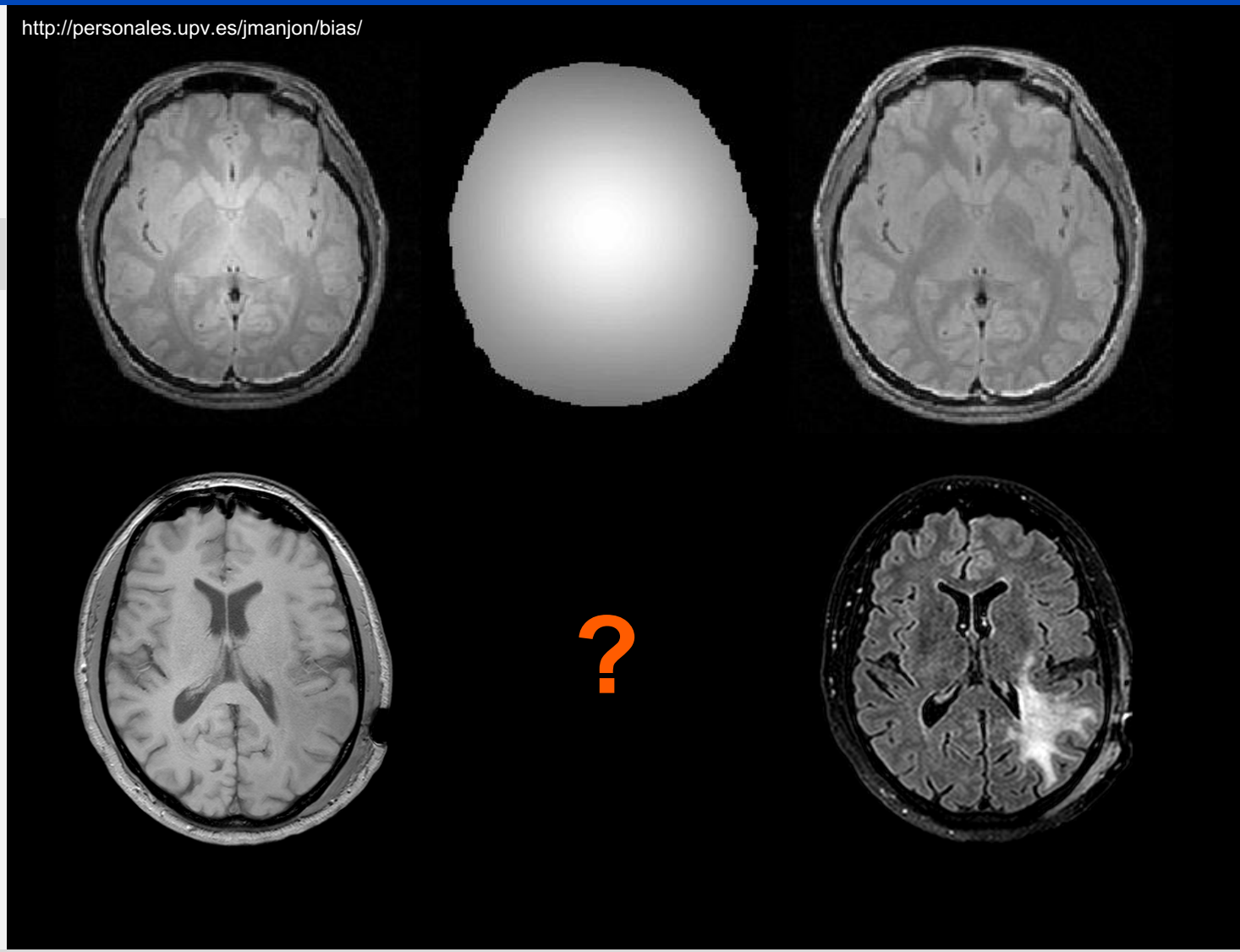
Kleesiek, J. et al.: *Deep MRI brain extraction: A 3D convolutional neural network for skull stripping,* NeuroImage 129, 2016, pp. 460-469

Preprocessing

dkfz.
50 Years – Research for
A Life Without Cancer

- Resampling
- Registration
- Brain Extraction
- **Bias Field Correction**
- Normalization

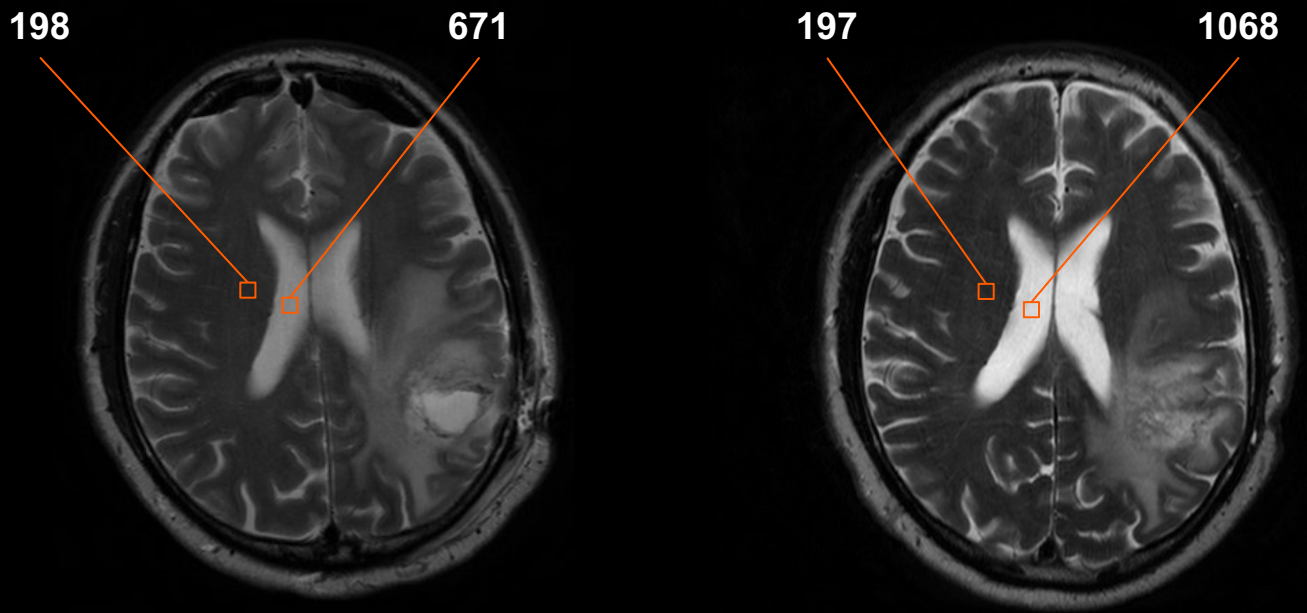
http://personales.upv.es/jmanjon/bias/



N4ITK FSL-FAST FREESURFER BrainSuite-BFC AFNI-3duniformize

Preprocessing – Normalization

Resampling
Registration
Brain Extraction
Bias Field Correction
Normalization



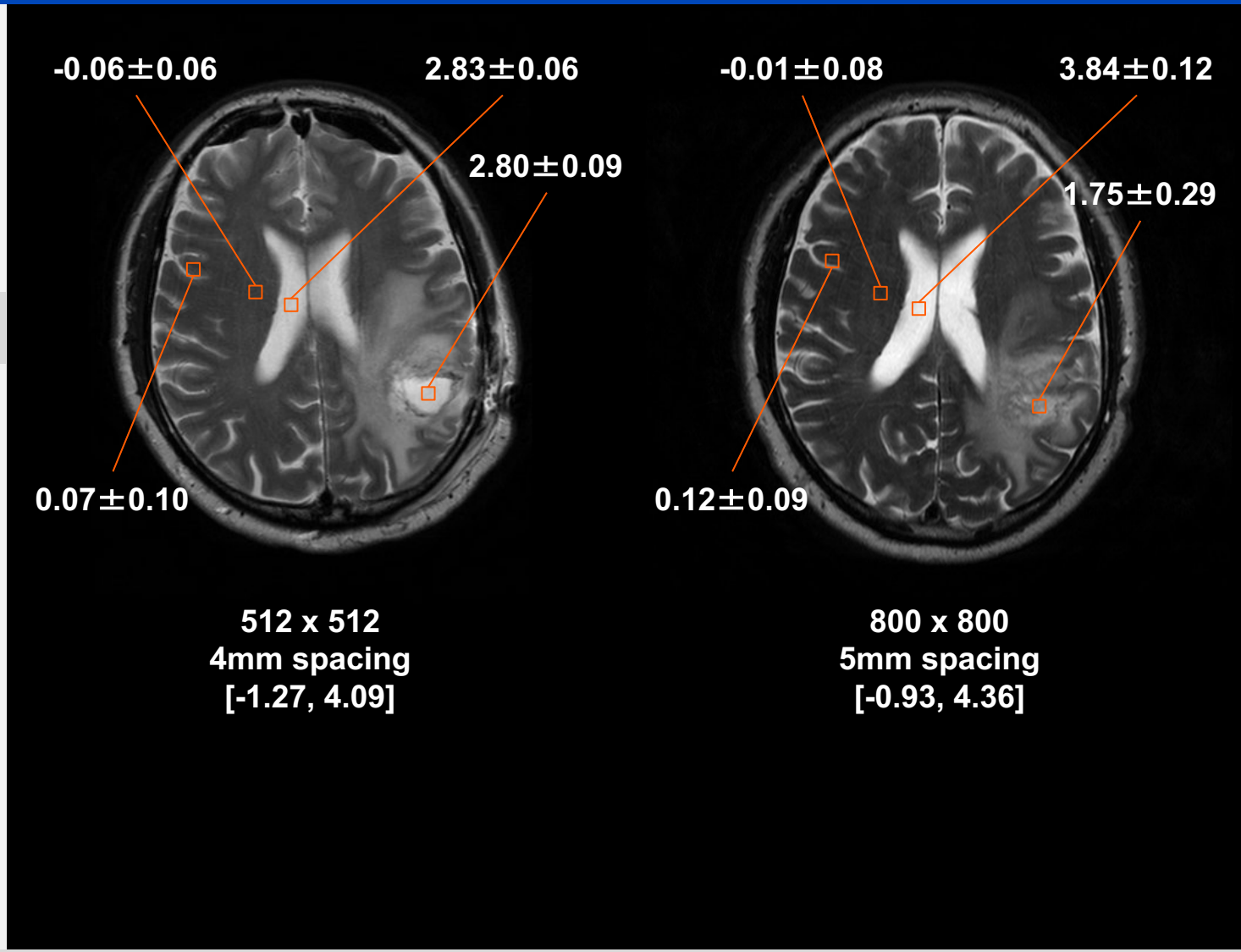
Can we model bias field and transfer functions to learn invariant representation?
Works well for noise correction.

Burger, H. et al.: *Image Denoising: Can plain neural networks compete with BM3D?,* Computer Vision and Pattern Recognition, Proceedings, 2012, pp. 2392-2399

Shinohara, R. T. et al.: *Statistical normalization techniques for magnetic resonance imaging,* NeuroImage: Clinical 6, 2014, pp. 9-19

Preprocessing

- Resampling
- Registration
- Brain Extraction
- Bias Field Correction
- **Normalization**



Shinohara, R. T. et al.: *Statistical normalization techniques for magnetic resonance imaging,* NeuroImage: Clinical 6, 2014, pp. 9-19