Surgical Planning Laboratory
Brigham and Women's Hospital
Boston, Massachusetts USA

a teaching affiliate of
Harvard Medical School

Fraunhofer MEVIS

Universität Bremen

# 3D Slicer

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- Founding Director, Surgical Planning Laboratory, Brigham and Women's Hospital
- Institutsleiter, Fraunhofer MEVIS
- Principal Investigator, National Alliance for Medical Image Computing, Quantitative Image Informatics for Cancer Research, and Neuroimage Analysis Center,
- Research Director, National Center for Image Guided Therapy

# Acknowledgments


**National Alliance for Medical Image Computing**
www.na-mic.org

**Neuroimage Analysis Center**
nac.spl.harvard.edu

**Surgical Planning Laboratory, Brigham and Women's Hospital**
spl.harvard.edu

**National Center For Image Guided Therapy**
www.ncigt.org

- Ferenc Jolesz, MD, my mentor
- Collaborators and colleagues


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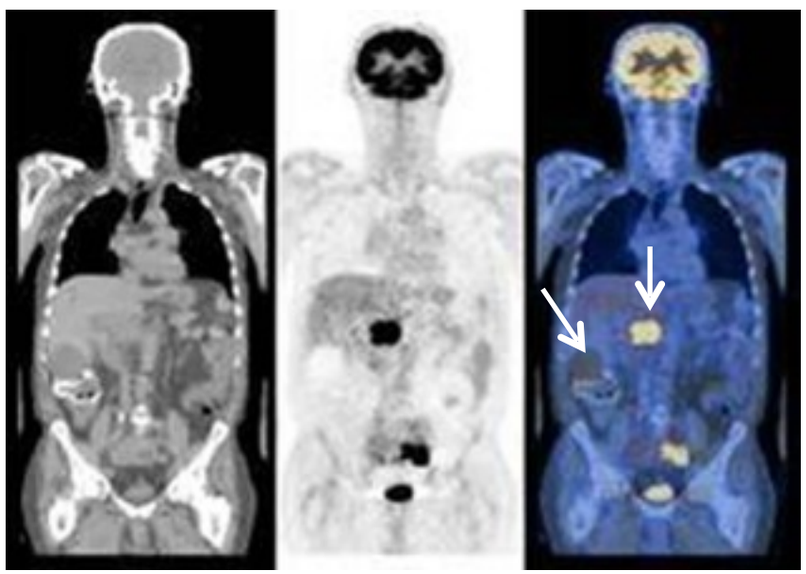
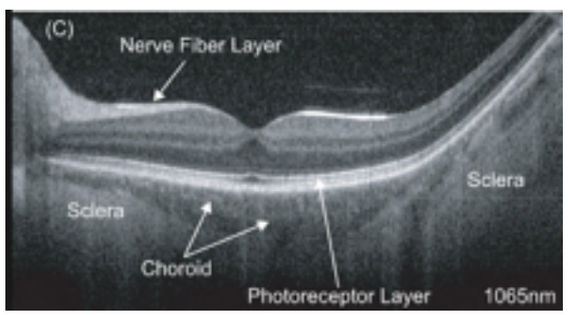
# Imaging Modalities

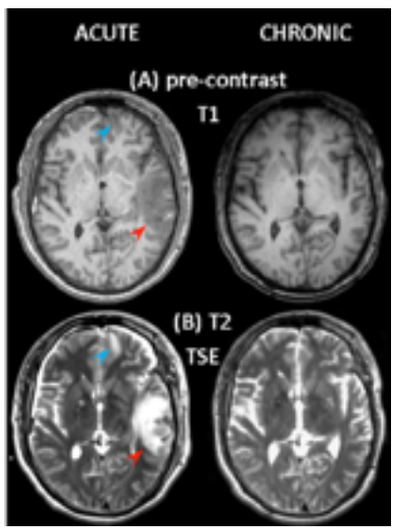
PET CT: http://nucmed.wikispaces.com/Wendt+Talk+6



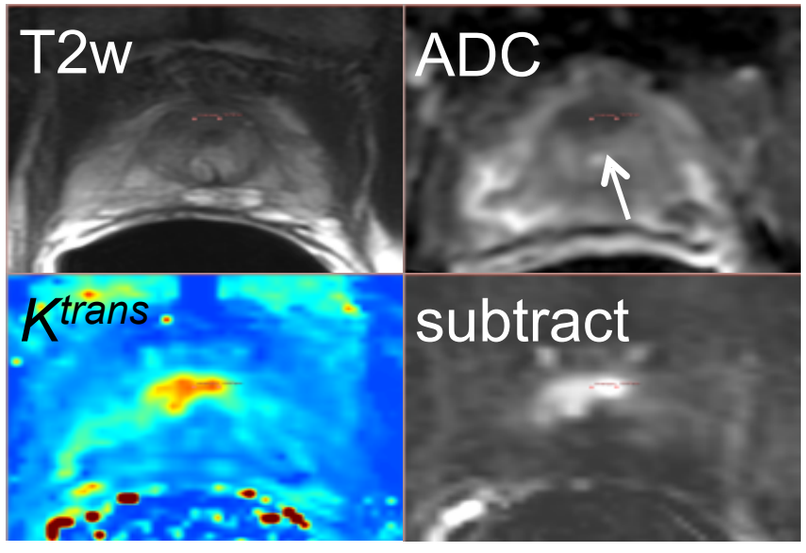



OCT: http://spie.org/x88950.xml?pf=true&ArticleID=x88950

MR Images: P. Vespa, J. Alger, UCLA




Complex MRI: Fedorov et al. 2012. JMRI. 36(4): 987–992.




4D Ultrasound: http://ultrasoundcarespecialist.com/html/anib_3d4d.html

Chubby Cheeks

## This is just a partial list

- X ray radiography
- Magnetic resonance imaging (MRI)
- Nuclear medicine
- Computed Tomography
- Tomography
- Ultrasound
- Optical Coherence Tomography
- Photoacoustic imaging
- Thermography
- Light Microscopy
  - Bright, dark field
  - Phase contrast
  - Fluorescence
  - Confocal

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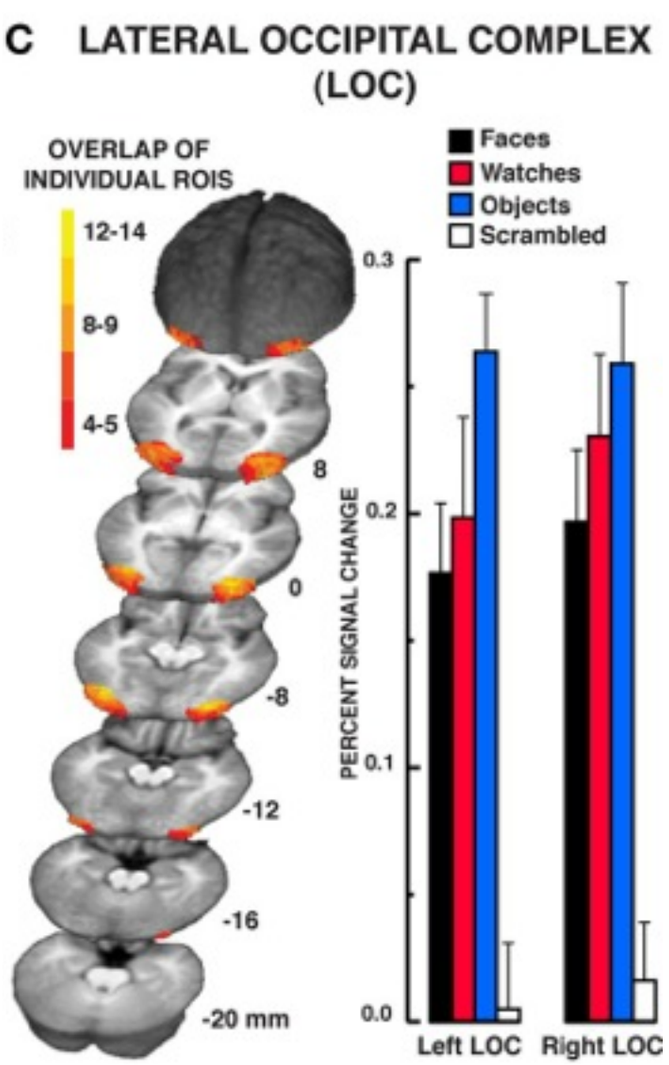
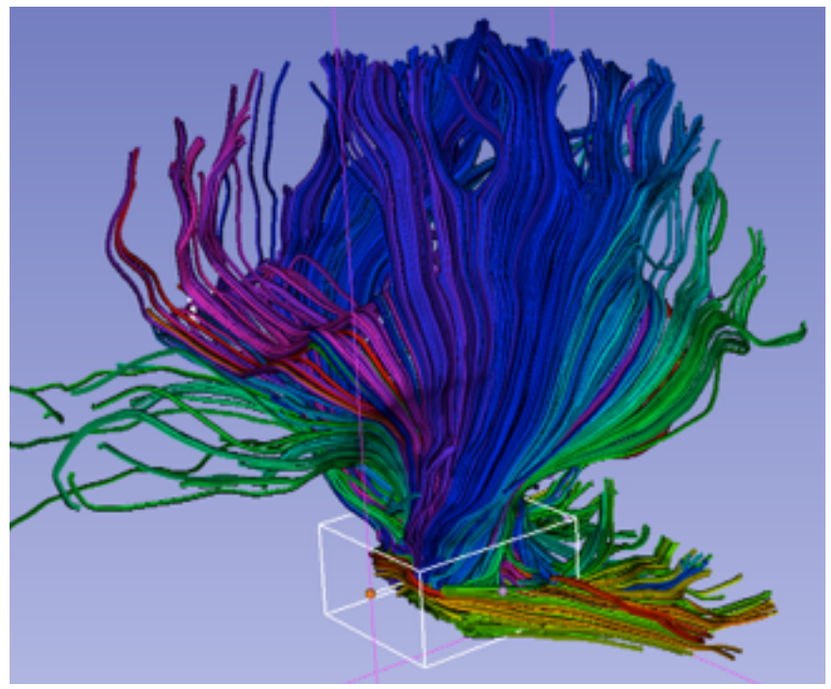
# Examples of Complexity

fMRI

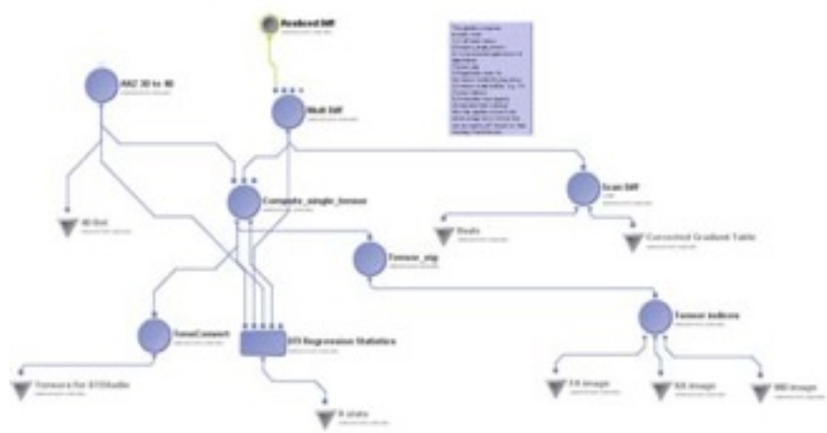
http://www.frontiersin.org/human_neuroscience/10.3389/fnhum.2010.00181/full

dMRI



DTI streamlines: http://wiki.slicer.org/slicerWiki/index.php/Slicer4:VisualBlog



DTI processing: http://www.loni.ucla.edu/~ophillip/DTIPipelines.html

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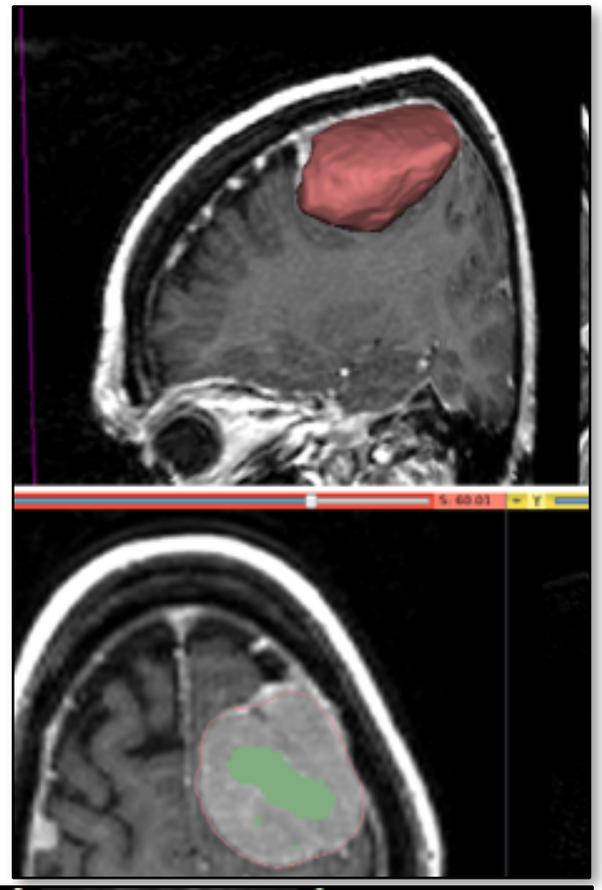
# What is MIC

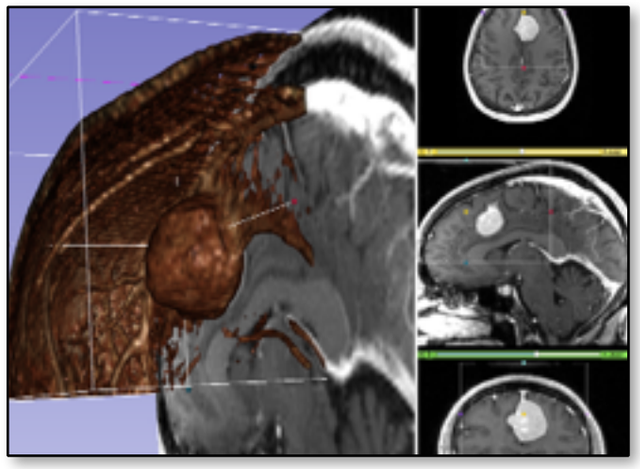
- Goal: extraction of clinically relevant information and knowledge from medical images using computational methods such as:
  - image segmentation
  - image registration
  - image-based physiological modeling
  - visualization

http://wiki.slicer.org/slicerWiki/index.php/Documentation/Nightly/Modules/RobustStatisticsSegmenter

result



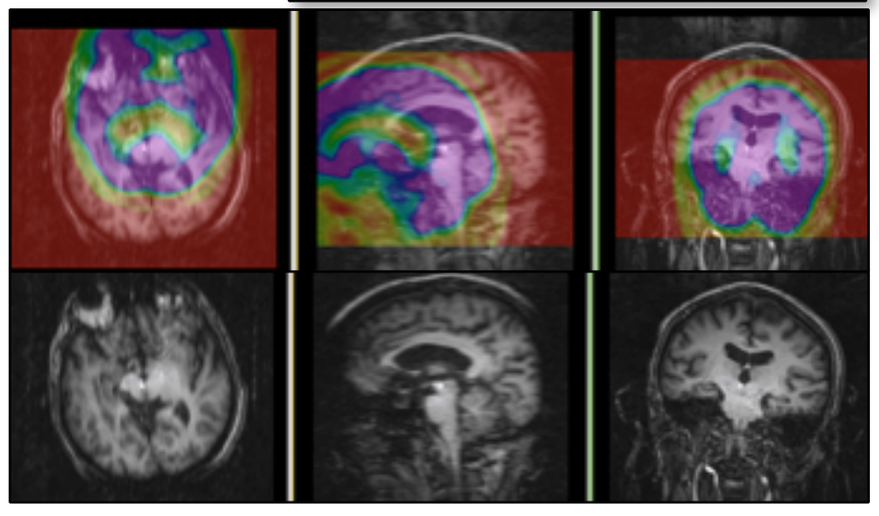
initialization



Volume rendering

before

after



http://wiki.slicer.org/slicerWiki/index.php/Documentation:Nightly:Registration:RegistrationLibrary:RegLib_C14

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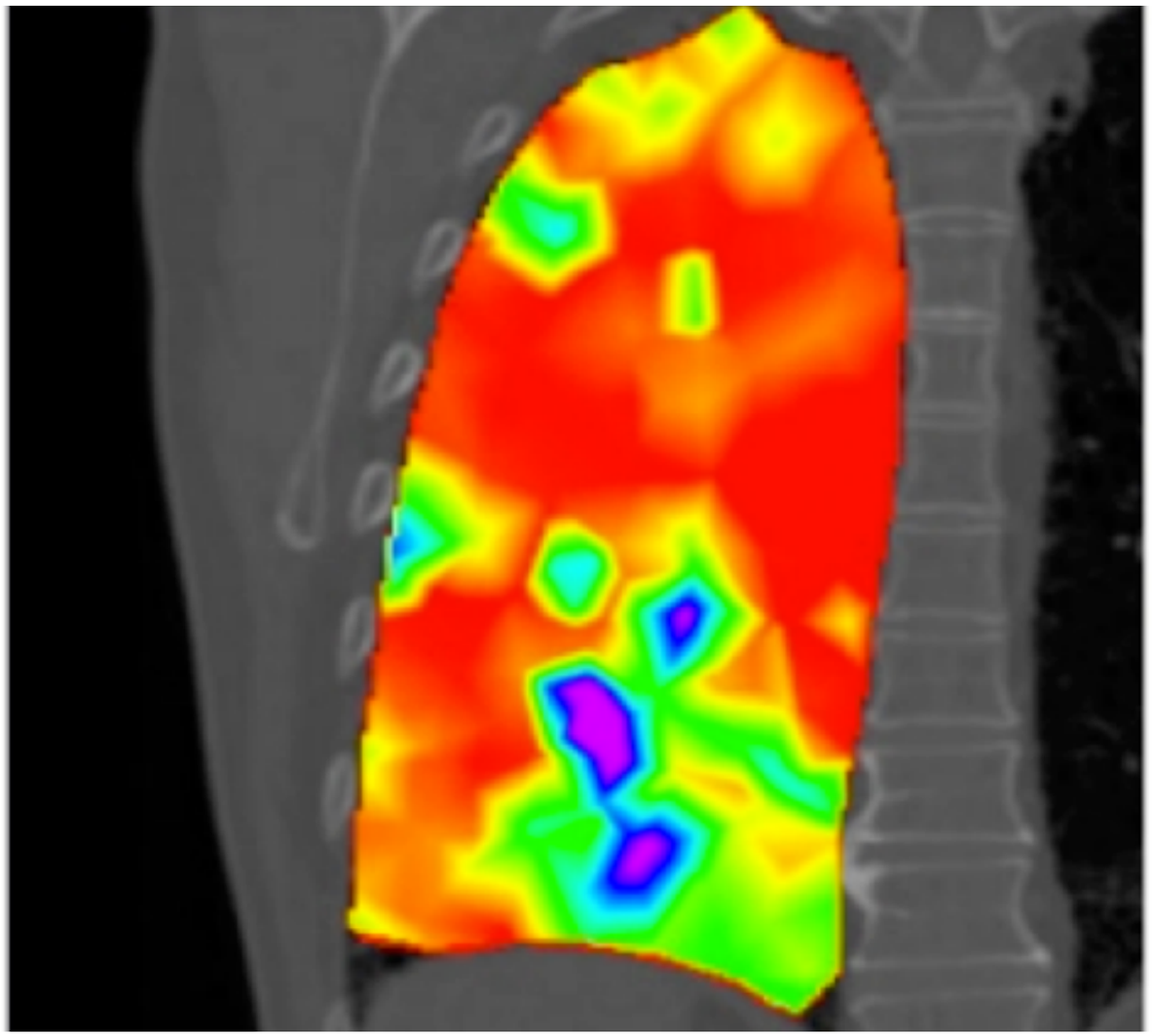
# The Increasing Importance of MIC

– More data and modalities: gigabytes to terabytes
– More complexity
  • fMRI, molecular imaging dMRI, 4DUS
– More applications
  • Discovery, Diagnosis
  • Therapy monitoring



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Risholm P., Ross J., Washko G.R., Wells III W.M. *Probabilistic Elastography: Estimating Lung Elasticity*. Inf Process Med Imaging. 2011;22:699-710. PMID: 21761697. PMCID: PMC3249413.

# Different Styles of Research

- Group Comparisons
- Subject Specific Analysis (SSA)

- Technologies are often developed for group comparisons
- Additional scientific research is necessary to use such technologies for SSA

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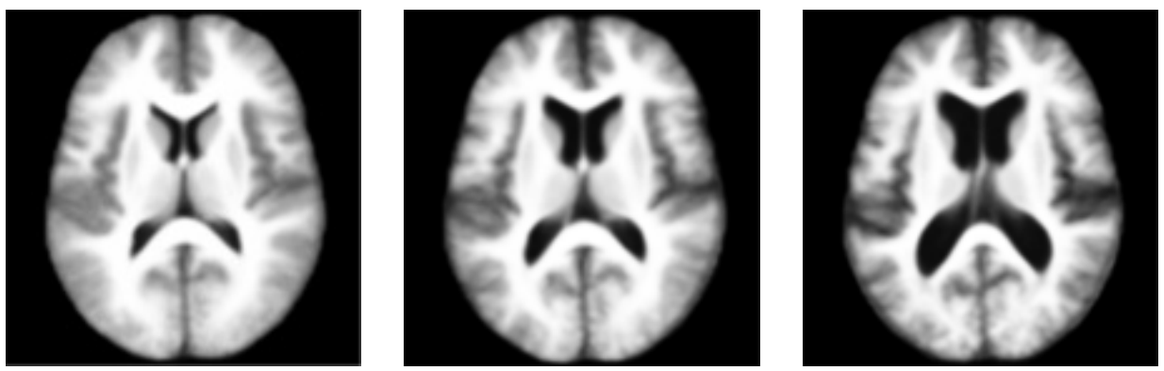
# Group Comparisons

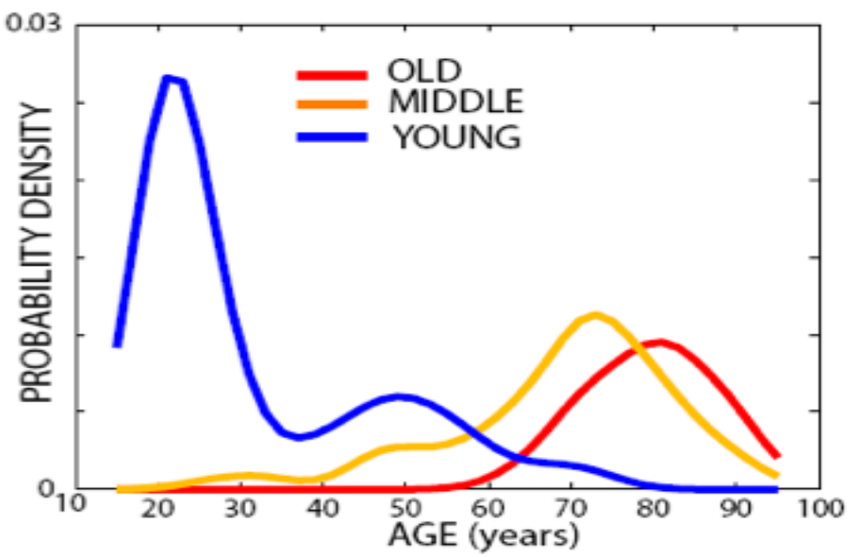
- Often used in basic imaging research
- Targets normal appearing structures. Questions: What is the….
  - Typical appearance
  - Normal variability
- Extensive resources are deployed: personnel, computational
- Most of our research is of this type, it's the easiest way to get results suitable for publication

M.R. Sabuncu, S.K. Balci, M.E. Shenton, and P. Golland. Image-Driven Population Analysis Through Mixture Modeling.
IEEE Transactions on Medical Imaging, 28(9):1473 - 1487, 2009



Young Middle Old

*3 Templates*

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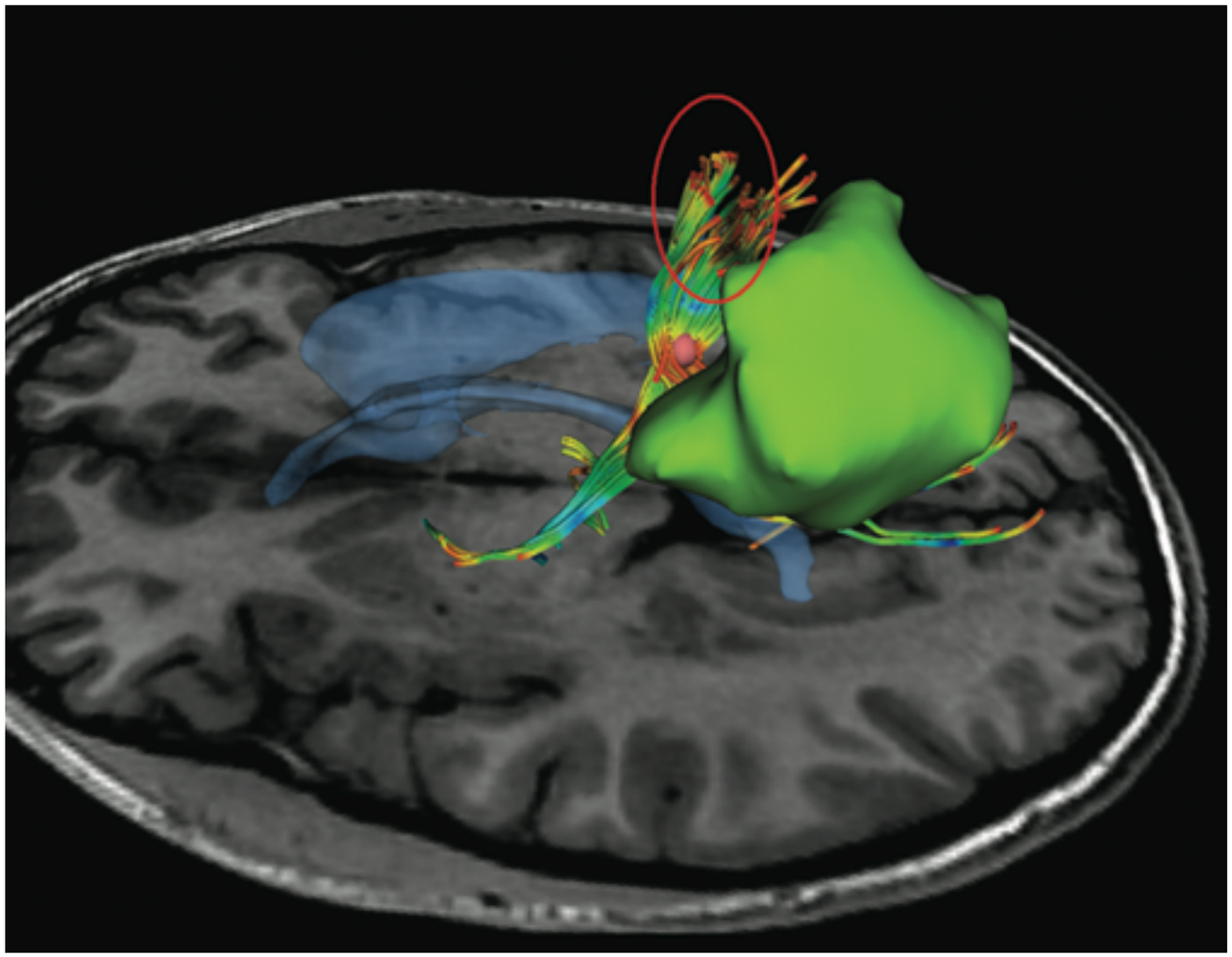
# Subject Specific Analysis

- Targets focal pathology:
  - Where is the pathology?
  - What are important surrounding structures
- Limited resources:
  - Time
  - Personnel
  - Computational
- Interactive work is the norm



Lack of quality in the processing pipeline can **NOT** be compensated by adding subjects
(you have only one subject)

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Golby A.J., Kindlmann G., Norton I., Yarmarkovich A., Pieper S., Kikinis R. *Interactive Diffusion Tensor Tractography Visualization for Neurosurgical Planning*. Neurosurgery. 2011 Feb; 68(2):496-505. PMID: 21135713

# Subject Specific Analysis (SSA)

- Quick and good enough is better than slow and perfect!
- Image processing problems cannot be compensated by adding subjects (you have only one)
- Interactive work is the norm

"**Ron's rules for tools**" is an informal set of rules that developers should keep in mind when working on interactive tools for translational clinical research. If you follow them, you will create tools that many people will use.

- You make it, I break it.
- Your tool does not exist, until it works on my laptop with my data.
- I am lazy. I do not like to move the mouse or to type.
- No more than one simple parameter.
- I have Attention deficit disorder: Make your algorithm fast.

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# SSA Challenges

- Many patients have visible pathology. Most MIC technology was developed for analysis of healthy looking subjects
- Tools need to be robust, easy to learn, and quick
- Due to the “valley of death”, very little technology has made it from research into clinical devices

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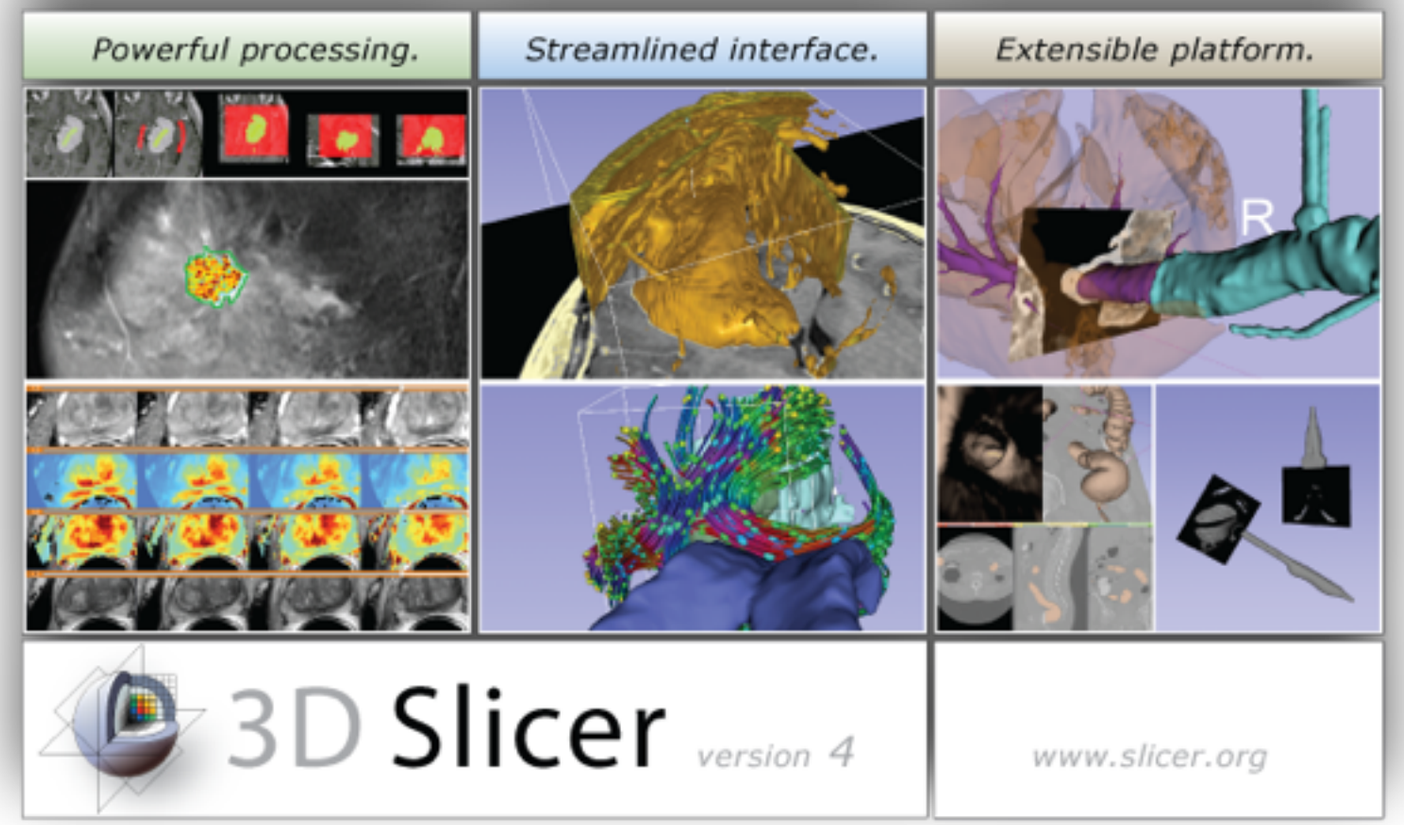
# 3D Slicer

- Platform for subject specific analysis
- An end-user application
- A platform for delivering software tools




  - Free open source software
    - Enables scientific collaboration
    - License allows painless translation to proprietary clinical tools
  - Well-engineered high-performance core
    - Software engineering methodology, multi-platform
  - Many options for extensions and for sharing them
  - Cross-platform

3DSlicer

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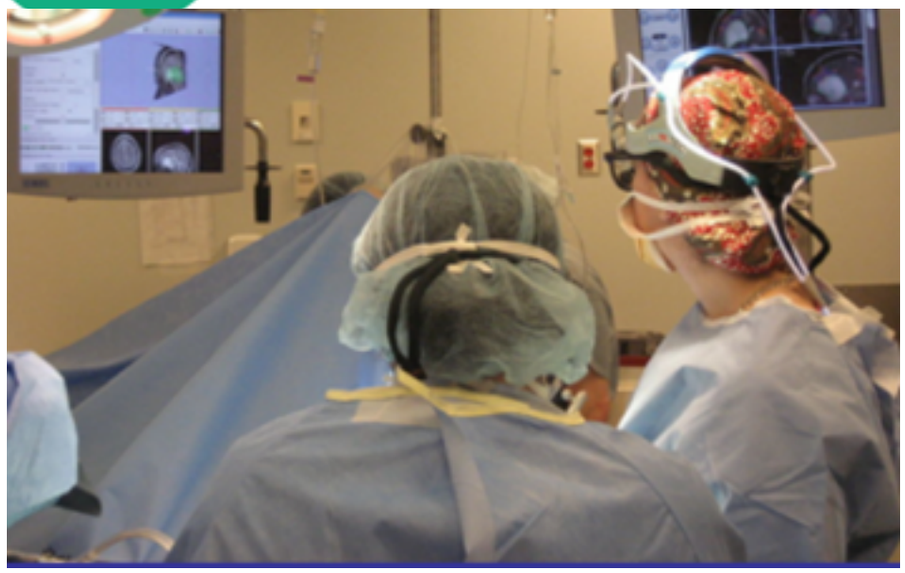
Picture courtesy Wendy Plesniak

# Easy to Use, Easy to Extend



## What does a user expect ?

- Easy Install and Upgrade
- “Standard” Clinical Behavior
- Advanced Functionality
- Consistent Interface
- Easily Deployable
- Extensible and Reconfigurable
- Rich Utility Libraries

3DSlicer

## What does a developer need ?

- Easily Deployable
- Extensible and Reconfigurable
- Rich Utility Libraries
- Stable Base

3D Slicer: a cross platform system for translating innovative algorithms into clinical research applications

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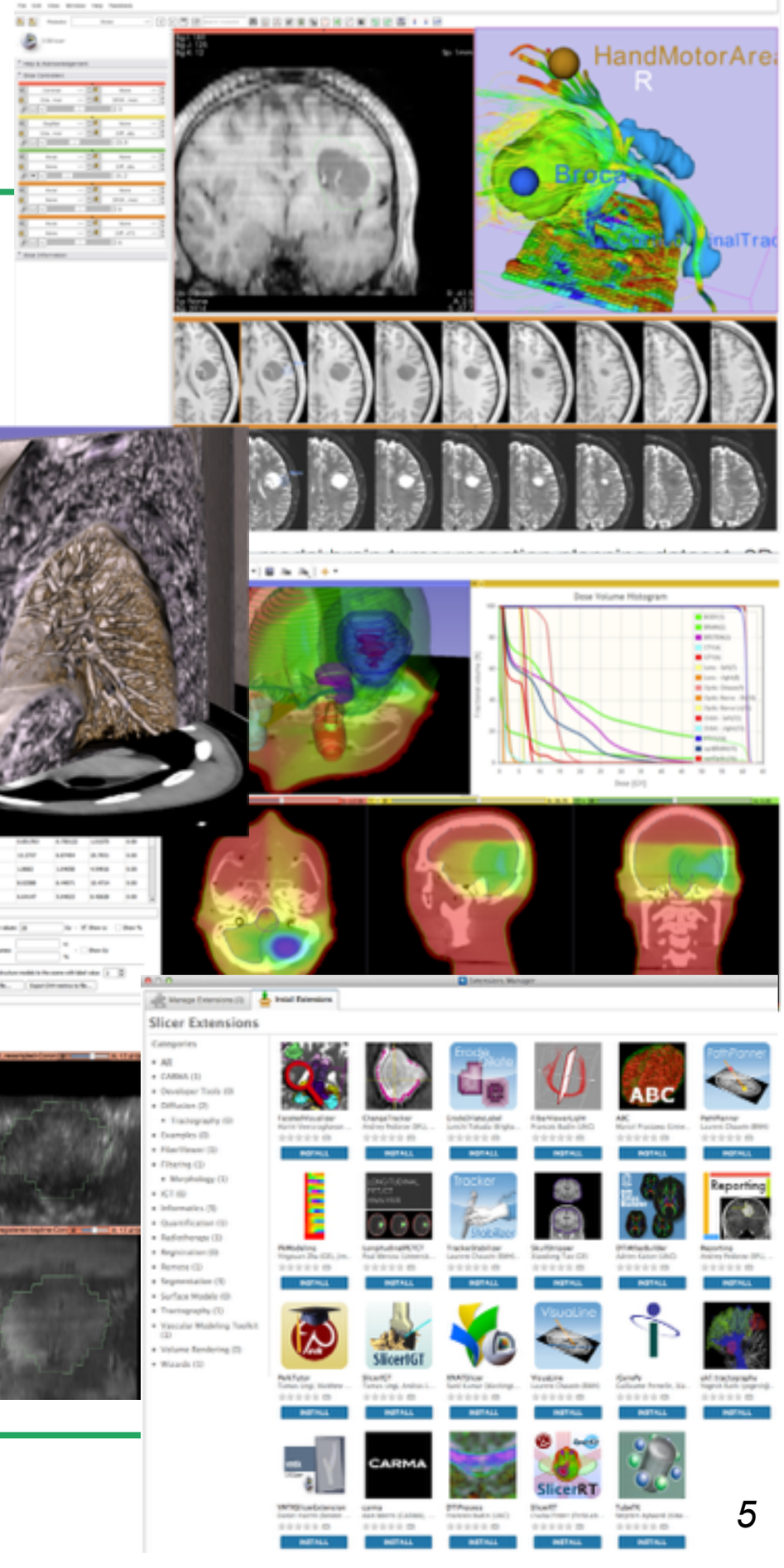
Courtesy S. Pujol, S. Pieper

# Slicer As A Platform

- Both basic and high-end features
  - Powerful visualization and layouts
  - Multi-modality, time series, segmentation, registration, dMRI
  - Dicom, PACS, device interfaces
  - Extensible through Python, Plug-ins
  - “App store” for sharing extensions

- Support and training
- Cross-platform
- *Research software*
  - *not FDA approved*

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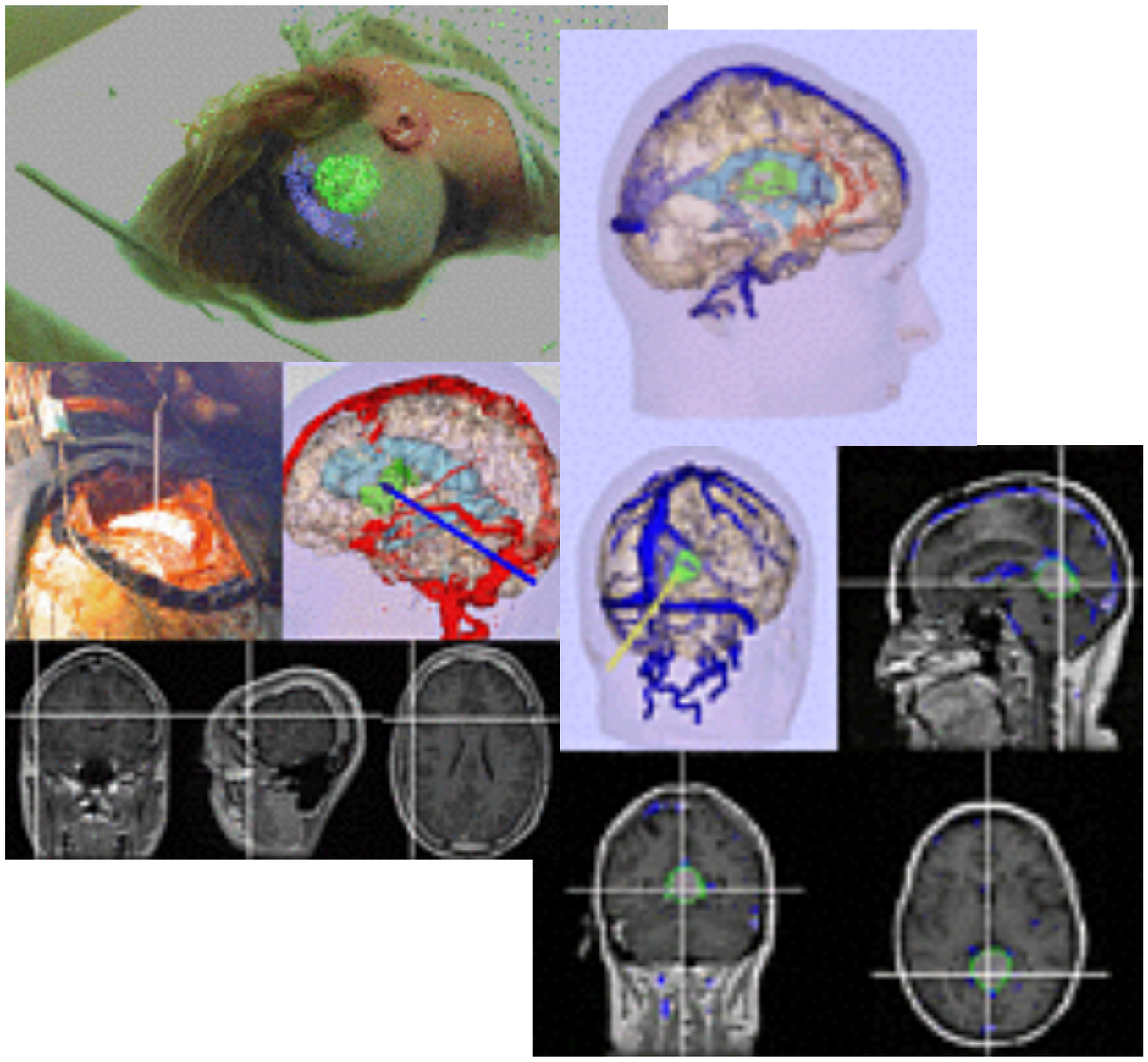
# 3D Slicer History

1997: Slicer started as the masters thesis of David Gering, in a collaboration between the Surgical Planning Lab (Harvard) and CSAIL (MIT)



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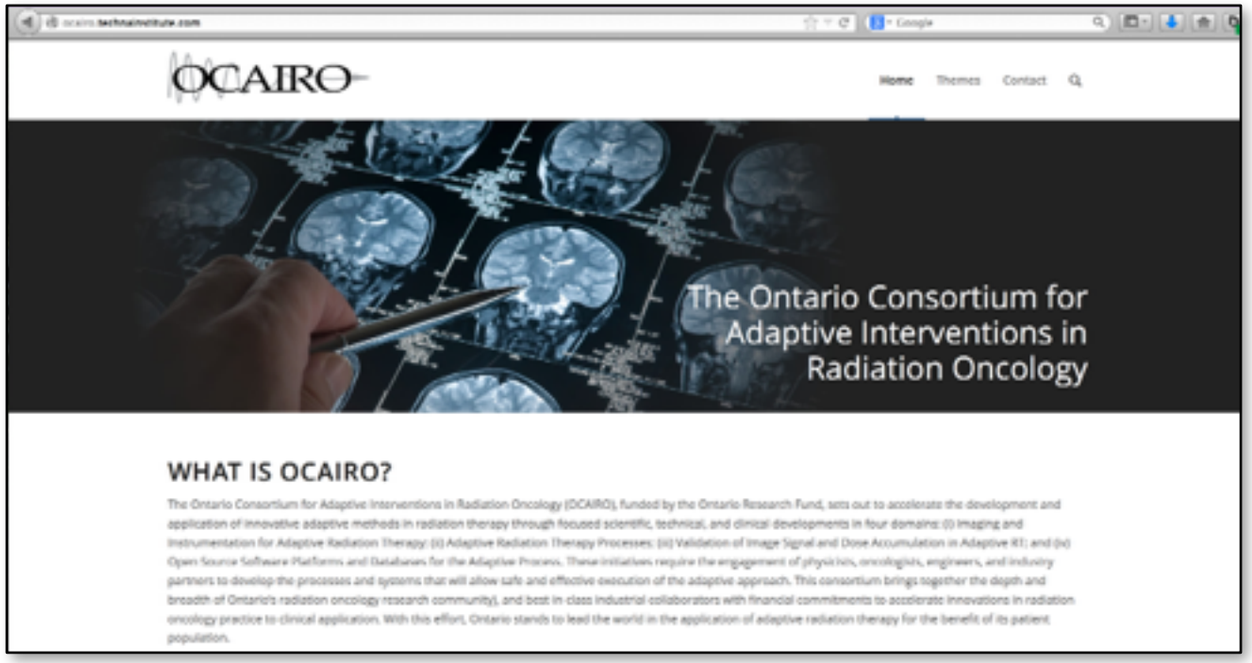
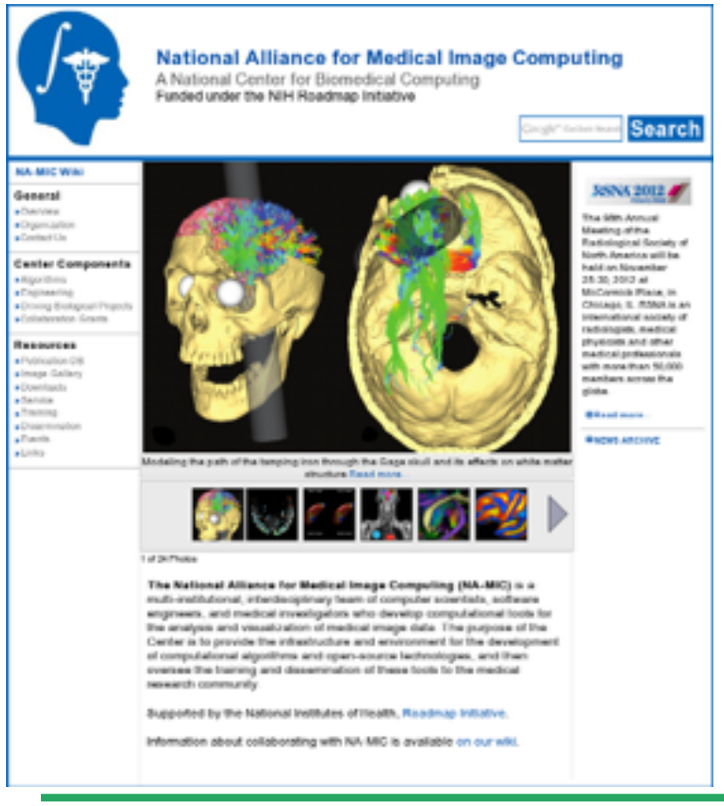
Images Courtesy of the CSAIL, MIT

# 3D Slicer Today

- Community Effort

quantitative image informatics
QIICR
for cancer research



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# Slicer Community At A Glance

3D Slicer project analysis from Ohloh.net http://www.ohloh.net/p/3376

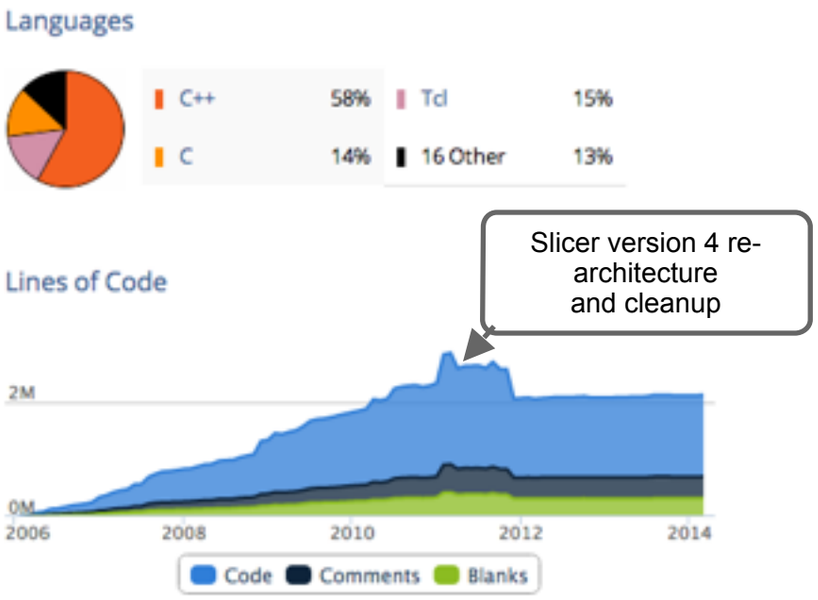
In a Nutshell, Slicer...

... has had 33,653 commits made by 91 contributors representing 1,427,063 lines of code

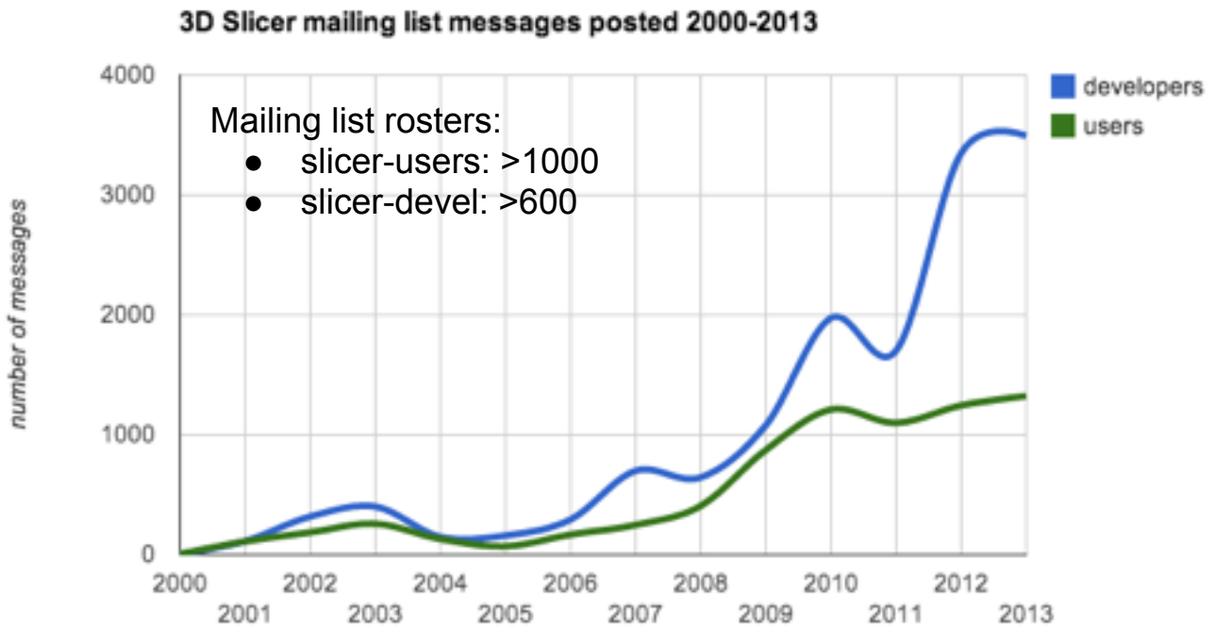
... is mostly written in C++ with an average number of source code comments

... has a well established, mature codebase maintained by a large development team with decreasing Y-O-Y commits

... took an estimated 403 years of effort (COCOMO model) starting with its first commit in January, 2006 ending with its most recent commit about 20 hours ago

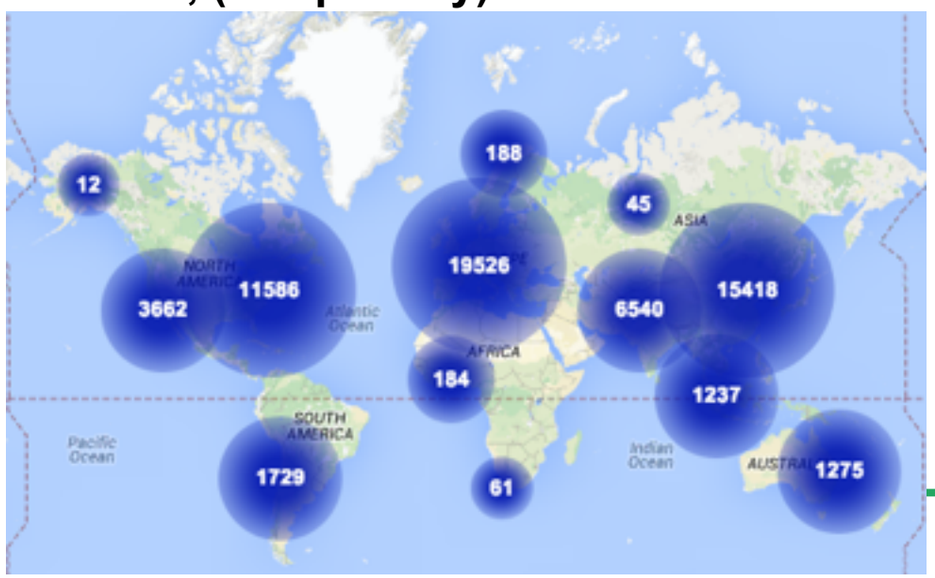


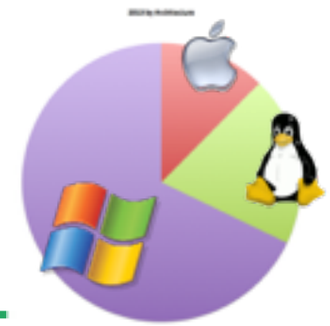

http://commontk.org




http://massmail.spl.harvard.edu/public-archives/slicer-users/
http://massmail.spl.harvard.edu/public-archives/slicer-devel/

Total number of 3D Slicer downloads in 2013:
**61463, (160 per day)**

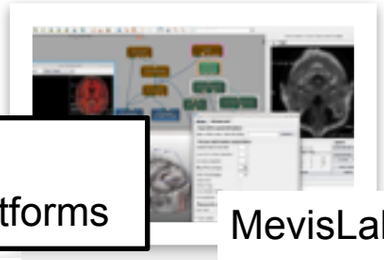


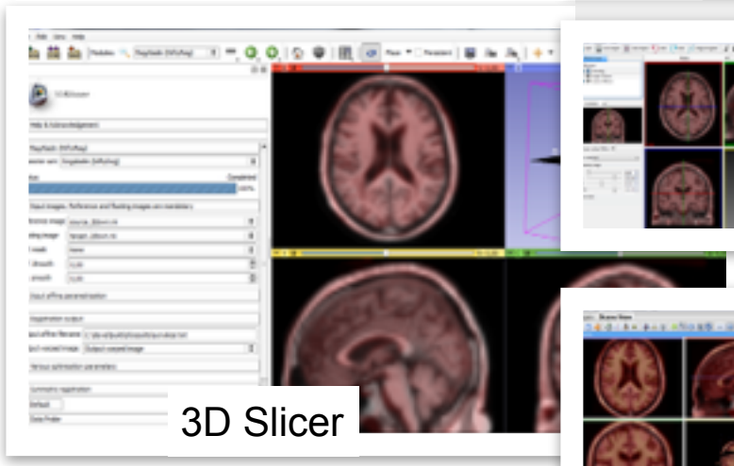
http://download.slicer.org/stats

# Features

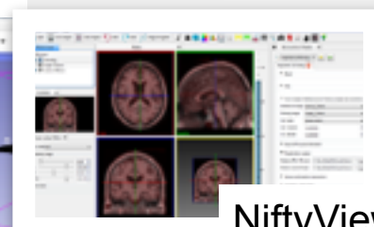
CLI Plug-ins
Shareable across several platforms



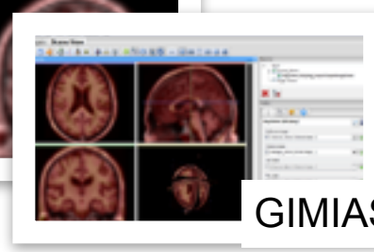
MevisLab



3D Slicer



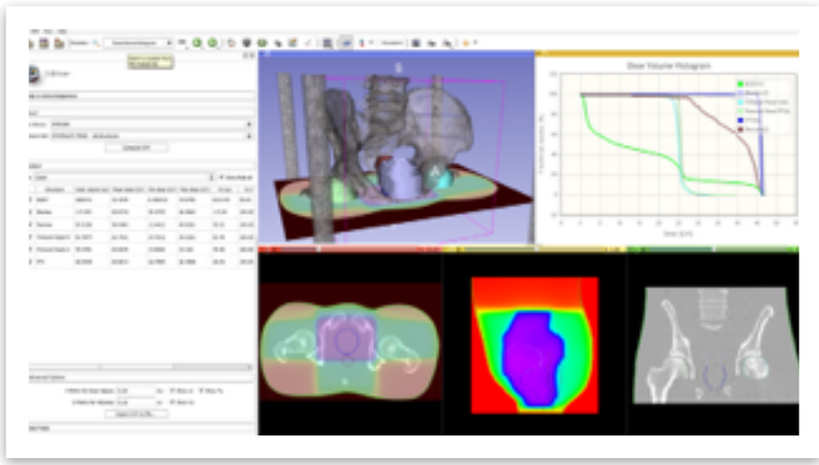
NiftyView



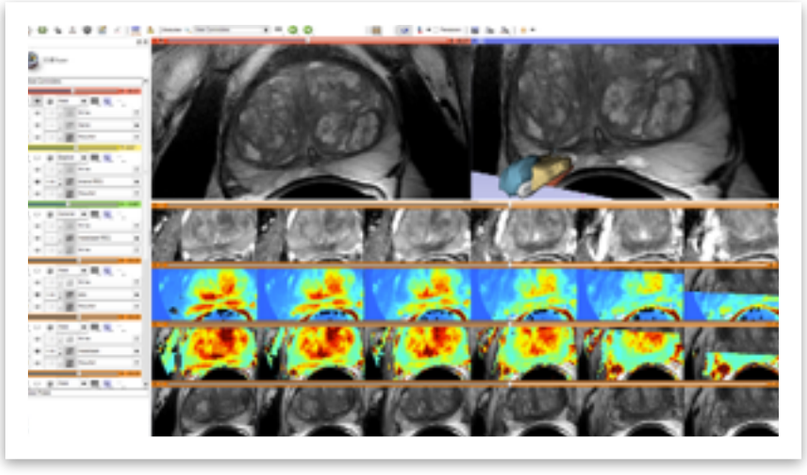
GIMIAS

- Volume Rendering
- .mrb files
- Layouts
- Sceneviews
- Annotations
- DICOM

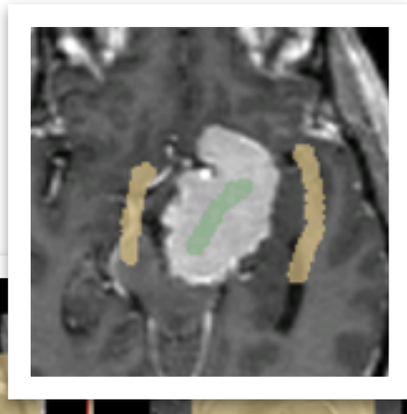
Quantitative imaging
Line, scatter, bar charts

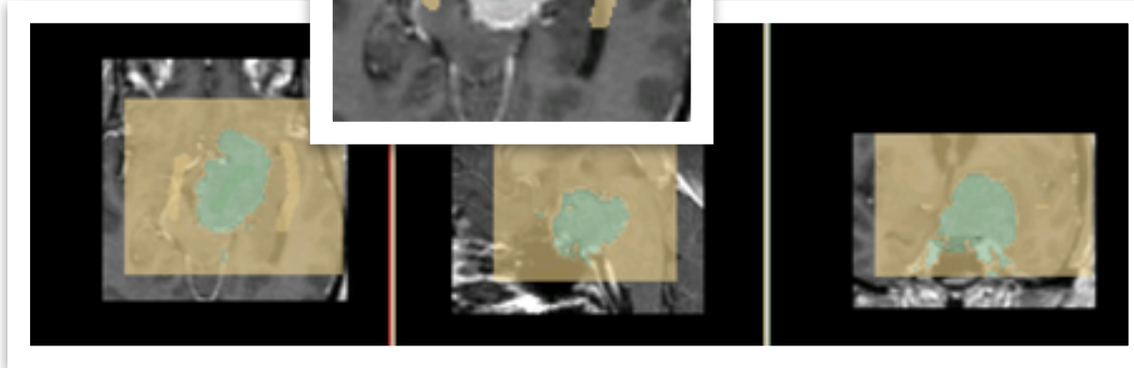


Support for multi-dimensional data
Compare view, Lightbox, crosshair



Interactive
Segmentation





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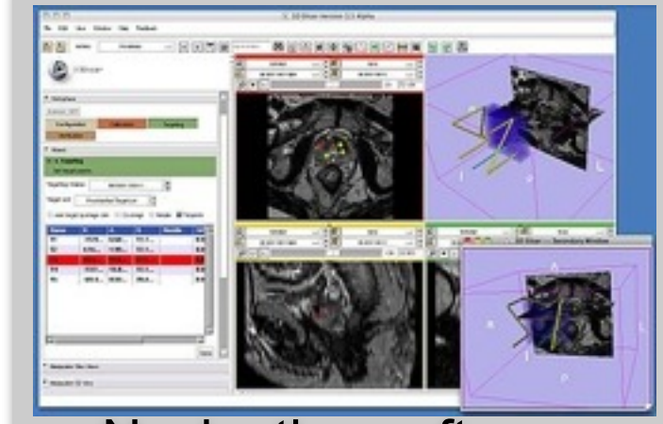
# Slicer and Devices

- Two-way communication
  - Imaging devices
  - Optical tracking devices
  - Robotic devices
  - More



Navigation software

Image

Transform

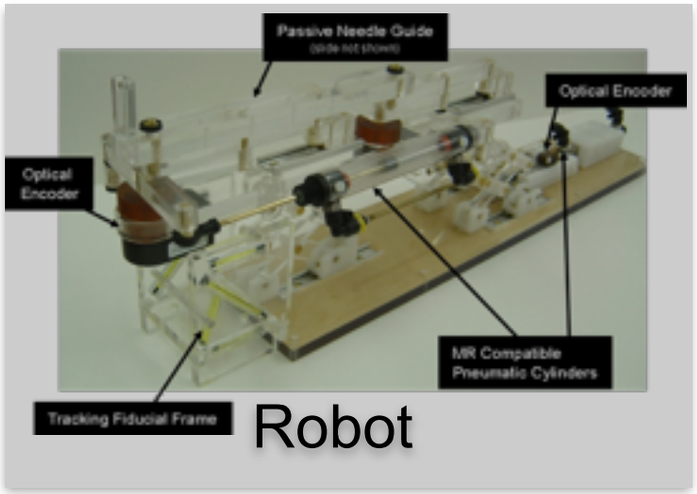
Scanner

OpenIGTLink

Tracking devices

Status

Command




Robot

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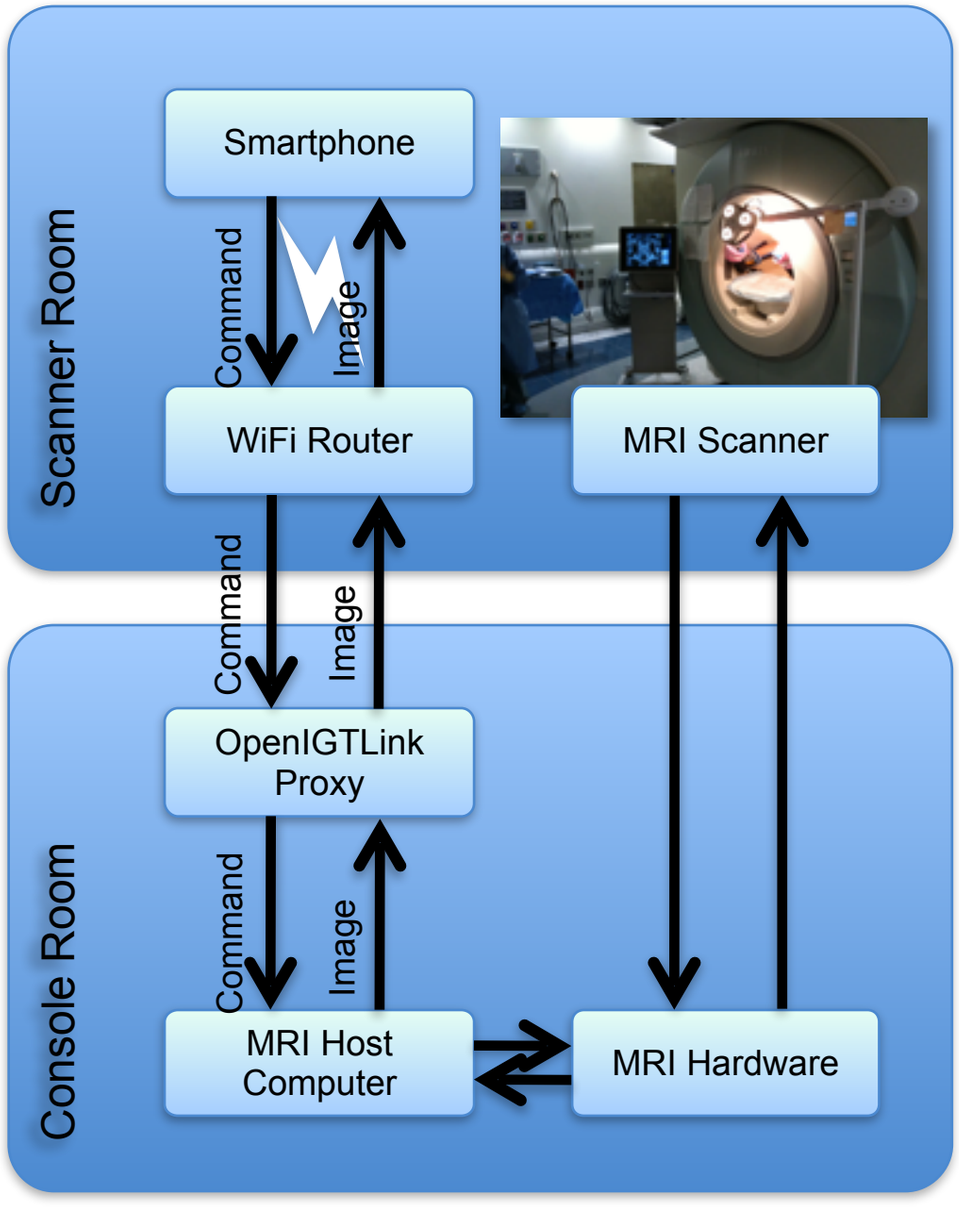
Slide courtesy J. Tokuda

# OpenIGTLink: API for Devices

## Use an iPhone to control scan plane acquisition



Tokuda J., et al. CARS 2012, June 27-30, Pisa Italy

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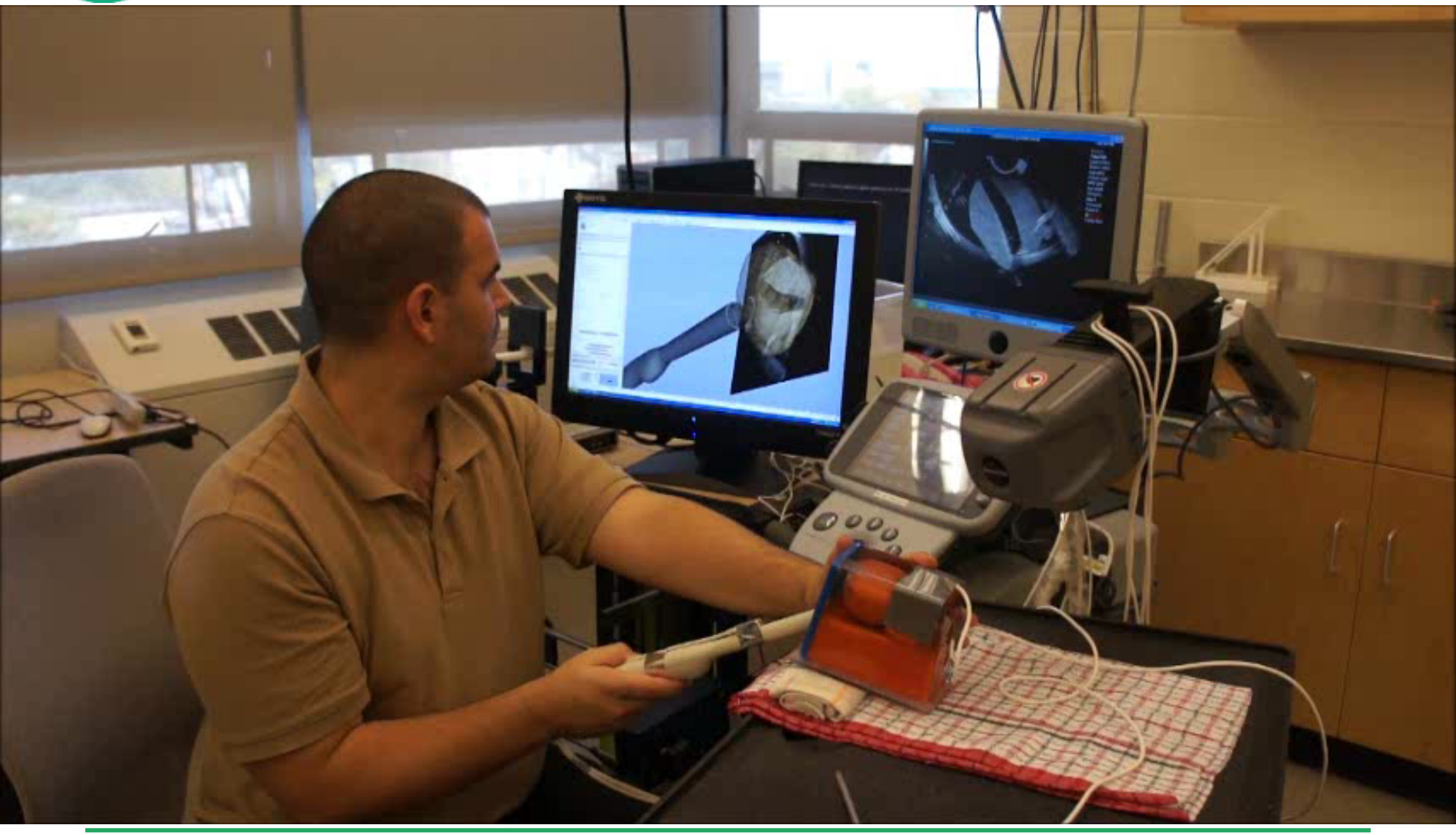
# US Tracking: 2011: Bench



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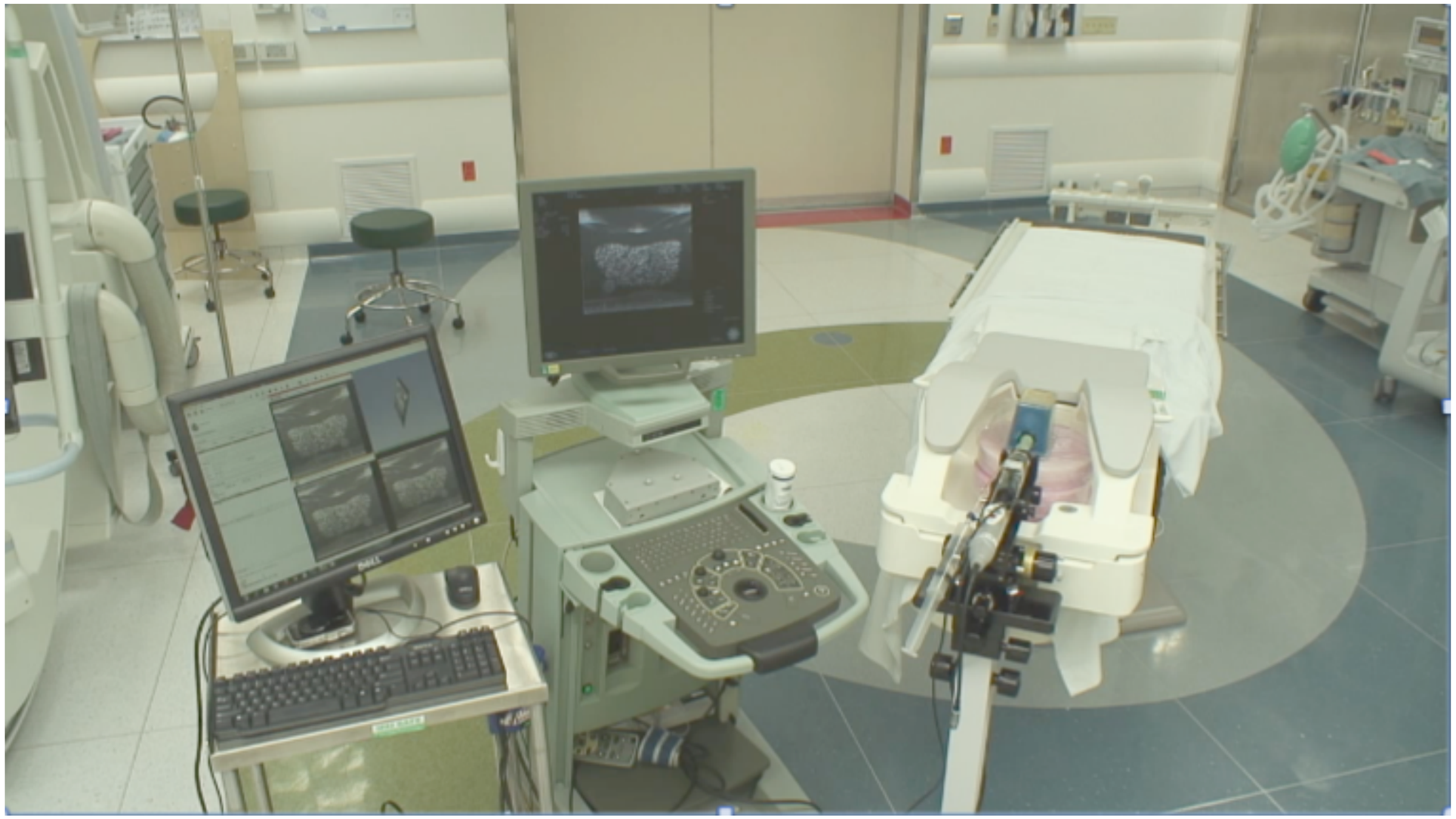
Movie courtesy Ungi, Lasso, Fichtinger

# US Tracking 2012: To Bedside

Sketch courtesy Wendy Plesniak

Research setup in AMIGO showing BK ProFocus and TRUS BK 8848 transrectal probe with orientation spatial sensor, interfaced to 3DSlicer via PlusServer library and OpenIGTLink.



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# 3D Printing

- 3D printing is a commodity today
- Is revolutionizing prototyping
- Hardware increasingly resembles software: the value is in the design

Image courtesy N. Farhat

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# Web Capabilities

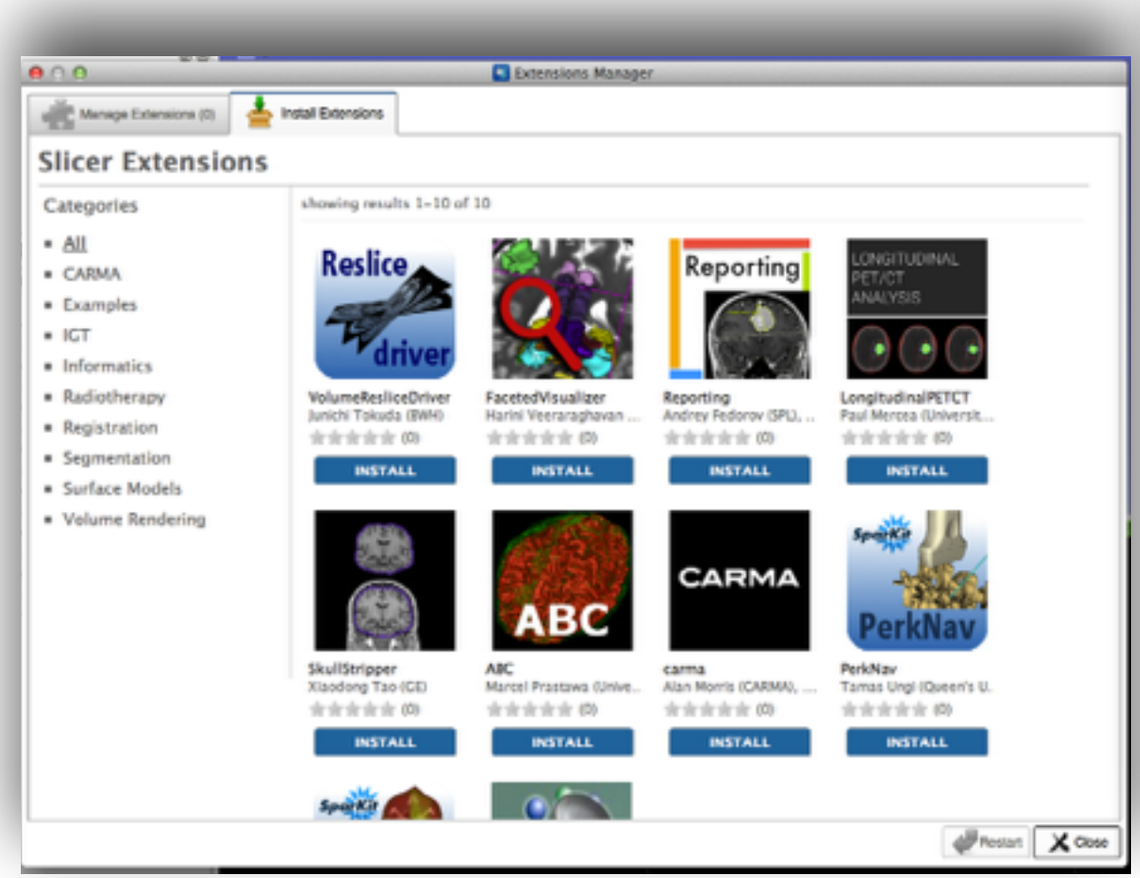
## QtWebKit enables Web services

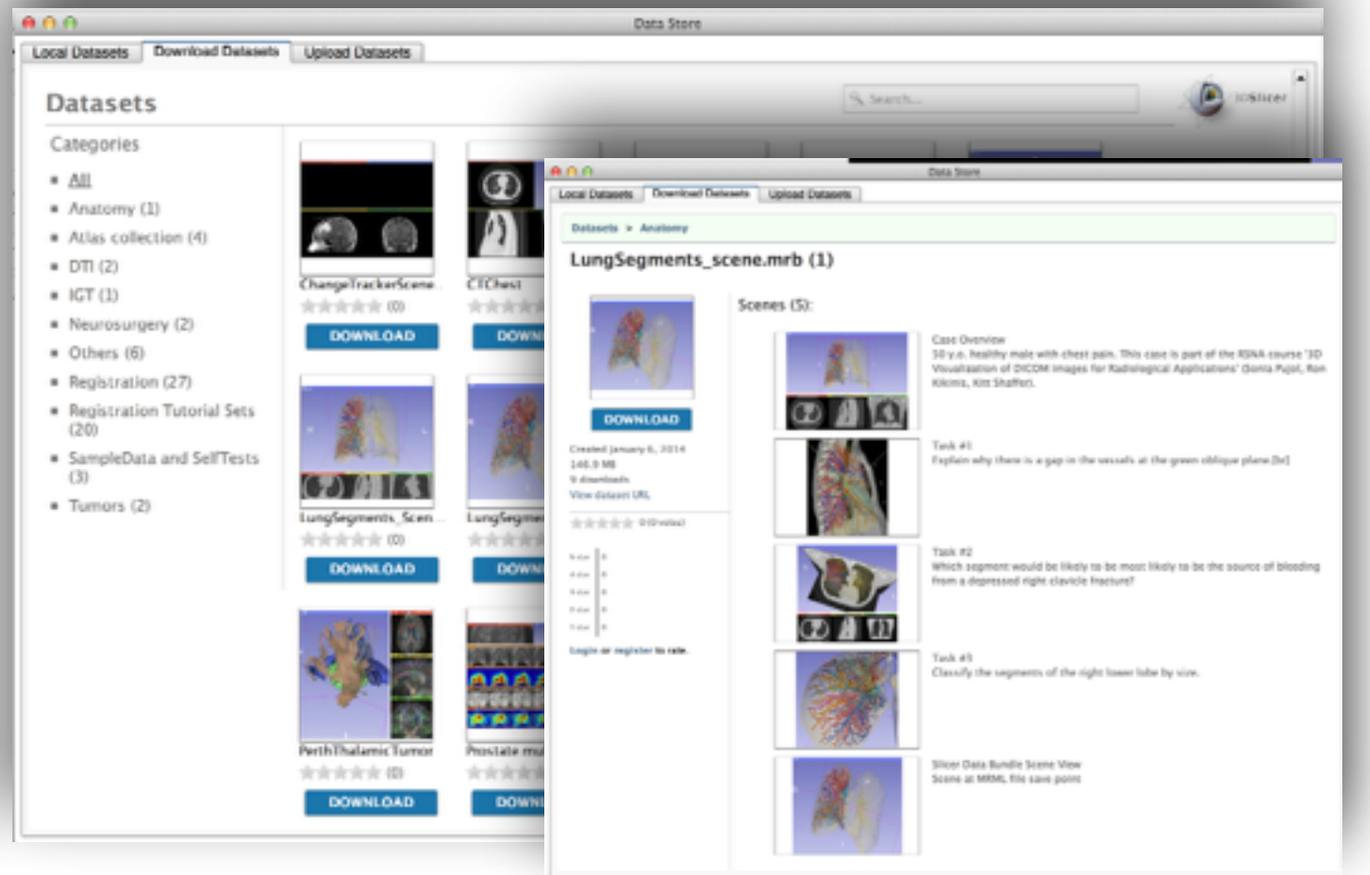
**Extension Manager and catalog**

- Share plug-ins with users
- Easy Installation

**Data Store**

- Web-based public repository of .mrb files allows sharing
- Sceneviews are exposed in the web interface

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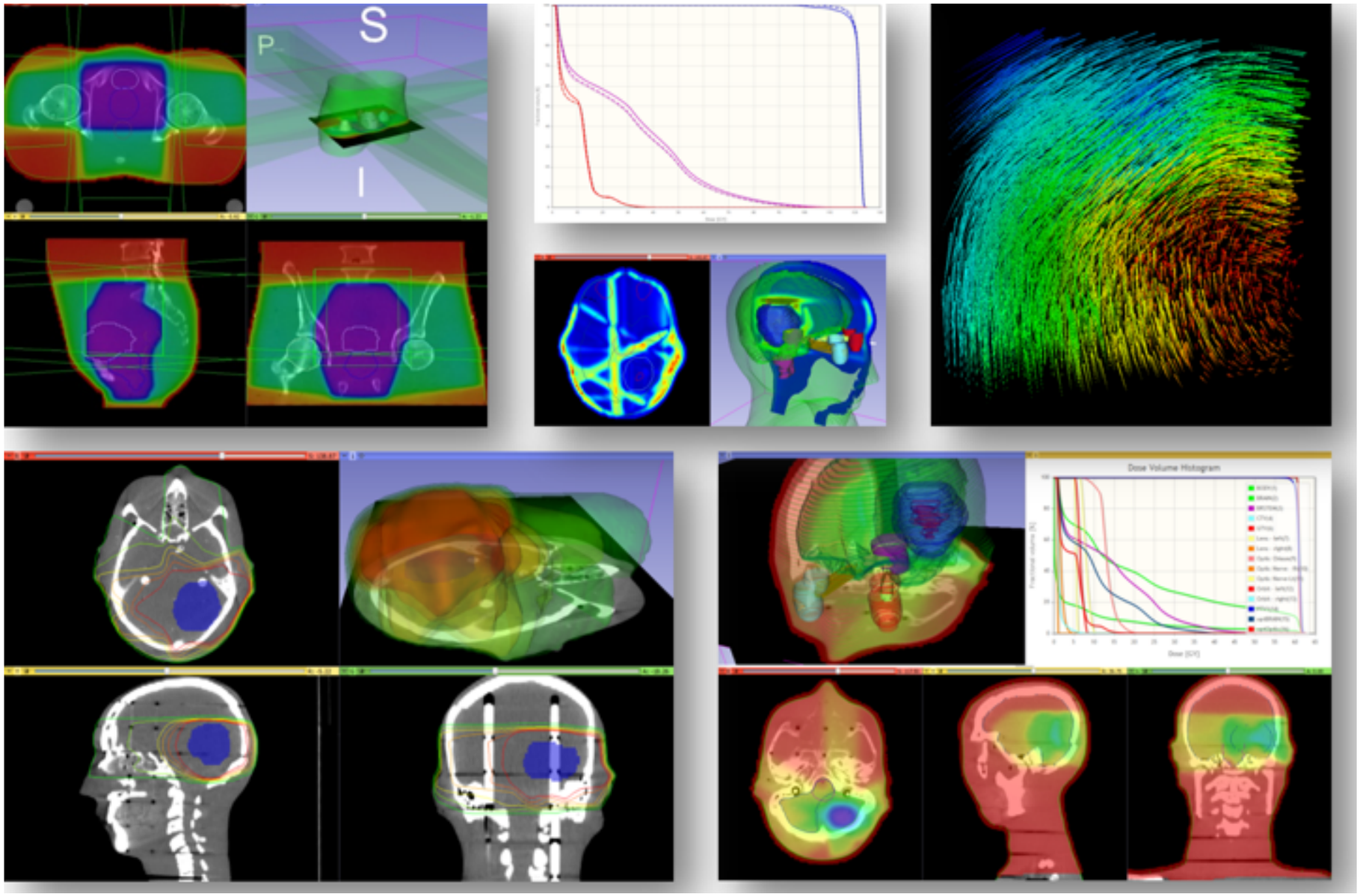
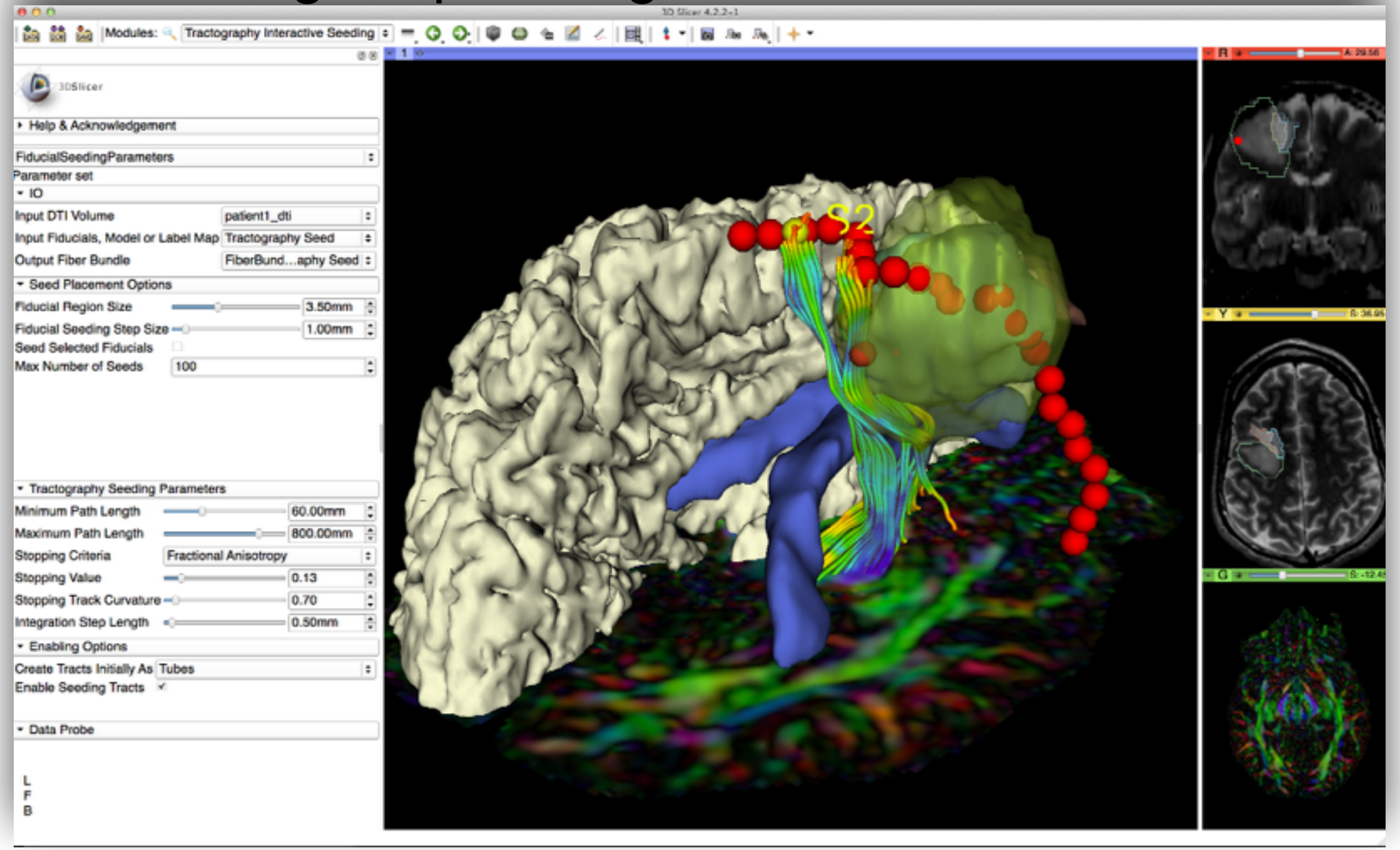
# Clinical Example 1

- Radiotherapy research extensions: Dicom RT, dose distributions and many more….



# Clinical Example 2

- Surgical planning

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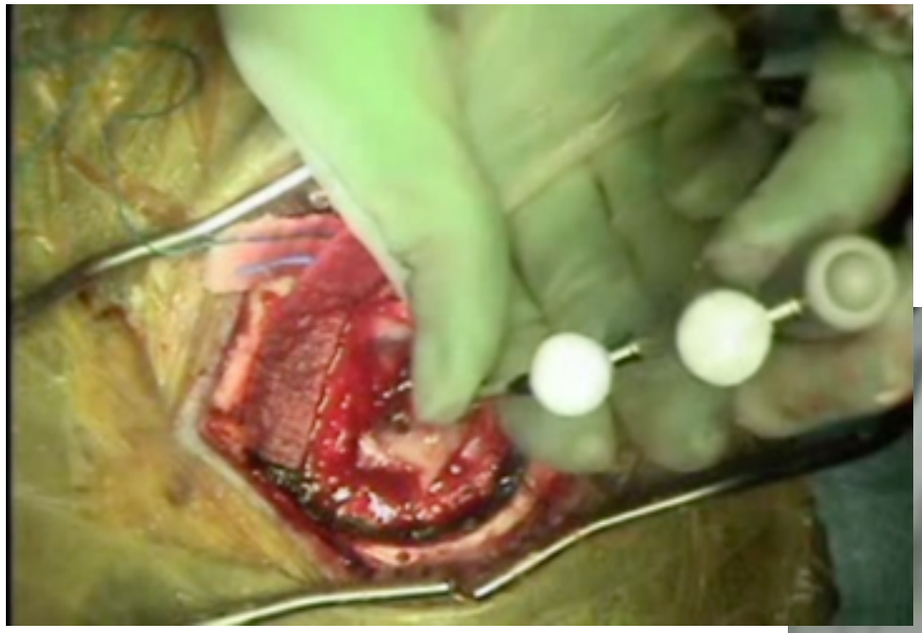
Courtesy S. Pujol, A. Golby

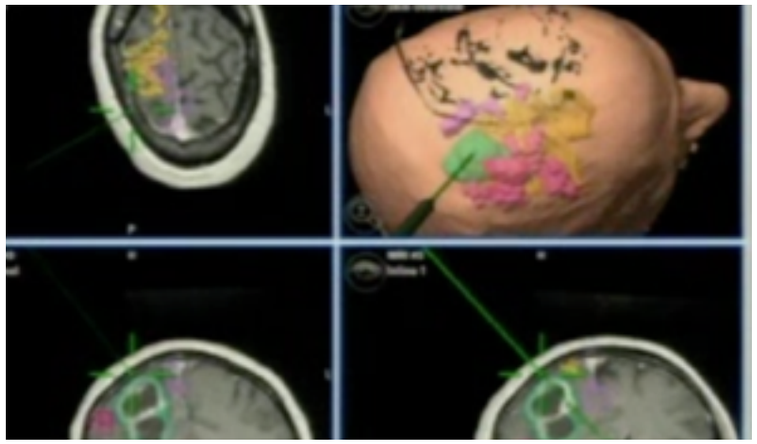
# Clinical Example 3

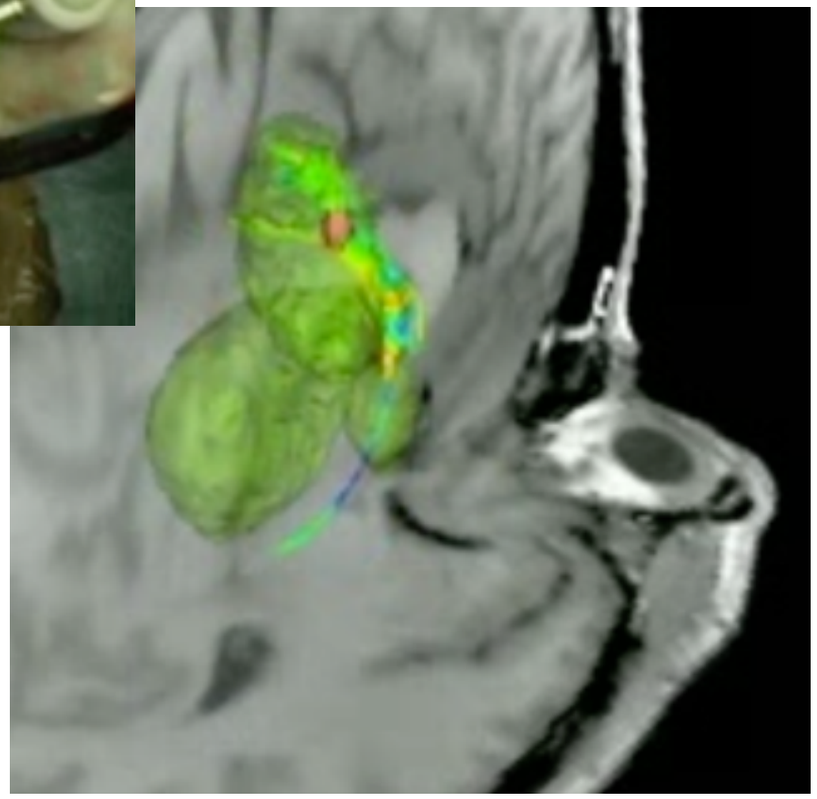
Image Guided Therapy

Interfacing to clinical devices

- Intraoperative Fiber Tracking
- Relies on pre-op data
- Slicer+Brainlab







©2013 Surgical Planning Laboratory, ARR

Images courtesy A. Golby

# Clinical Example 4

Image-guided navigation to localize and excise parathyroid adenoma

©2013 Surgical Planning Laboratory, ARR



Slide courtesy of Jayender Jagadeesan

# AMIGO Parathyroid Team

- Surgeon: Daniel Ruan, MD
- Radiologist:  Thomas Lee, MD
- Navigation Scientist: Jayender Jagadeesan, PhD

## AMIGO Support Team

- Techs/Nurses: Dan Kacher, Janice Fairhurst, Angela Kanan, Shivon Cesar, Sue Sheehan, Sandra Lawson, Julia Bousquet, Sean Jackson, Nikita Aristarkhov

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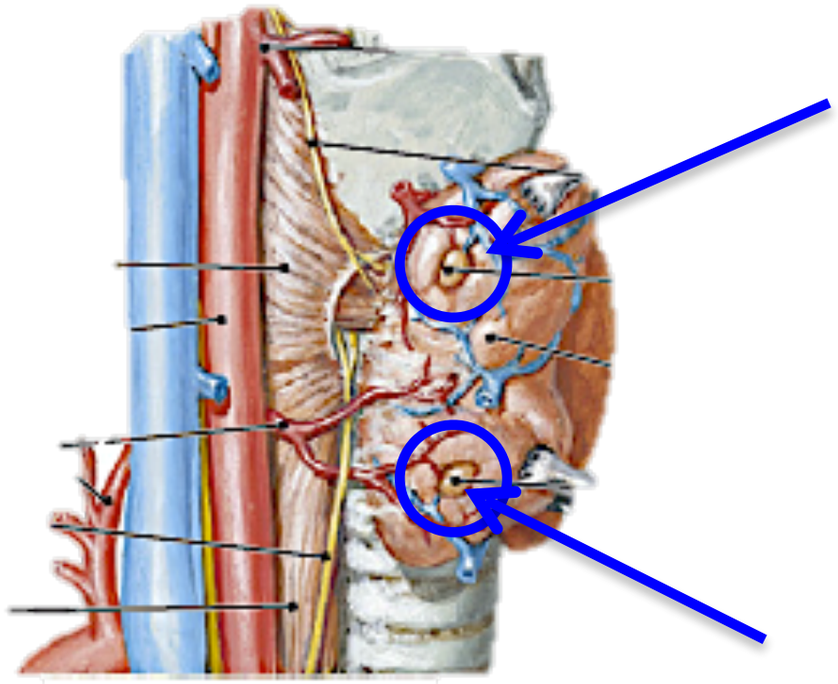
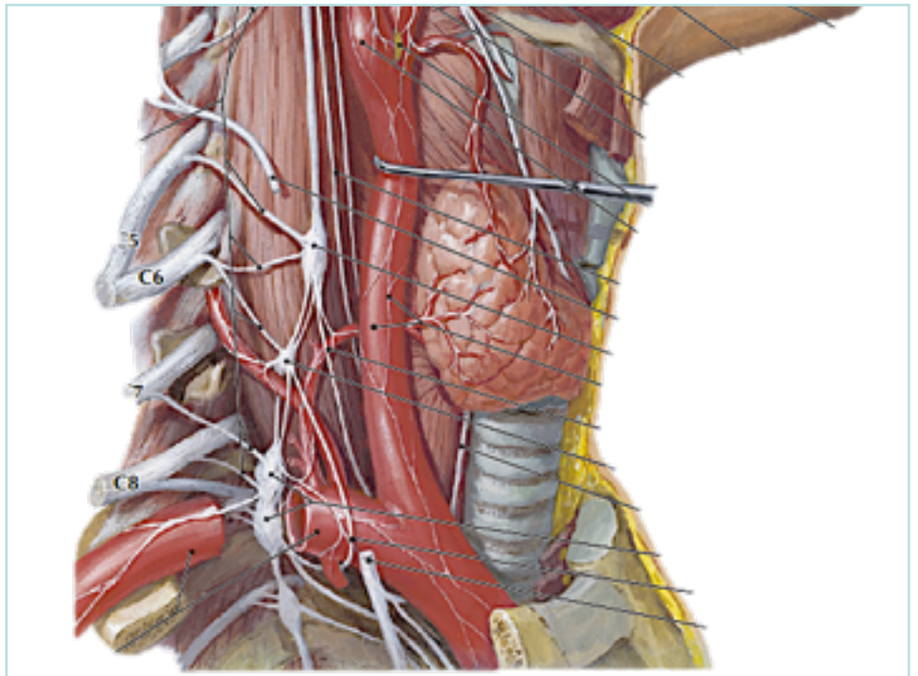
# Problems with Diagnosis and Surgical Resection






- Small glands hidden behind the thyroid gland
- As small as a rice grain
- Numerous sensitive structures around the parathyroid making surgical resection difficult
- Damage to laryngeal nerve could lead to hoarseness, inability to speak and difficulty in breathing

©2013 Surgical Planning Laboratory, ARR



Photo: Netter

# Intraoperative MRI

- Fiducials placed on the patient for enabling “Patient-to-Image” registration
- Cardiac coil utilized for imaging the patient
- Cartridge built to house the cardiac coil and EM flat plate transmitter
- Imaging
  - Gross T1 3mm slices
  - Hi-res T2 images

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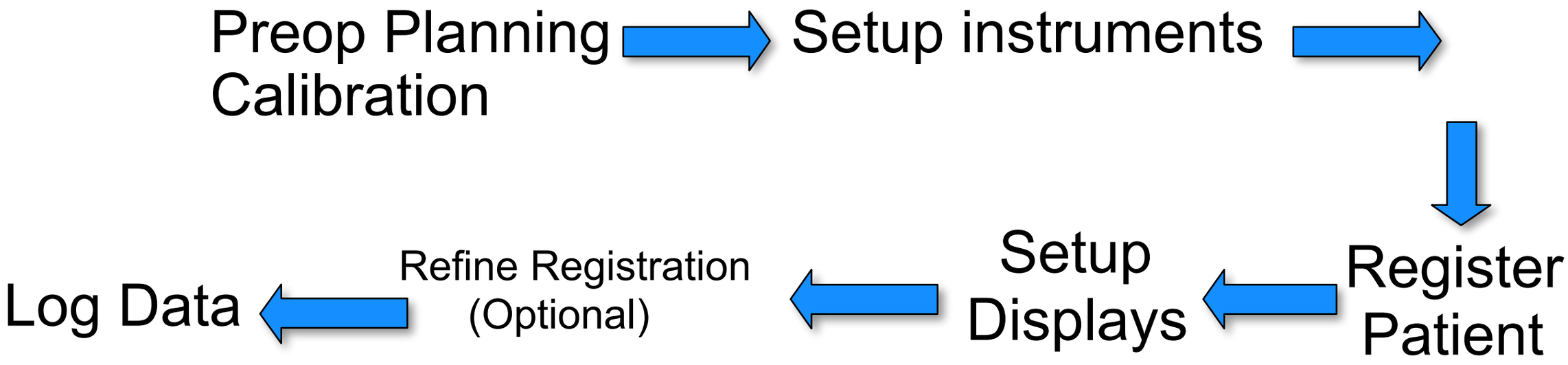
# Intraoperative Guidance

- Module developed in 3D Slicer
- Software and ATC hardware decoupled
  – OpenIGTLink communication
- Wizard Workflow

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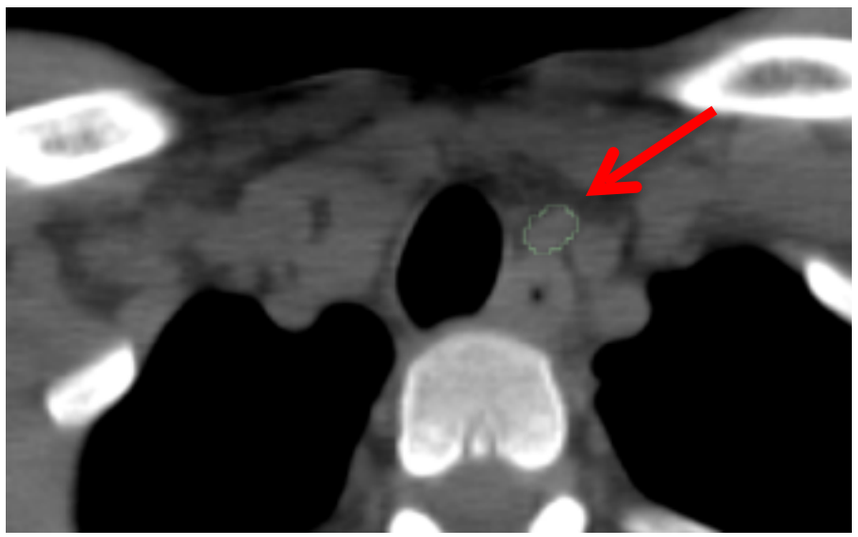
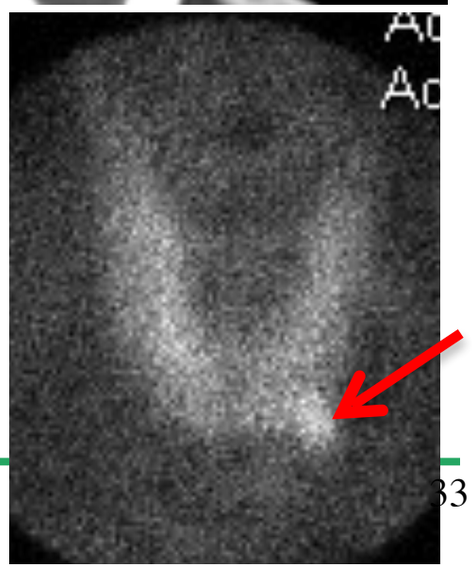
# Diagnostic Imaging

DCE MRI

CT



Sestamibi scans



Jayender et. al, Segmentation of parathyroid tumors from DCE-MRI using Linear Dynamic System analysis, ISBI 2013

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# Intraoperative Video

x 2 speed

©2013 Surgical Planning Laboratory, ARR



Slide courtesy of Jayender Jagadeesan

# Result of Navigation System

**Smart Pointer**

How accurate was the smart pointer in localizing the tumor?

Not accurate

Very accurate

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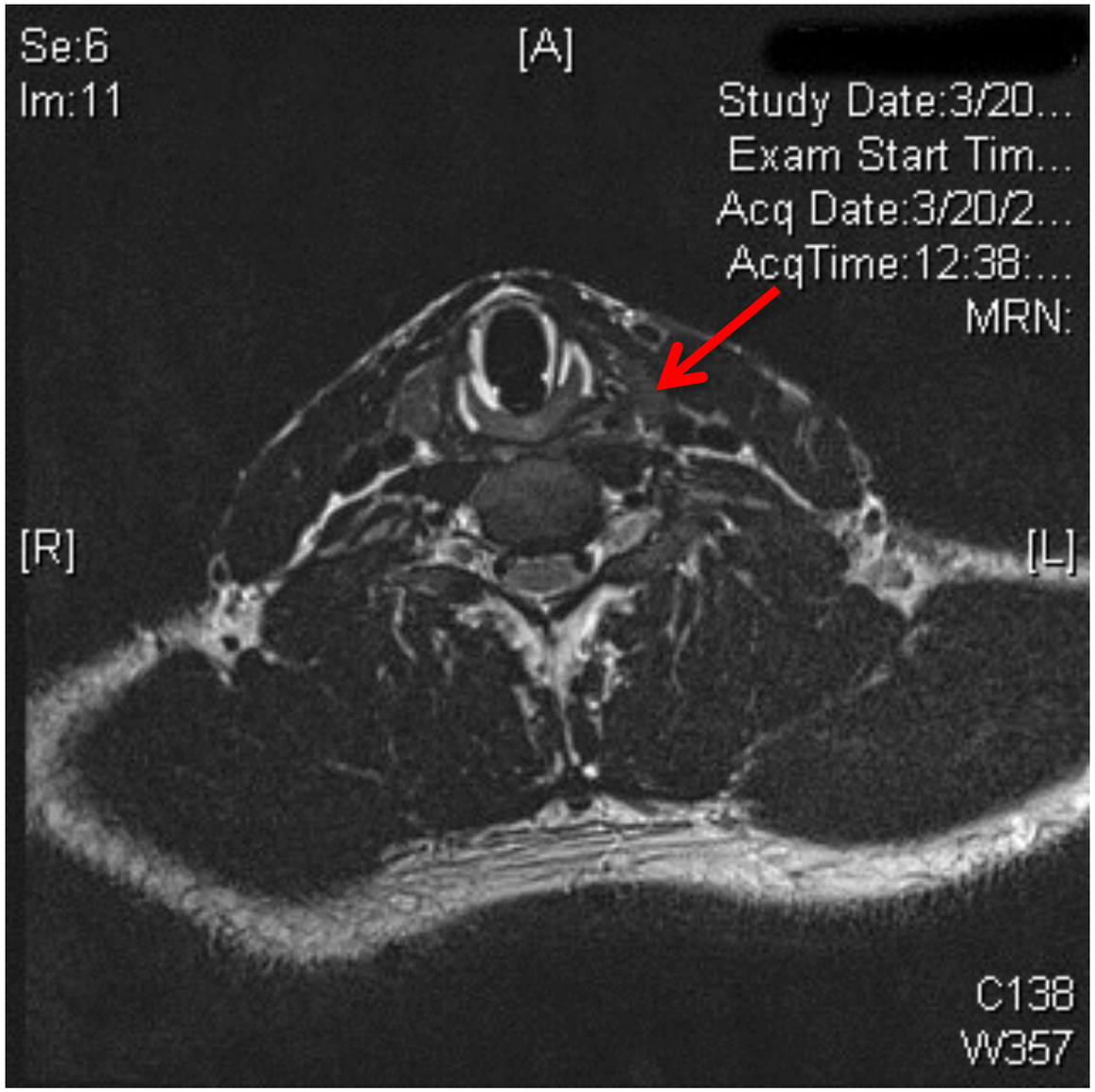
Slide courtesy of Jayender Jagadeesan

# Postoperative scan

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Slide courtesy of Jayender Jagadeesan

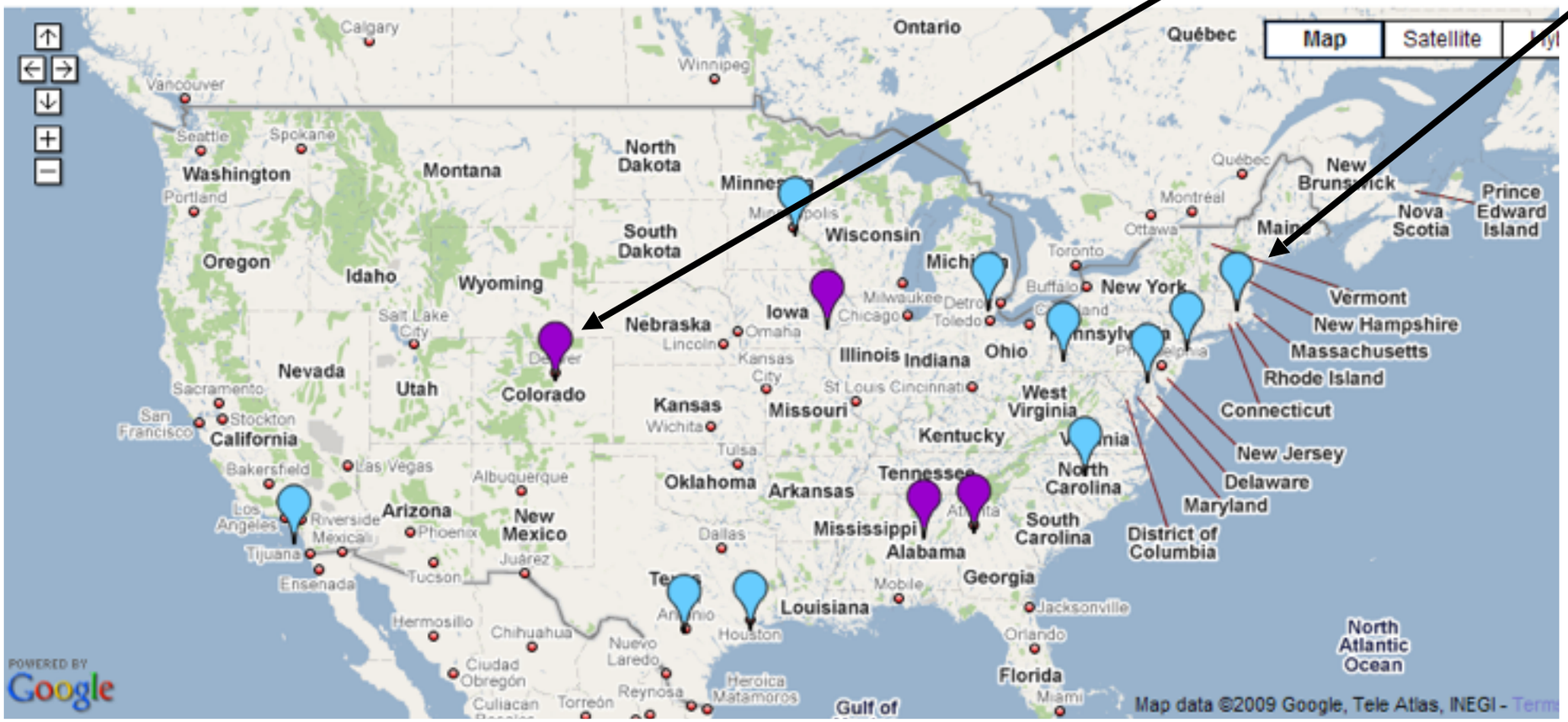
# Clinical Research Example 5

Only 20% of smokers develop COPD → Genetic factors

COPDGene®
COPD Genetic Epidemiology

Multi-center study funded by the National Heart, Lung and Blood Institute (NHLBI).

Co-PIs: Drs. James Crapo, Edwin Silverman.




***21 clinical sites***

***3 image analysis centers:***

- Denver
- Boston
- Iowa

***2 imaging platforms:***

- VIDA
- Slicer

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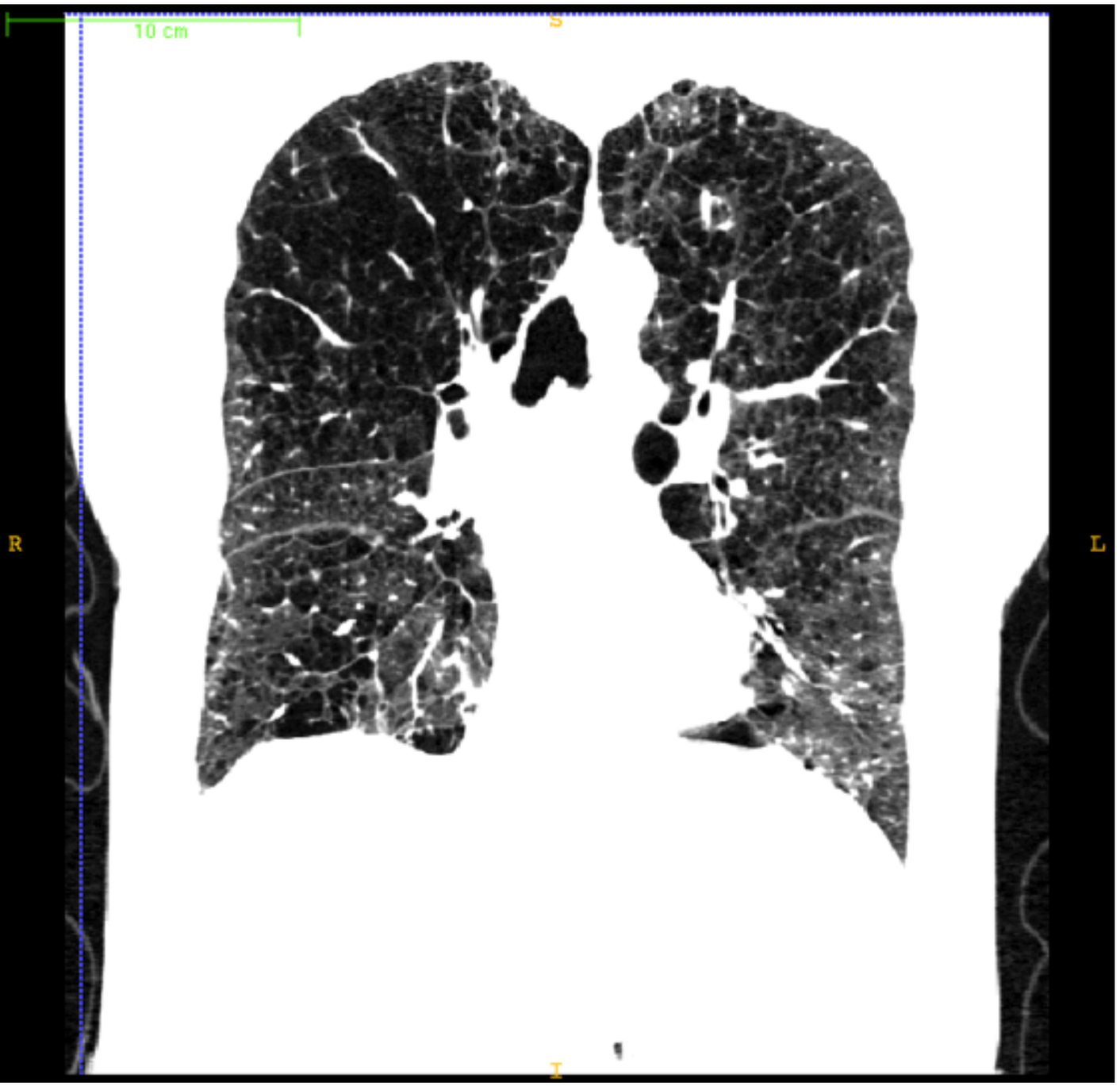
Slide courtesy R. San Jose

# Emphysema Classification for Gene Discovery




- Identification of emphysema patterns based on local histogram classification

| | |
|---|---|
| Normal | Severe CLE |
| Mild CLE | PLE |
| Moderate CLE | Paraseptal |

- Centrilobular (CLE) and panacinar (PLE) emphysema
- GWAS in 9000 smokers
- New genetic markers for emphysema were found near the CHRNA3/5 locus on 15q25 and near MMP12 and MMP3 on 11q22

*Castaldi PJ, San Jose Estepar R, Sanchez Mendoza C, Crapo JD, Lynch D, Beaty TH, Washko GR, Silverman EK, Proc. ATS, 2012, p.A3808.*

©2013 Surgical Planning Laboratory, ARR

Slide courtesy R. San Jose

# Phenotype Extraction In The Lung

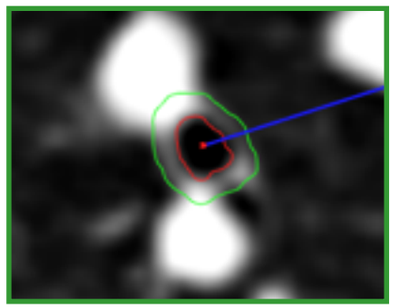
## Extraction

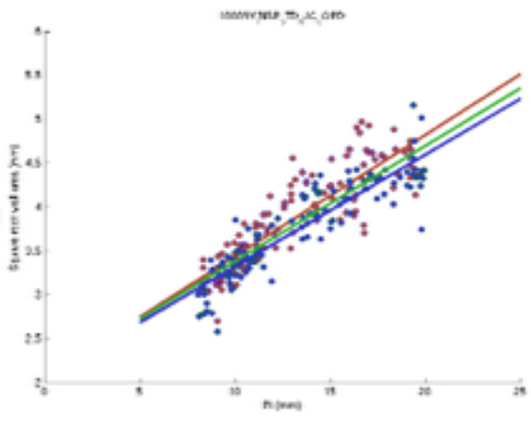
## Sizing

## Phenotype

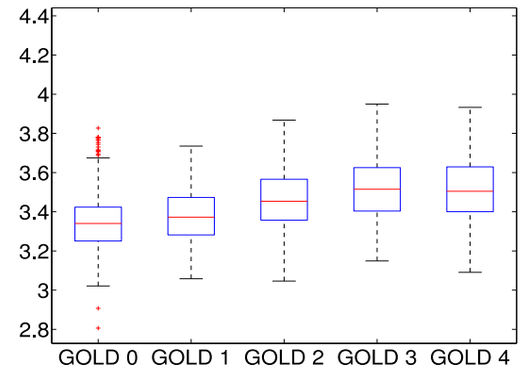
## Population Study

**Airways**





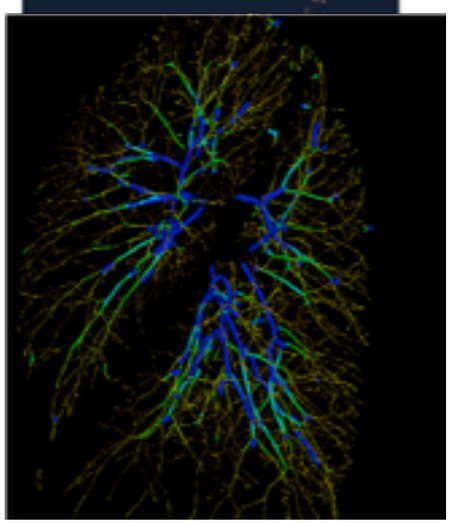
Airway Wall corresponding to a 10 mm internal Perimeter



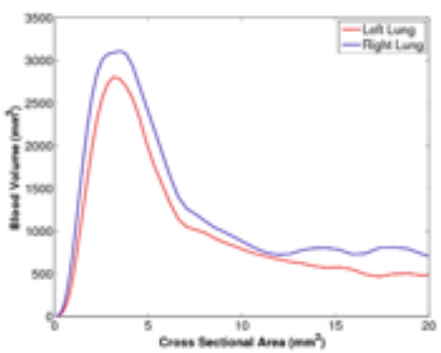

Smoker Controls → Severe Disease

San Jose Estepar R et al, **Automatic Airway Analysis for Genome-Wide Association Studies in COPD,** ISBI 2012

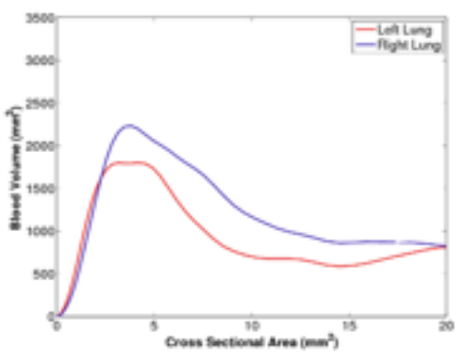
**Vessels**



### Smoker control




### Severe disease



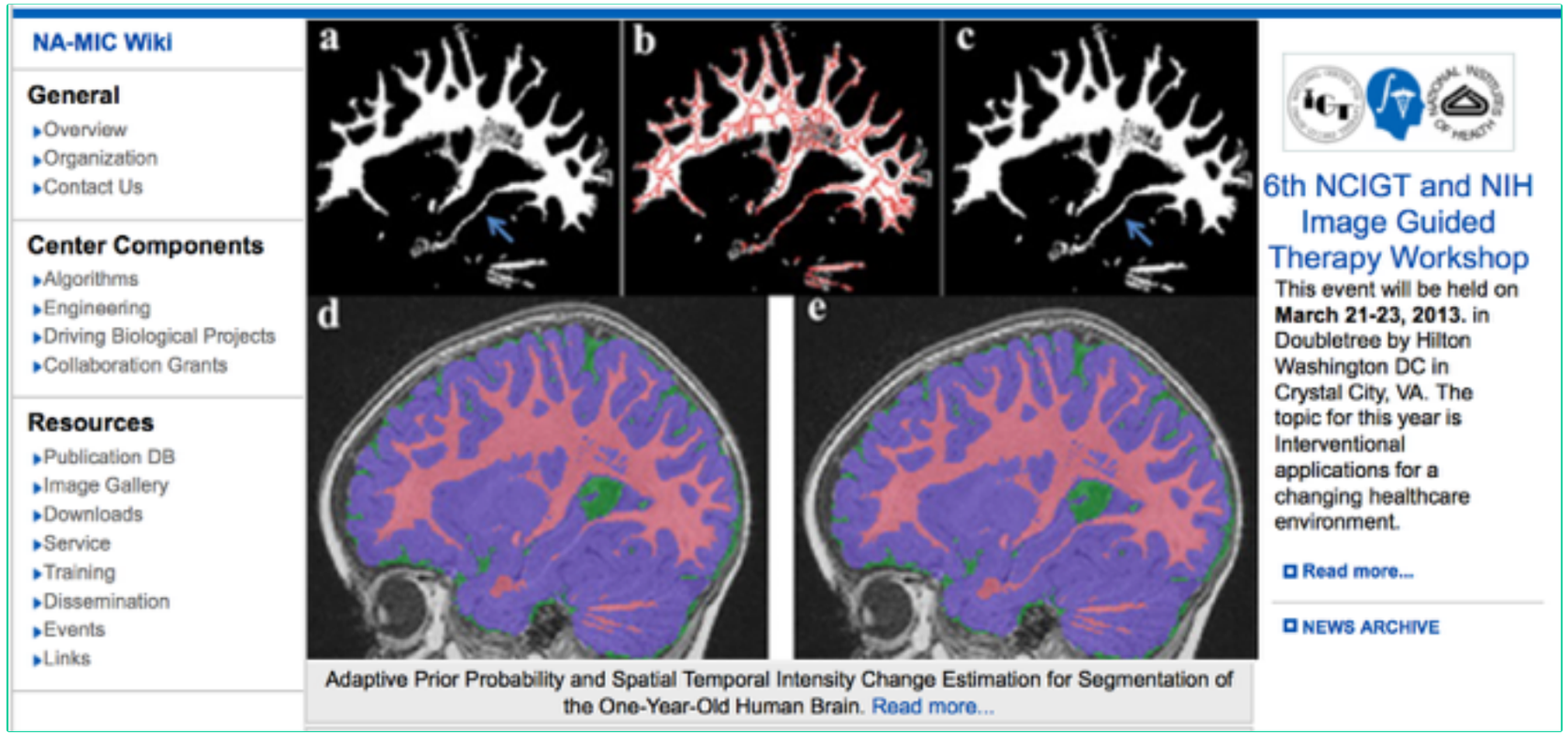

Shift in blood volume per cross sectional area indicating distal pruning and proximal remodeling with disease progression

Kindlmann G, San José Estépar R, Smith SM, Westin CF**. Sampling and visualizing creases with scale-space particles**. IEEE Transactions on Visualization and Computer Graphics 2009;15(6): 1415-1424. PMID: 19834216.

San Jose Estepar R et al, **Computational Vascular Morphometry for the Assessment of Pulmonary Vascular Disease based on Scale-Space Particles,** ISBI 2012

# NA-MIC

- The National Alliance for Medical Image Computing (NA-MIC), is a distributed community of researchers
- Focus on
  - Subject specific image analysis
  - NA-MIC kit, including 3D Slicer as a platform for dissemination
- Funded by NIH through the NCBC program since 2004

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# NA-MIC in Numbers

- 3D Slicer software used worldwide as platform for development and sharing
- Large impact on NIH grantees: 31 funded collaborations across schizophrenia, lupus, autism, lung disease, cardiac disease, brain cancer, liver, colon, prostate, musculoskeletal disorders.
- International funding: Canada, Germany, Spain, Italy, Japan, Australia.
- “Common Toolkit”: joint transatlantic effort
- Trained 55 engineers, 35 grad students, 20 post-docs.
- 2000+ investigators trained in 63 worksho
- 500+ full size papers, including awards
- 15 “Project-weeks”, weeklong working e
  twice a year: over 650 participants

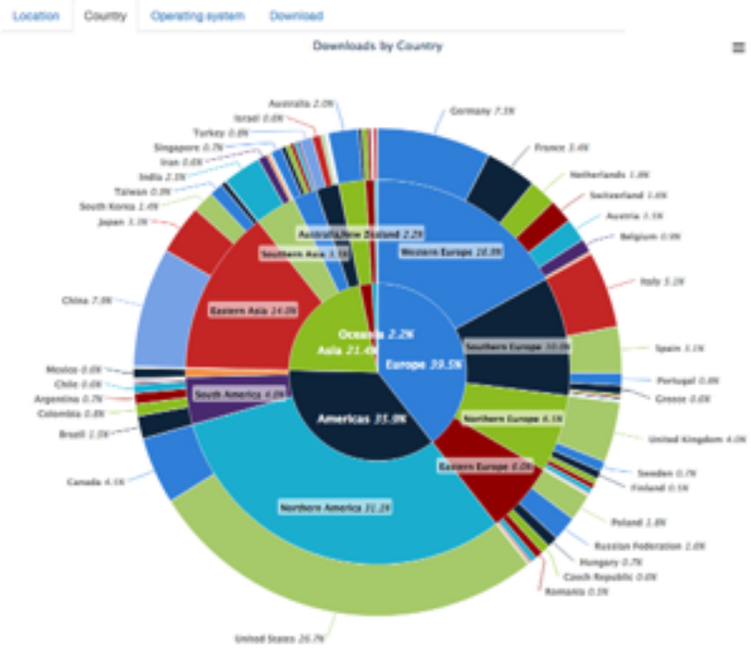


Image courtesy M. Halle

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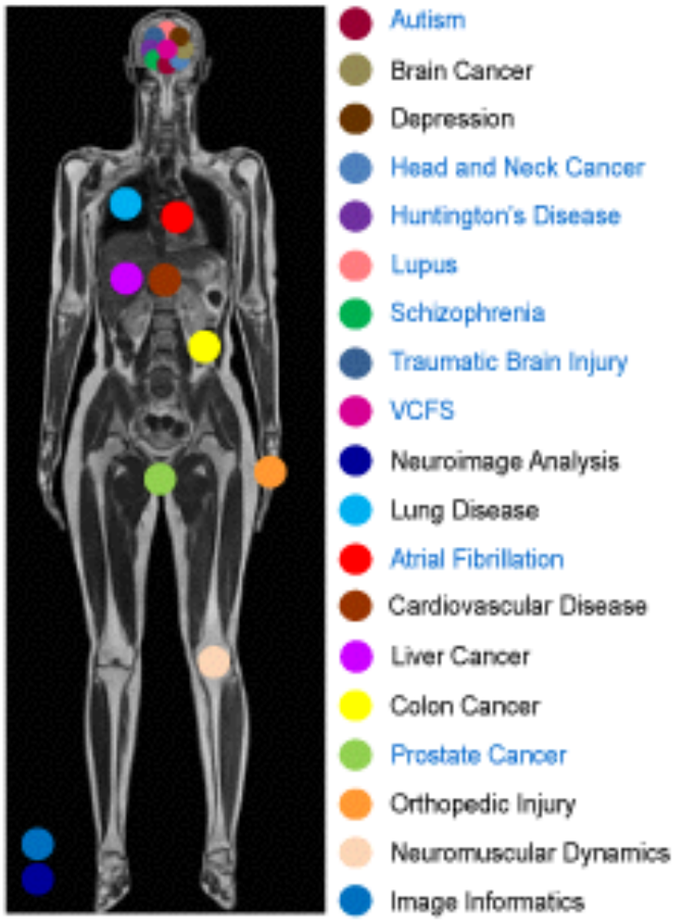
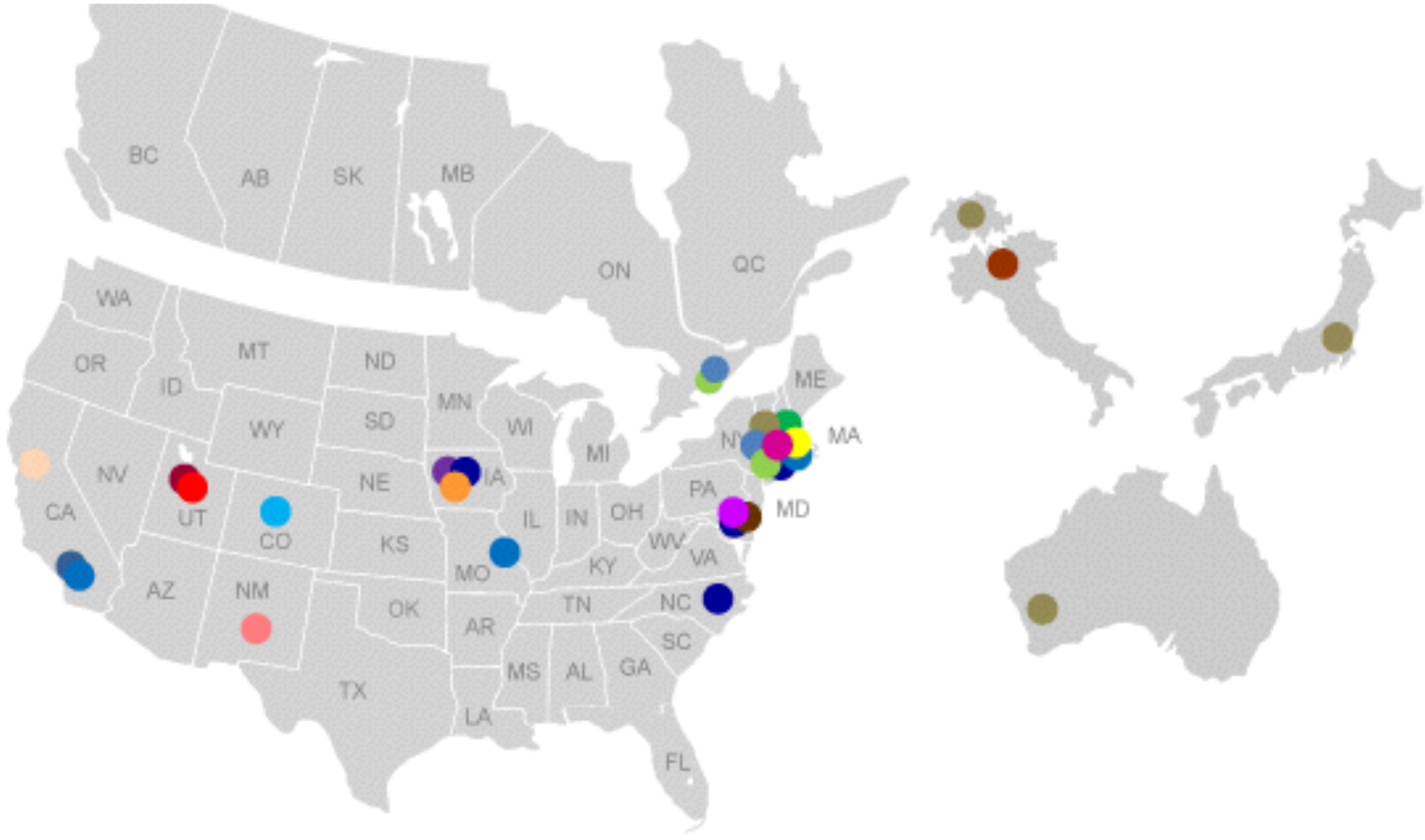
# NA-MIC Community



- Autism
- Brain Cancer
- Depression
- Head and Neck Cancer
- Huntington's Disease
- Lupus
- Schizophrenia
- Traumatic Brain Injury
- VCFS
- Neuroimage Analysis
- Lung Disease
- Atrial Fibrillation
- Cardiovascular Disease
- Liver Cancer
- Colon Cancer
- Prostate Cancer
- Orthopedic Injury
- Neuromuscular Dynamics
- Image Informatics




## Active

R01MH084795, U41RR019703, NSF CCF-0916526, R01EB008171, U01HL089897, R01CA124377, R01CA131718, R01CA11128
R01EB005973, U54EB005149-05S2, U54GM072970, P41RR013218, R01EB006733, R01NS050568, R21EB009900, U54EB005149-05S3
UL1RR025758, U54LM008748, U24RR025736, U24RR021992, U24RR021382, U24RR026057, AIST, Japan, UWA, Australia
Mario Negri Institute, Italy, CO-ME, Switzerland, OCAIRO, Canada

## Completed

U54EB005149-04S1

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Picture 2011, courtesy Kapur, Jakab, Kikinis

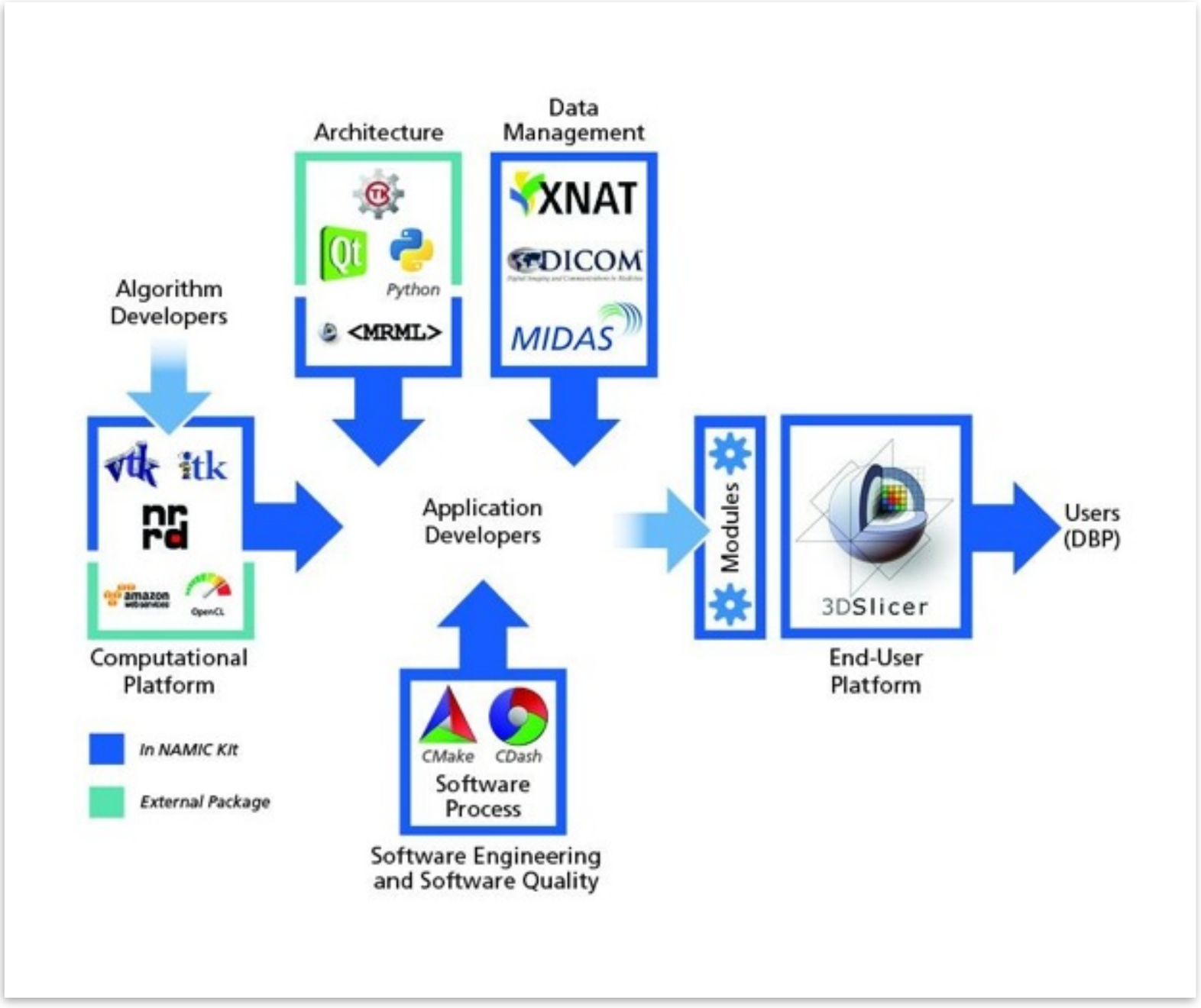
# The NA-MIC Kit

The NA-MIC Kit is a free open source platform to support translational research in MIC

**Slicer is built on the NA-MIC Kit**

**Common Features**

- BSD style Open Source
- No known IP liabilities
- Compiled on all supported platforms
- Optimized Interoperability of the components

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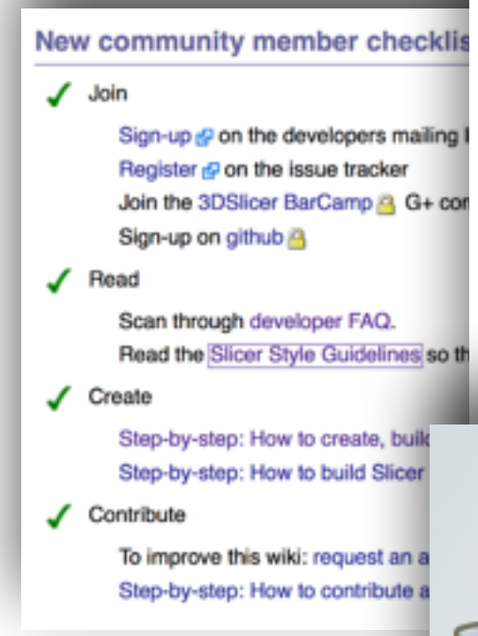
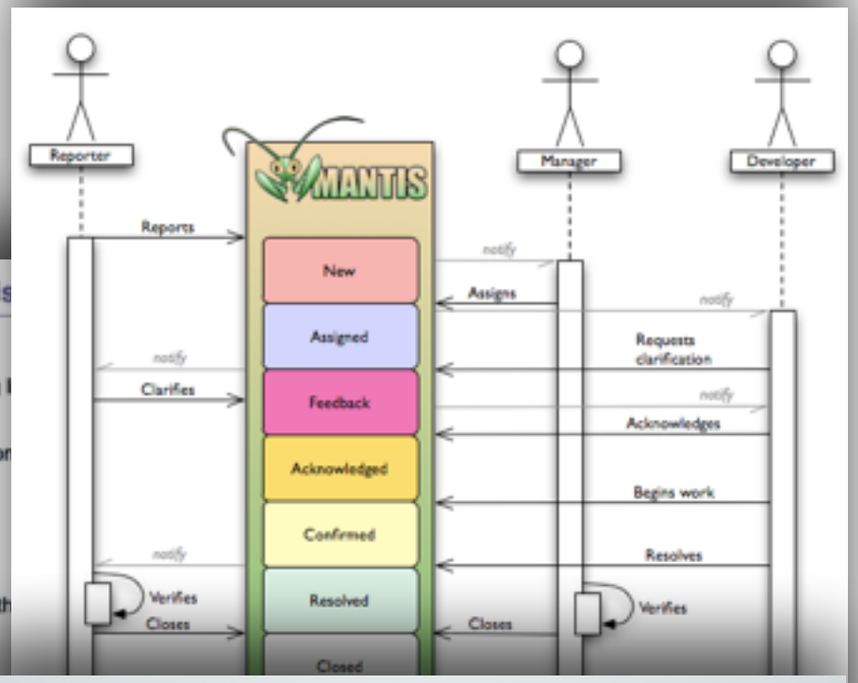
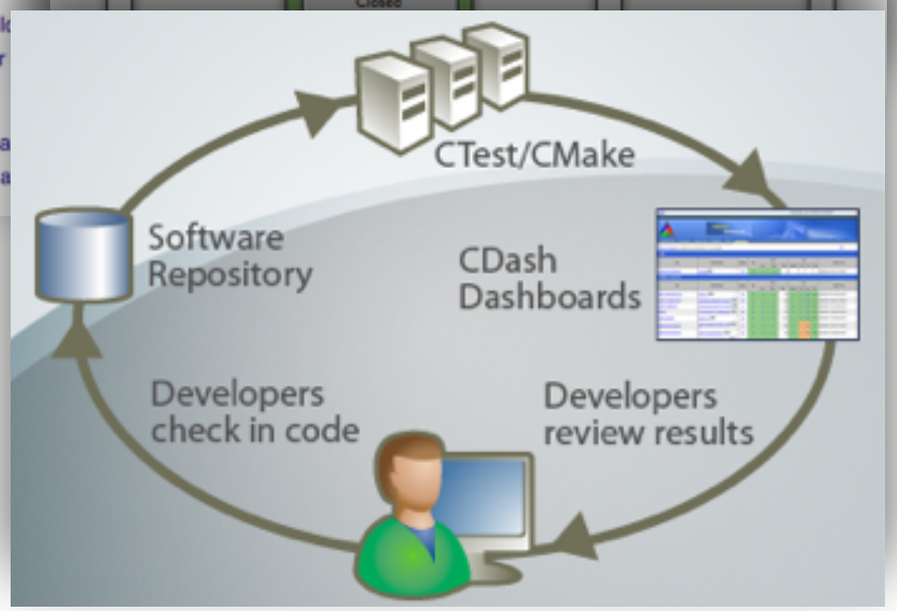
# Principled Software Process

- Documented workflows
- Github is used as repository
  - distributed
  - allows offline work
  - sharing with granularity
- Slim trunk, most functionality is in plug-ins

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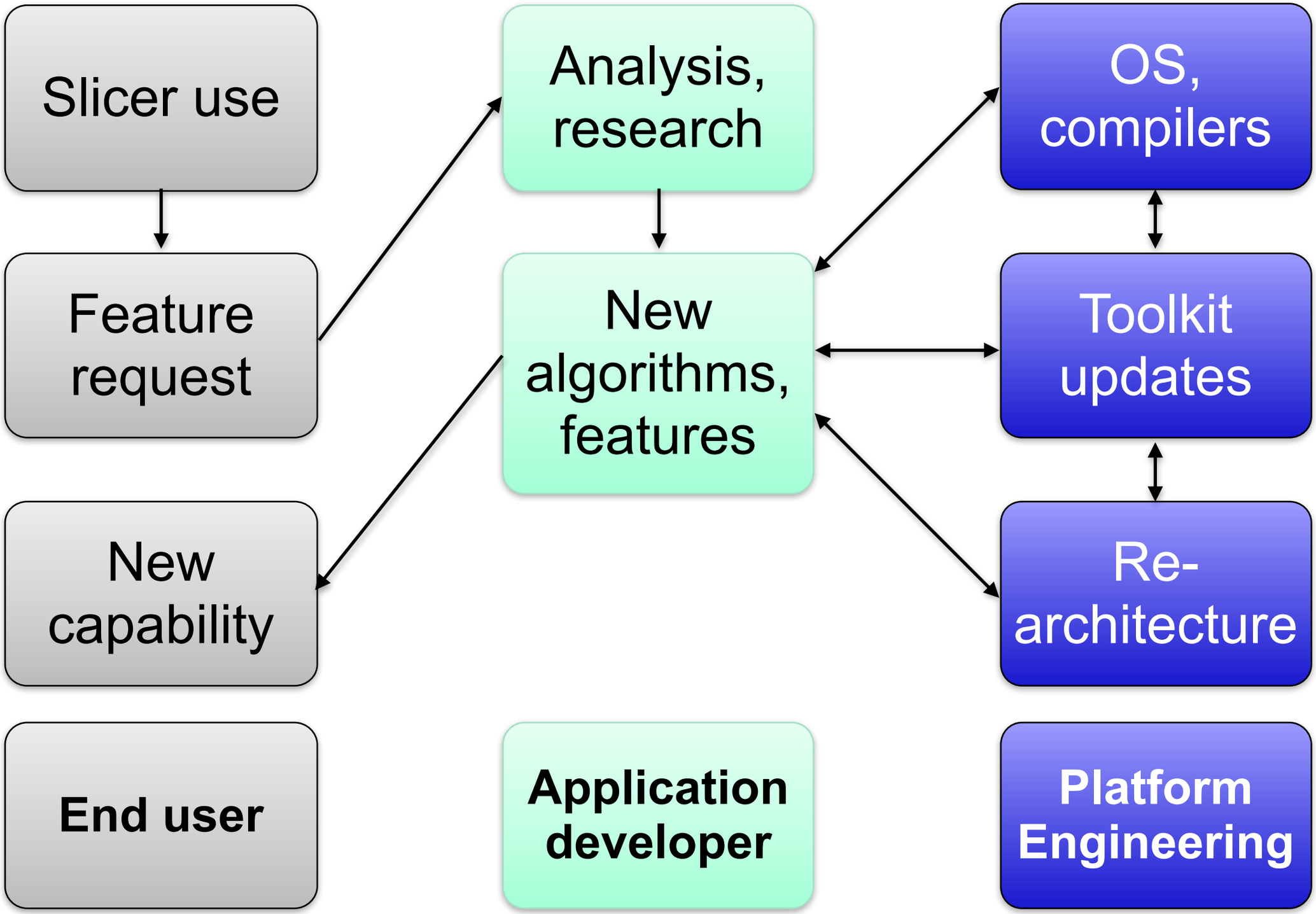
# Slicer Development Process

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# Application Development

- Algorithm research comes first
- Implementation workflow once the algorithms are known:
  - Create individual modules as plug-ins
  - Create workflows based on the modules
  - Use the extension manager for distribution

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# Platform Engineering

- The Slicer platform is based on many toolkits and libraries
- Operating systems change constantly
- Ongoing effort is needed for updating the versions used by the NA-MIC kit and Slicer
- Modifications and patches are pushed downstream to the toolkits and libraries

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# What it takes

- Money, money, money
- Time, time, time

  – Platform engineering for translational MIC is expensive and difficult to find funding for
  – It takes time to bring together an interdisciplinary community

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# Work

- 1 Ph.D. thesis is one to two person-years of actual work
- Slicer represents over 100 person years in direct effort

In a Nutshell, Slicer4...

... has had 20,538 commits made by 97 contributors
representing 397,670 lines of code

... is mostly written in C++
with an average number of source code comments

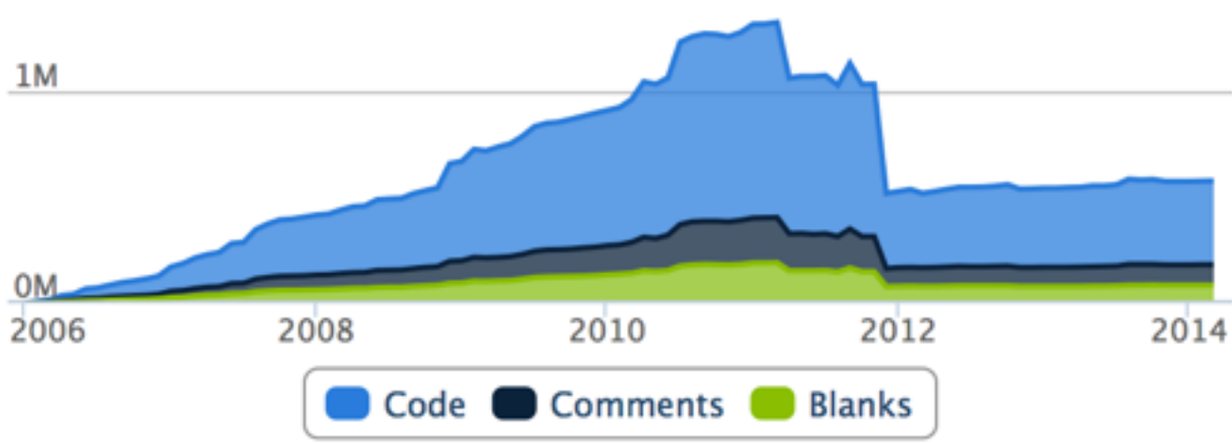
... has a well established, mature codebase
maintained by a large development team
with decreasing Y-O-Y commits ← work moved to plug-ins

... took an estimated 105 years of effort (COCOMO model)
starting with its first commit in January, 2006
ending with its most recent commit 2 days ago

Languages

| | | | |
|---|---|---|---|
| C++ | 51% | C | 27% |
| XML | 9% | 10 Other | 13% |

Lines of Code




http://www.ohloh.net/p/slicer

# NA-MIC Kit Engineering Team

FeiZhao
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bess
blezek
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christopher.mullins
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davisb
demian
domibel
dpace
fedorov
finetjul
francois_budin
freudling
gcasey
haehn
harveerar
hayes
hjohnson
hliu
hong
hyang
ibanez
ilknur.kabul
inorton
jcfr
jcross186
joe.snyder
johan.andruejol
jvs
karthik
kedar_p
kerstin
kquintus
lantiga
lassoan
lauren
lorensen
maddah
malaterre
matthew.bowman
mccormic
mike
millerjv
mscully
naucoin
nicky
nobyhata
padfield
partyd
pieper
pinter
pkarasev
pkarasev3
pohl
rjosest
rsierra
samset
sankhesh
sylvain
taox
taylor
tgl
tokuda
tringo
ungi
vmagnotta
vrnova
wjp
ygao
yumin
zach.mullen
zack.galbreath

*Special thanks to Jean-Christophe Fillion-Robin, Julien Finet, Steve Pieper, Nicole Aucoin, Andrey Fedorov, Jim Miller, Andas Lasso*

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# Open Source (OS)

- Collaborate and move freely
  - Good match for the migratory lifestyle of scientist
  - Advantageous for collaborations
  - Neutral territory in multi-vendor settings
- Extensible

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# Upsides for Industry

- Potential advantages:
  - Compared to closed systems more people track changes and detect problems
  - Easy access to world class algorithms and architectures.
  - Community can be engaged
- Open Source approaches are practical
  - Costs are potentially lower
  - They permit the organization to focus on its key product skills, not on commodity capabilities

# Challenges for Industry

- Avoid leakage of proprietary information through clear rules and strategies
- Monitor the open source community for shifting focus and direction
- Internal development is likely to be needed for key features.
- Summary:  Risks are manageable, but need to be managed

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# From Tools to Medical Product

- Open Source facilitates scientific exchange

  BTW: Open Source means
  no restriction on use
  (i.e. no restriction on commercial use)

- All Medical Products are closed source due to significant regulatory requirements

- How to bridge?

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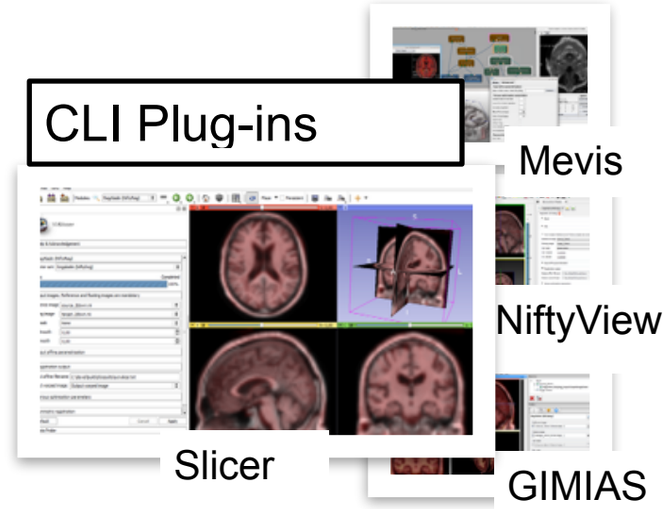
# From Open to Closed Source

Open source

3D Slicer

MITK

MedINRIA




Plug-ins

Mevis Lab

syngo.via , Advantage Windows, Vitrea

Closed source

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# CTK: An example of OPM

- Common infrastructure elements
- International and transatlantic group of contributors
- Free Open Source Software under a BSD license
- Dicom, application hosting, CLI, Widgets and more

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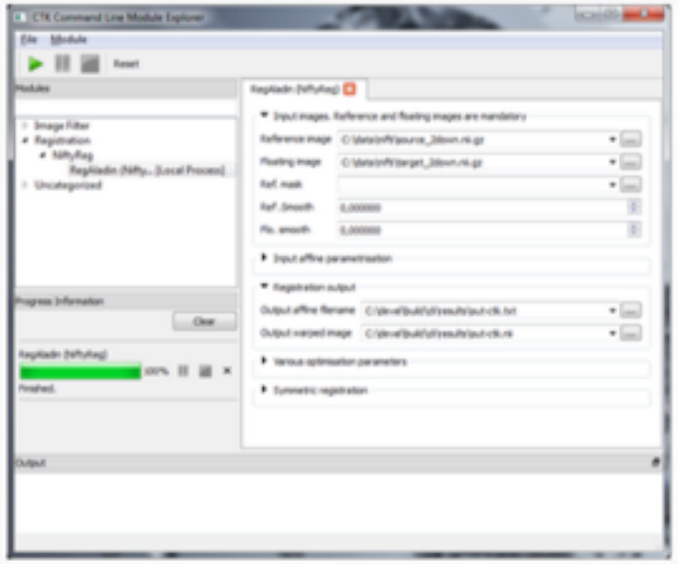
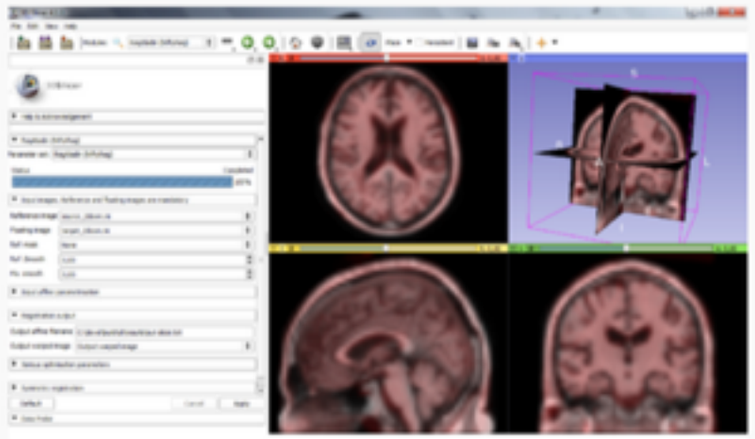
# Plug-Ins: The Key for Translation

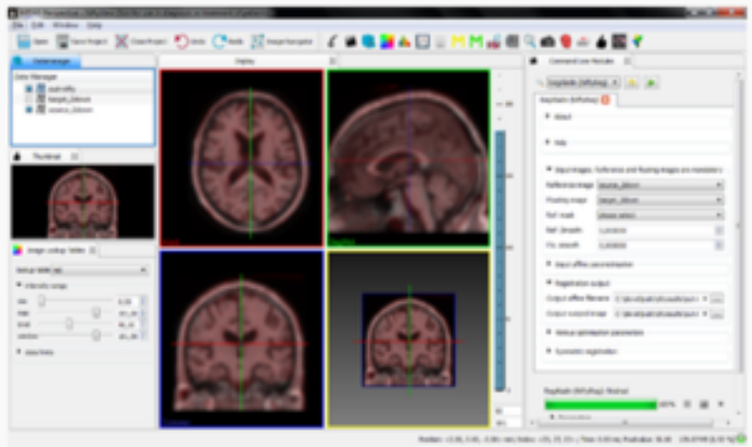
- Example: One CTK plug-in on different platforms



CTK command line module explorer

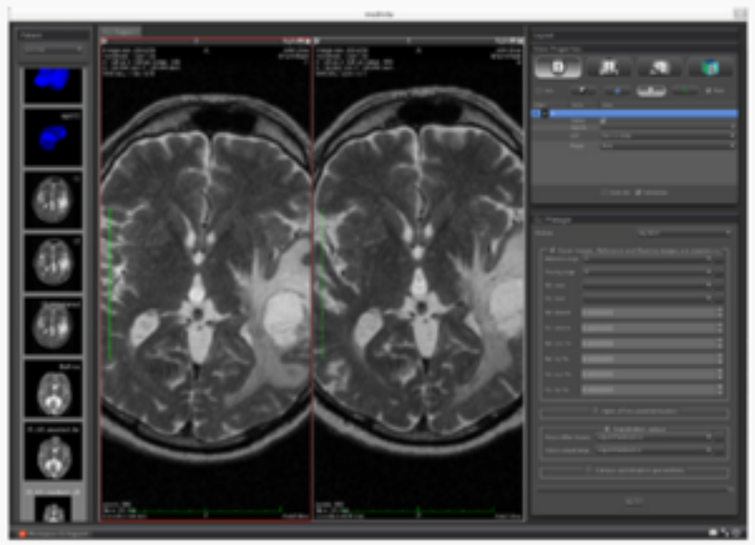


3D Slicer



NiftyView

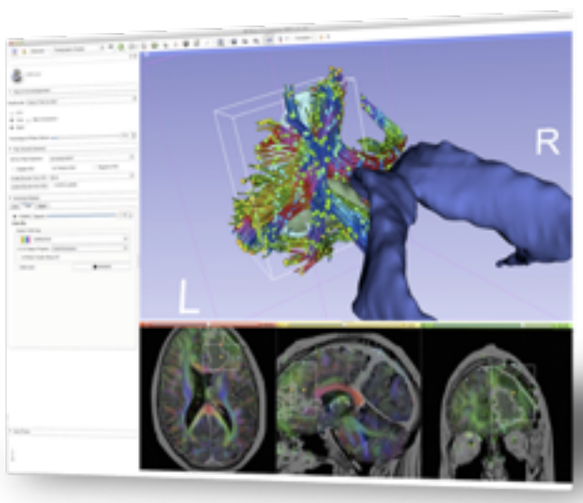
GIMIAS



MedInria

# Social Engineering

- How to build an Open Community?
  - Mutual Self Interest:
    If I get more out of something than I put into it, it is attractive
  - Community building:
    - Us versus them.




Combine social media with in-person events.

Interdisciplinary nature is an additional challenge

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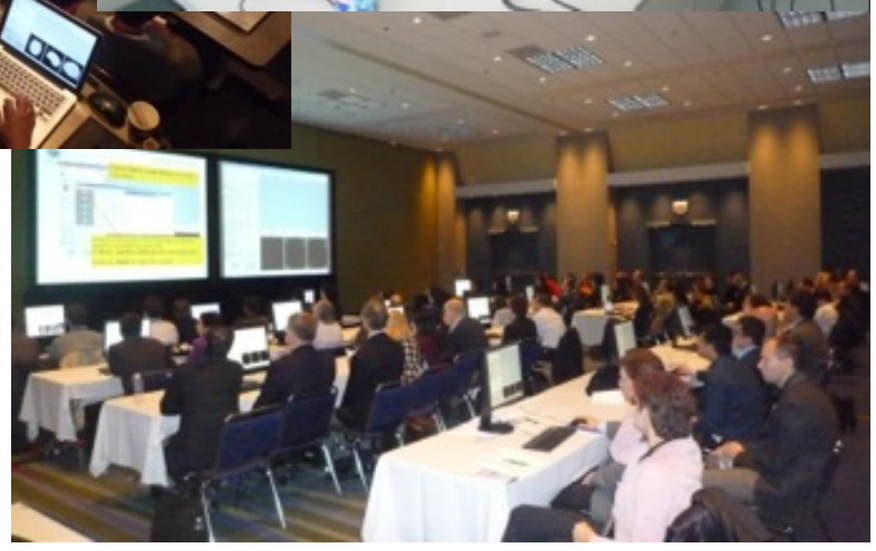
# User Training Events

- Hands-on training workshops at national and international venues
- More than 2,700 clinicians, clinical researchers and scientists trained since 2005



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# Project Week

- Every 6 months, alternating between Boston and Utah
- A working week: Focus on programming and platform updates
- In-person nature encourages socializing
- A key for community building

**16th Project Week: Salt Lake City, Utah, January 2013**

•80 attendees: 17 academic institutions, 4 companies

•54 Projects: TBI, Atrial Fibrillation, Slicer 4 Extensions, Huntington's Disease, Head and Neck Cancer, Stroke, IGT, Radiation Therapy, Medical Robotics, Infrastructure Engineering

**17th Project Week: MIT, Summer June 2013**

•104 attendees: 22 academic institutions, 13 companies

•75 Projects: Huntington's Disease, TBI, Atrial Fibrillation and Cardiac Image Analysis, Radiation Therapy, IGT and Device Integration with 3D Slicer, COPD, and Infrastructure Engineering

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# Conclusions

- Free Open Source Software
  - Facilitates translation: bridging the valley of death
  - Is a win-win proposition: the OPM principle
  - Requires proper policies and governance
- Slicer and the NA-MIC kit are a good example of FOSS for translational work

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# Acknowledgments


**National Alliance for Medical Image Computing**
www.na-mic.org

**Neuroimage Analysis Center**
nac.spl.harvard.edu

**Surgical Planning Laboratory, Brigham and Women's Hospital**
spl.harvard.edu

**National Center For Image Guided Therapy**
www.ncigt.org

- Ferenc Jolesz, MD, my mentor
- Collaborators and colleagues


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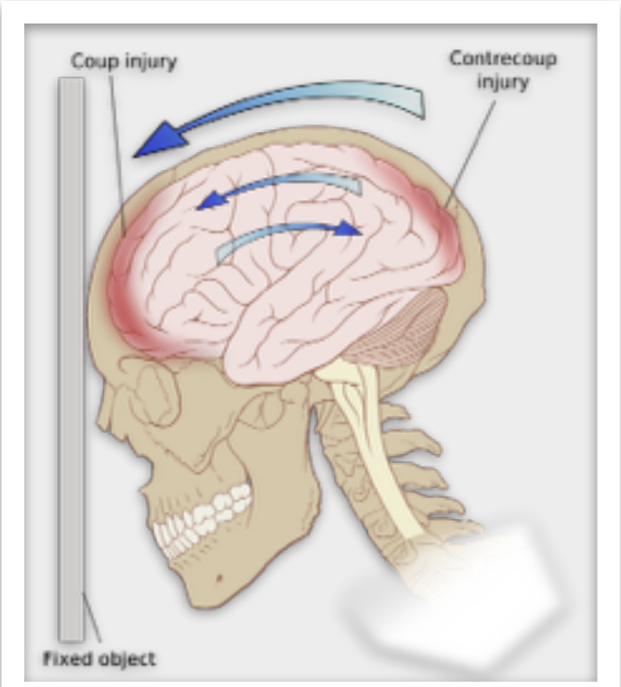
# Traumatic Brain Injury Facts

- There are approximately 1.5 million new cases of non-fatal traumatic brain injury (TBI) in the US every year.
- The worldwide incidence of this condition has been estimated to amount to at least 6.8 million TBI cases every year.
- The financial burden of this condition in the USA alone amounts to over $56 billion annually
- More than half of the cases are classified as moderate or severe

- NA-MIC collaboration:
  - UCLA: Jack vanHorn, Andrey Imiria, Paul Vespa
  - UTAH: Guido Gerig, Marcel Prastawa, Bo Wang
  - Kitware: Stephen Aylward, Danielle Pace

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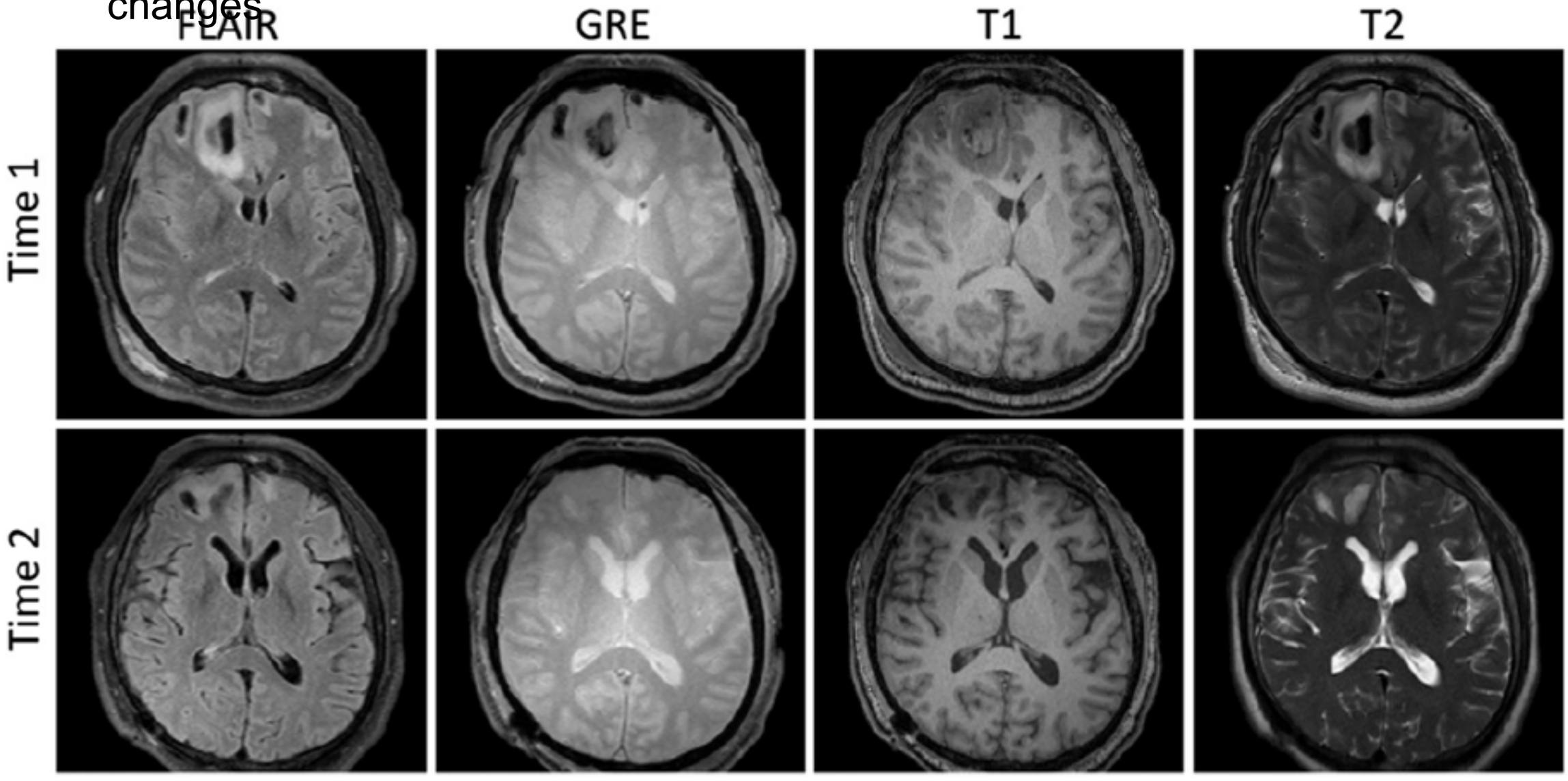
http://en.wikipedia.org/wiki/Traumatic_brain_injury

# Traumatic Brain Injury

Brain images of patients with traumatic brain injury undergo dramatic changes

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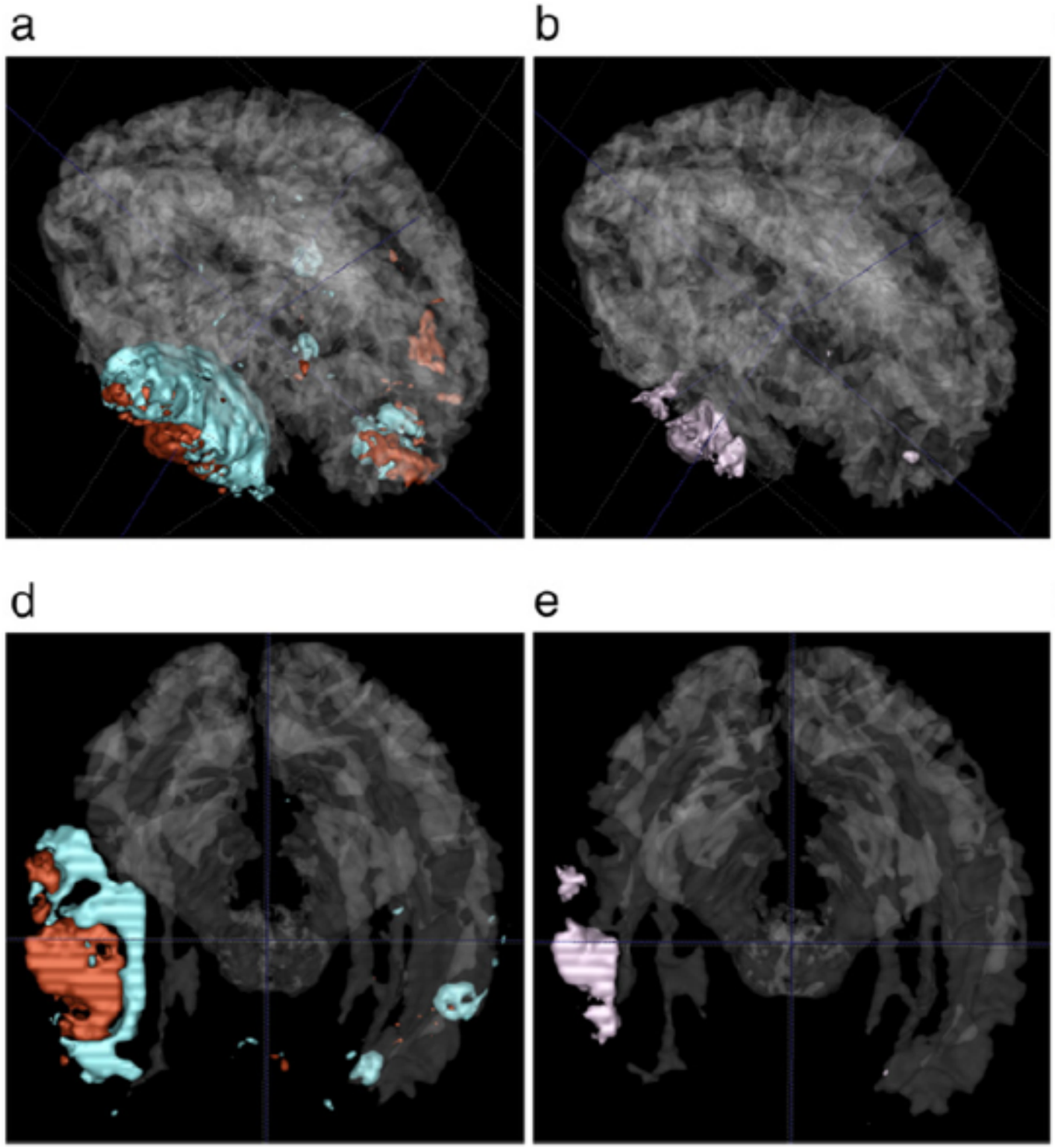
# Example Traumatic Brain Injury

Neuroimage anal
creation of techn

- EM segmenter
  (Prastawa et al.)
- Non-rigid regis
  (Pace et al.)

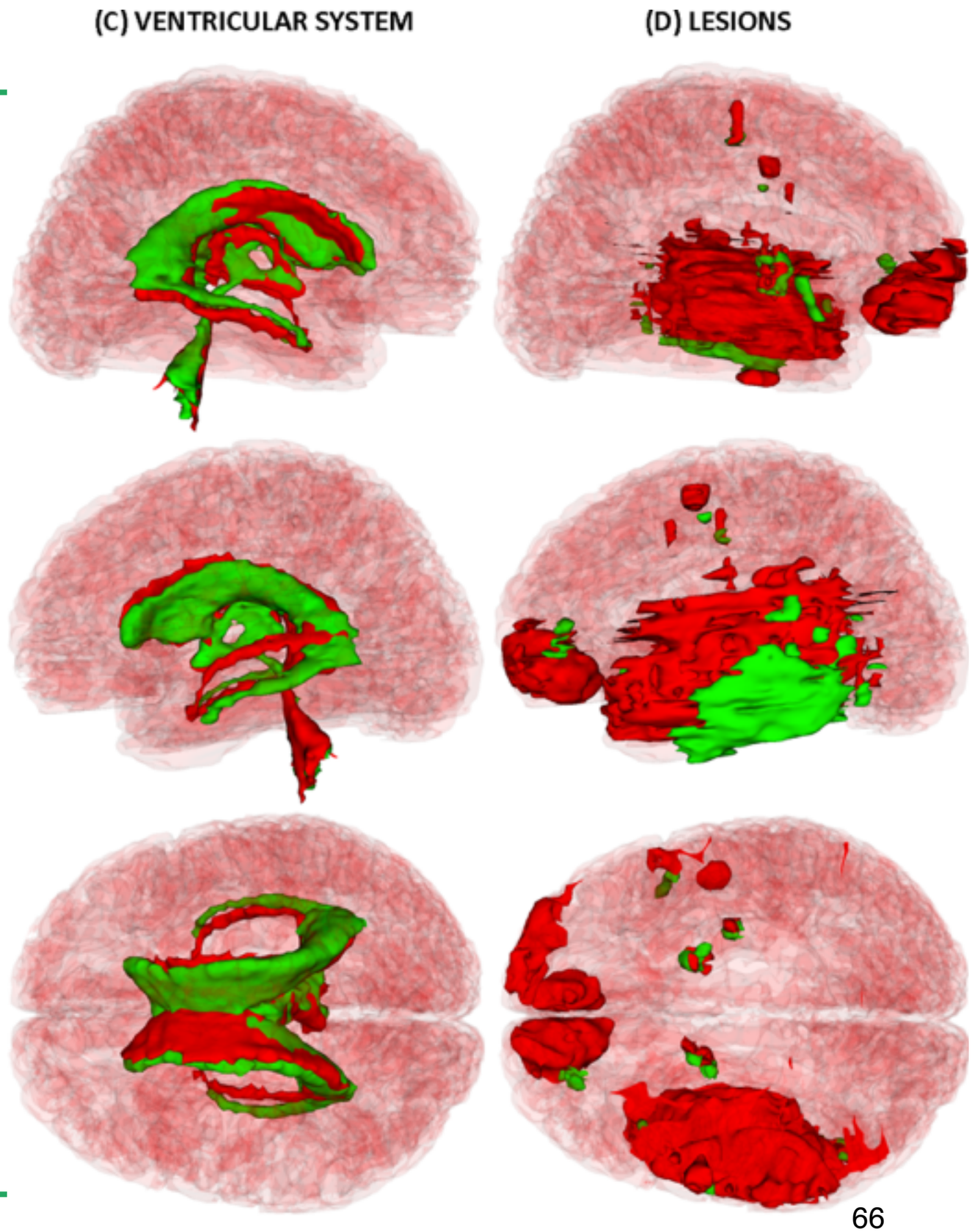



A. Irimia et al. / NeuroImage: Clinical 1 (2012) 1–17

# SSA 2

## Longitudinal change: acute vs. chronic

Wang B., Prastawa M., Irimia A., Chambers M.C., Vespa P.M., Van Horn J.D., Gerig G. *A Patient-specific Segmentation Framework for Longitudinal MR Images of Traumatic Brain Injury*. Proceedings of SPIE 2012;8314, 831402.




acute

chronic

Wang et al., Univ. Utah

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# DTI

- The UCLA group had acquired good quality DWI data in both acute and chronic patients
- Once segmentation and registration work on TBI subjects, parcellation of the grey matter and analysis of the white matter are possible

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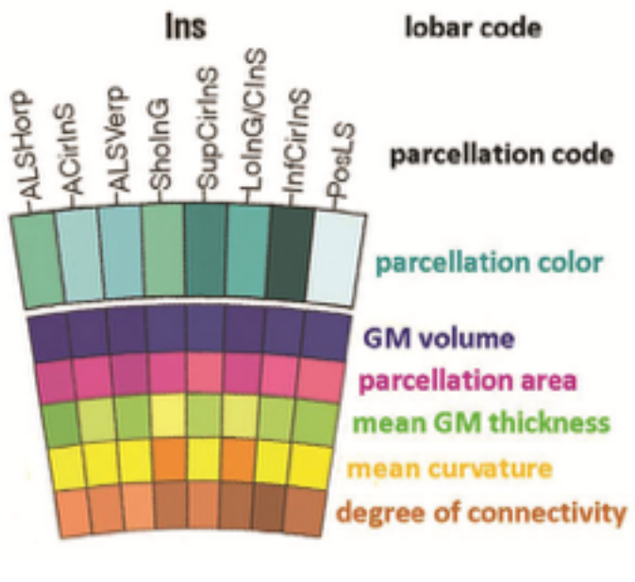
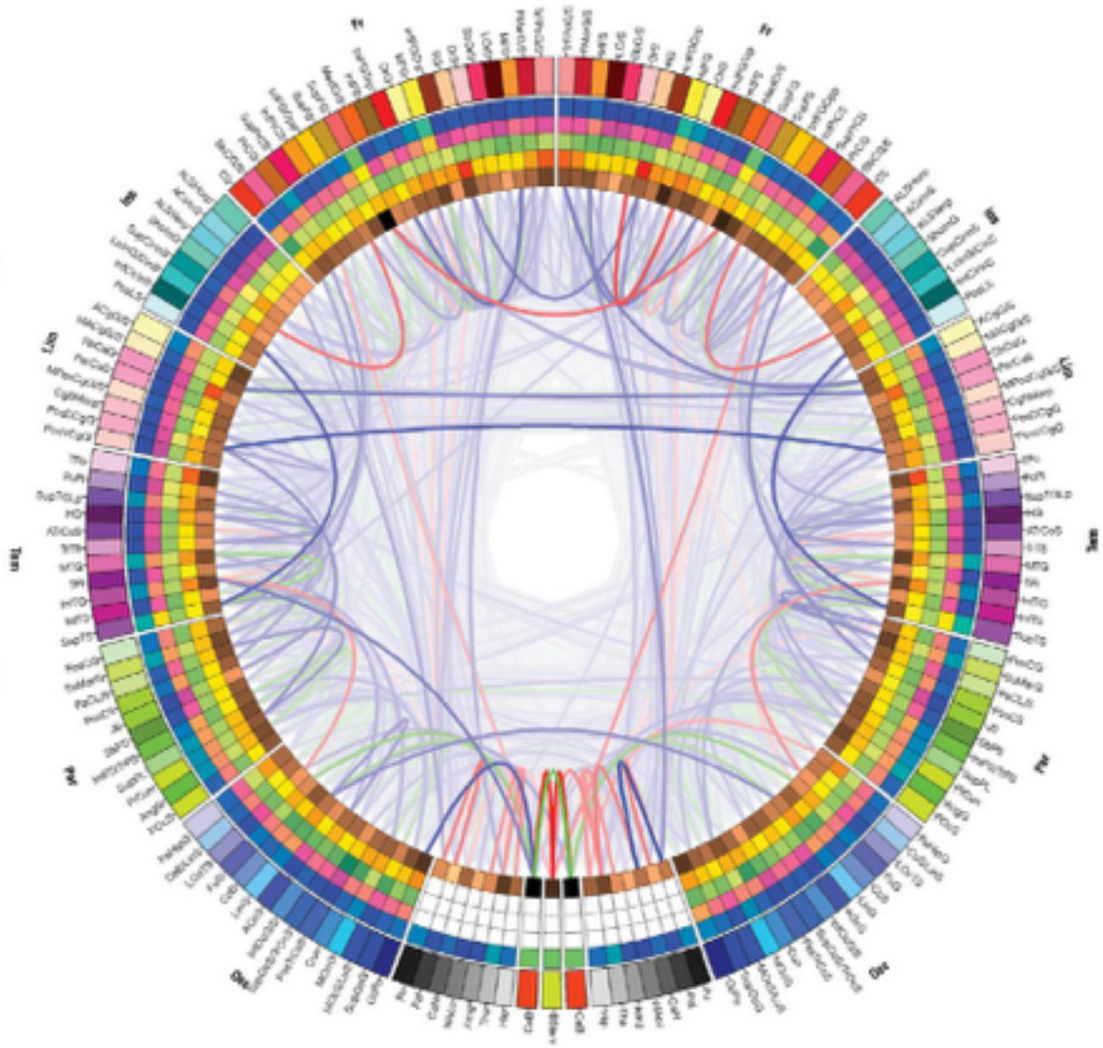
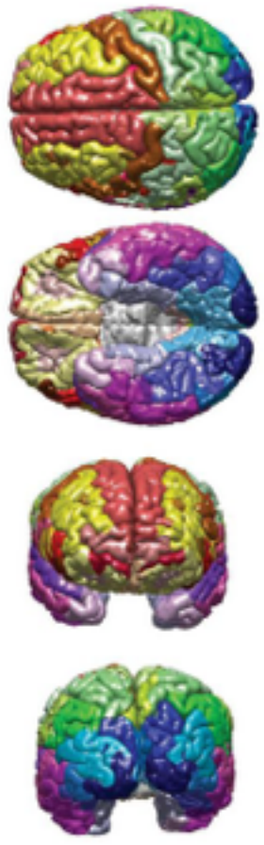
# Connectograms

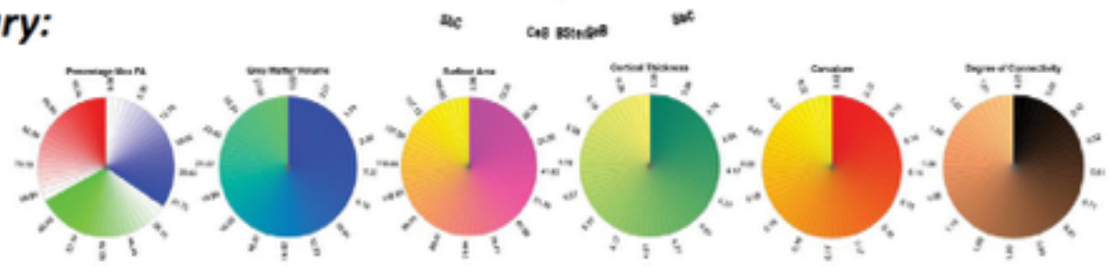






***Sample Summary:***

N=100
Right handed
Males
25-36 years old



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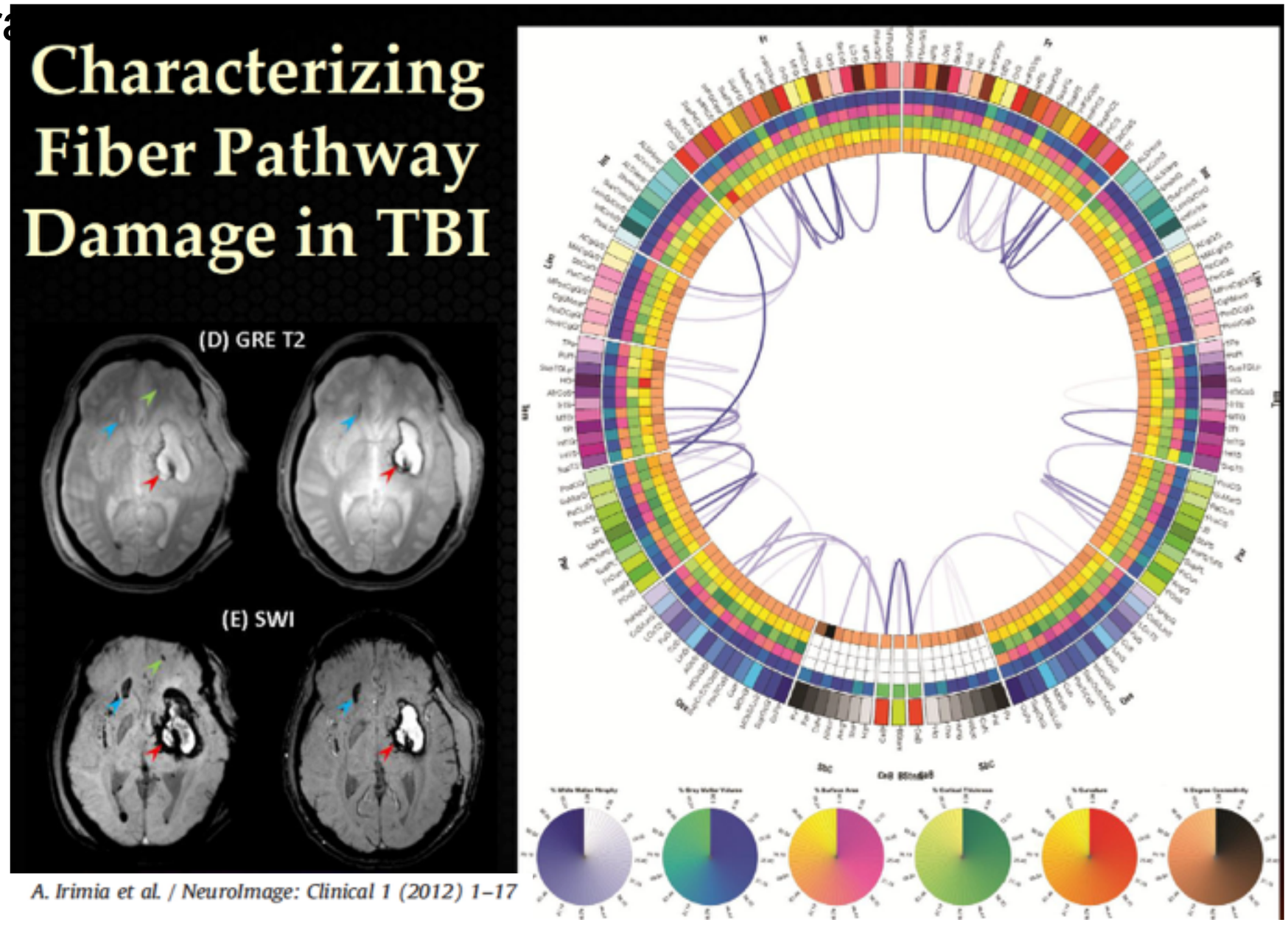
# Personalized Connectomics

Streamlines, which are reduced by more than 20% as a result of brain tra




A. Irimia et al. / NeuroImage: Clinical 1 (2012) 1–17

# SSA: The Effects of Pathology

- Focal pathology introduces focal changes, which make it difficult to define general rules upon which algorithms are based
- Example: Effect of brain tumors on fractional anisotropy of adjacent white matter.

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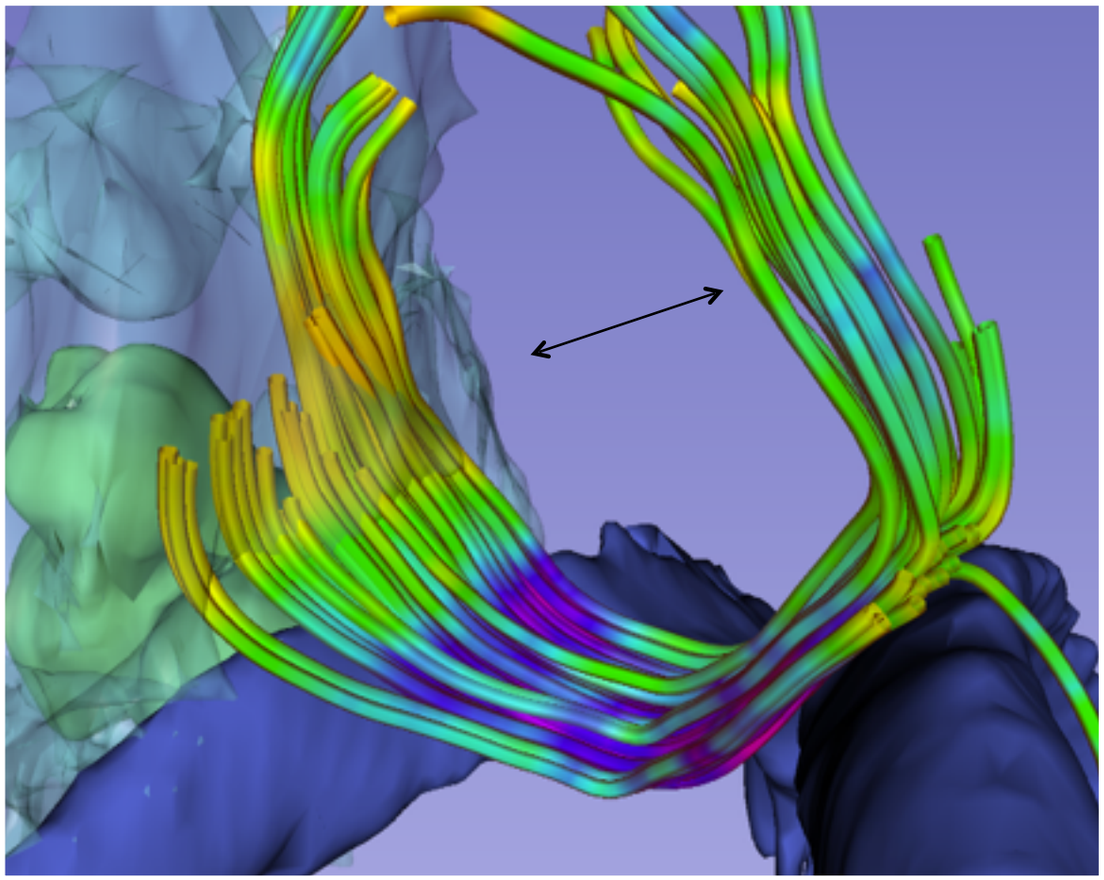
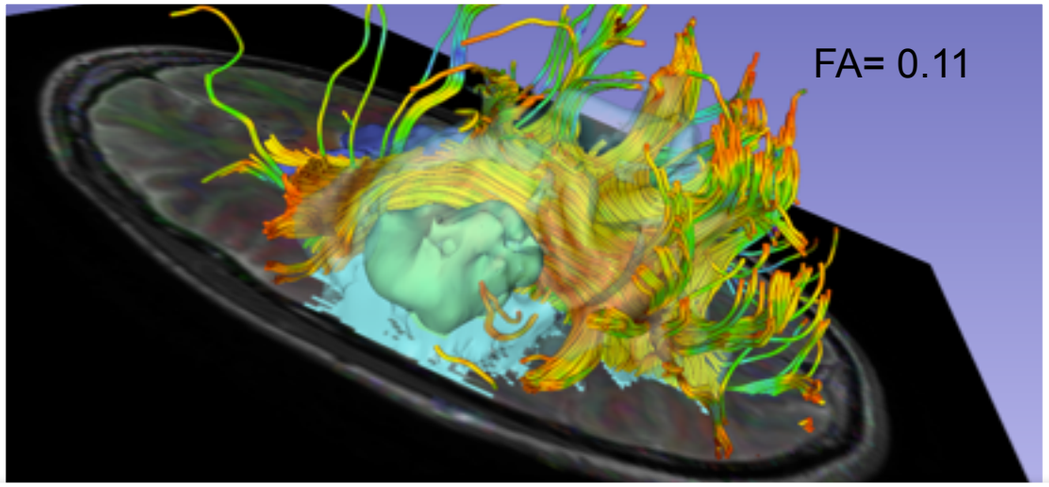
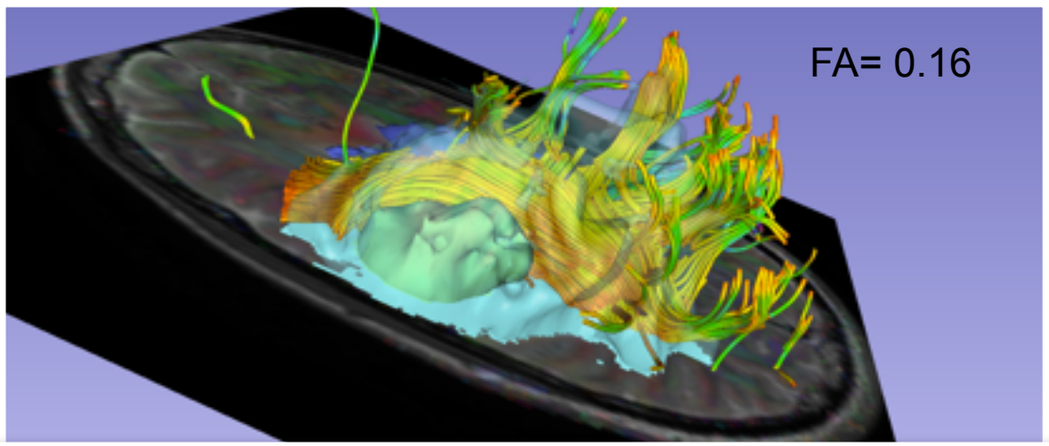
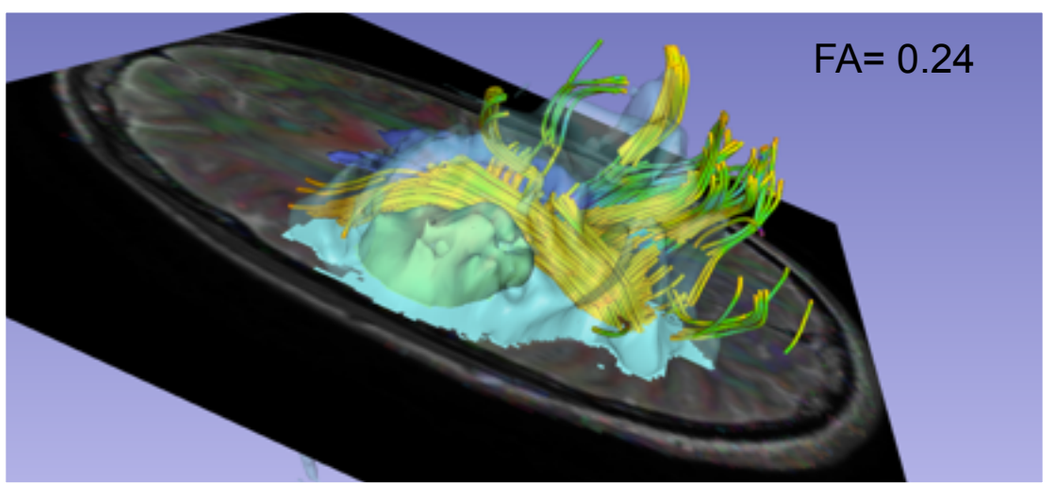
# FA Changes Around a Tumor



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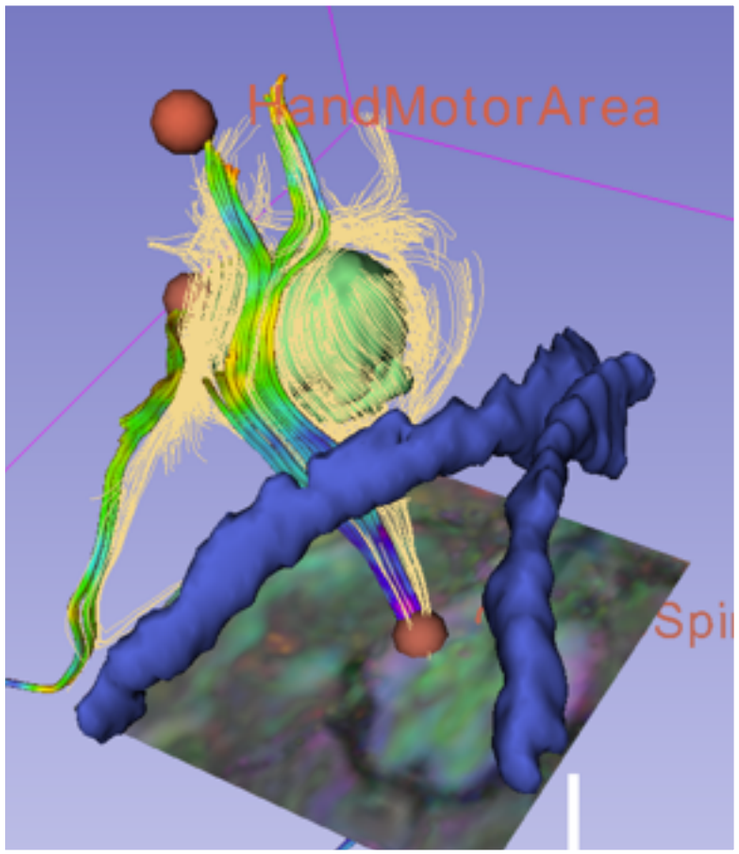
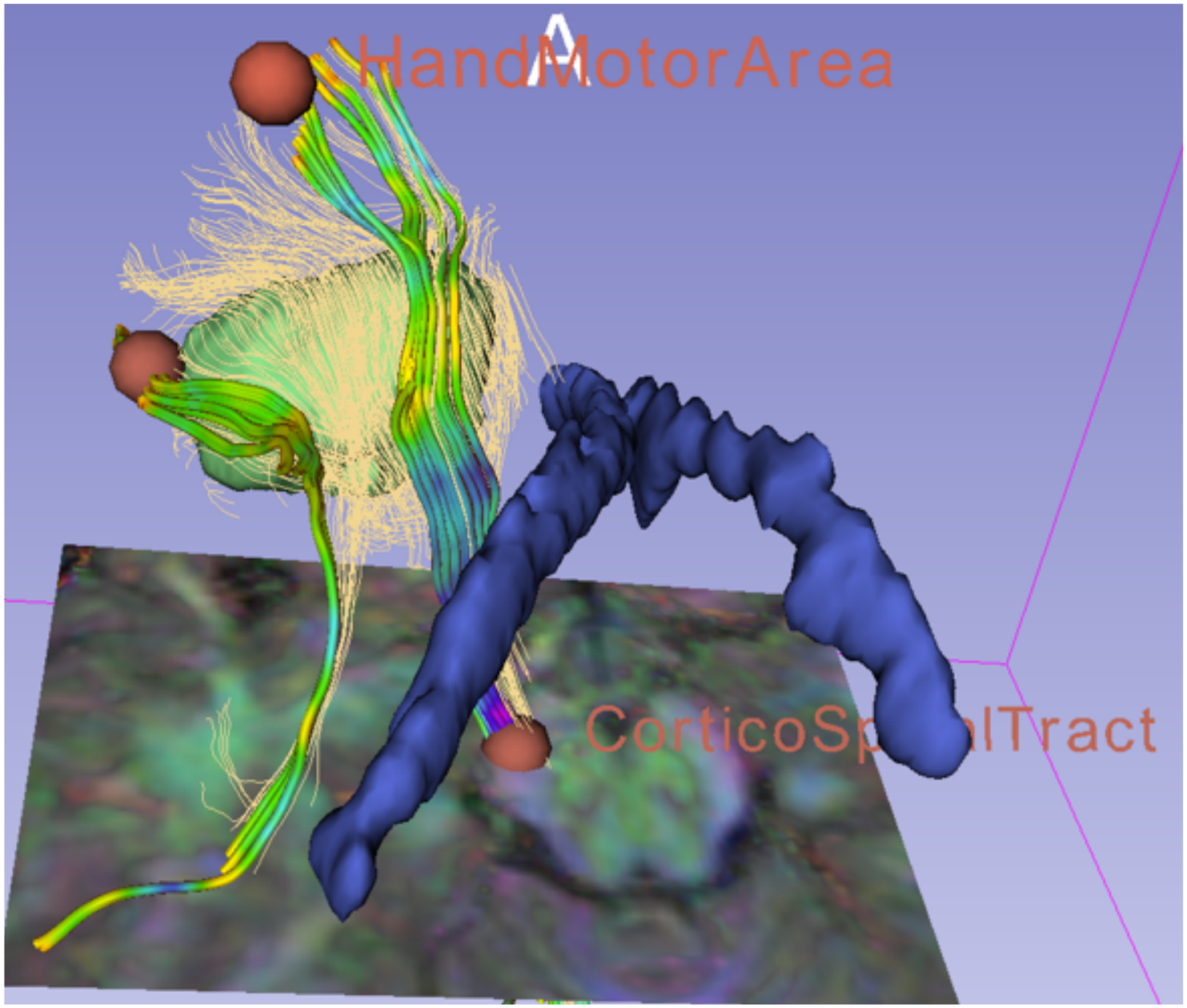
# Dislocation of Normal Anatomy

The cortico-spina
midline

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