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Medical Image Computing – Research and Boundary Conditions

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Research Director, National Center for Image Guided Therapy

Acknowledgments

Ferenc Jolesz, MD, my mentor
My collaborators and colleagues

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

Neuroimage Analysis Center
nac.spl.harvard.edu

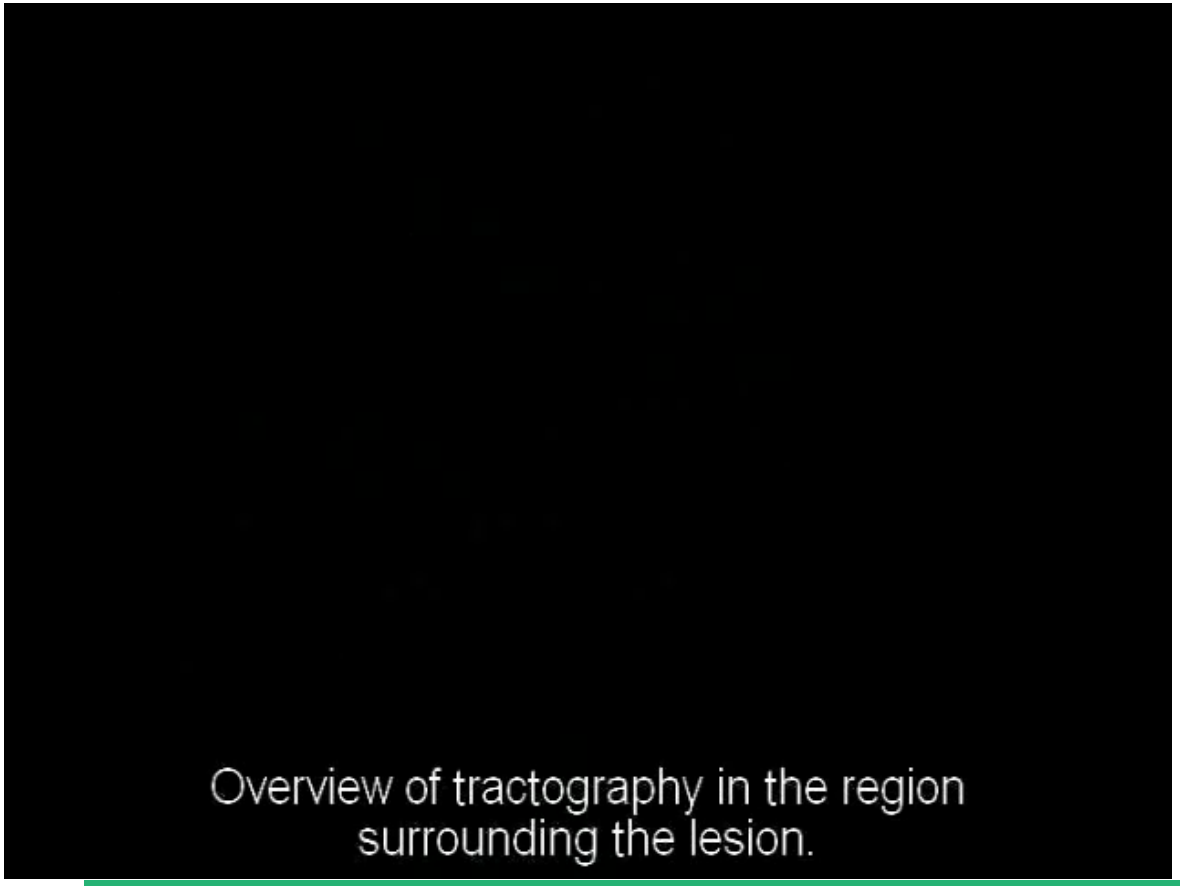
Surgical Planning Laboratory, Brigham and Women's Hospital
spl.harvard.edu

National Center For Image Guided Therapy
www.ncigt.org

Open Source and Closed Source

OpenIGTLink allows interfacing to proprietary devices

Research systems in parallel to FDA approved devices



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

Images courtesy A. Golby

Post-Processing Is Critical

- From image data to information
- From information to knowledge

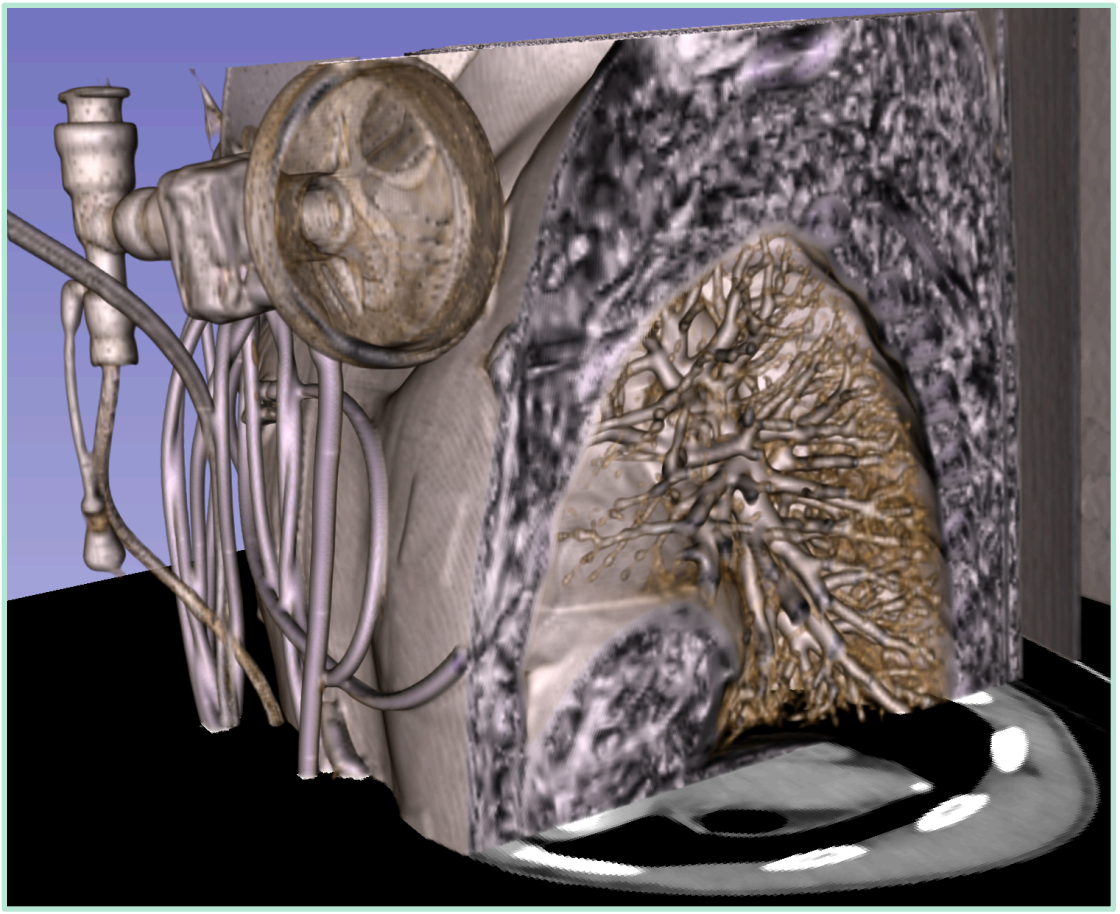


Image provided by Kikinis

Translation Pipeline

- Can it be done?
  - Technical Prototypes
- Is it worth doing?
  - Research Tools
- Standard of care
  - Medical products

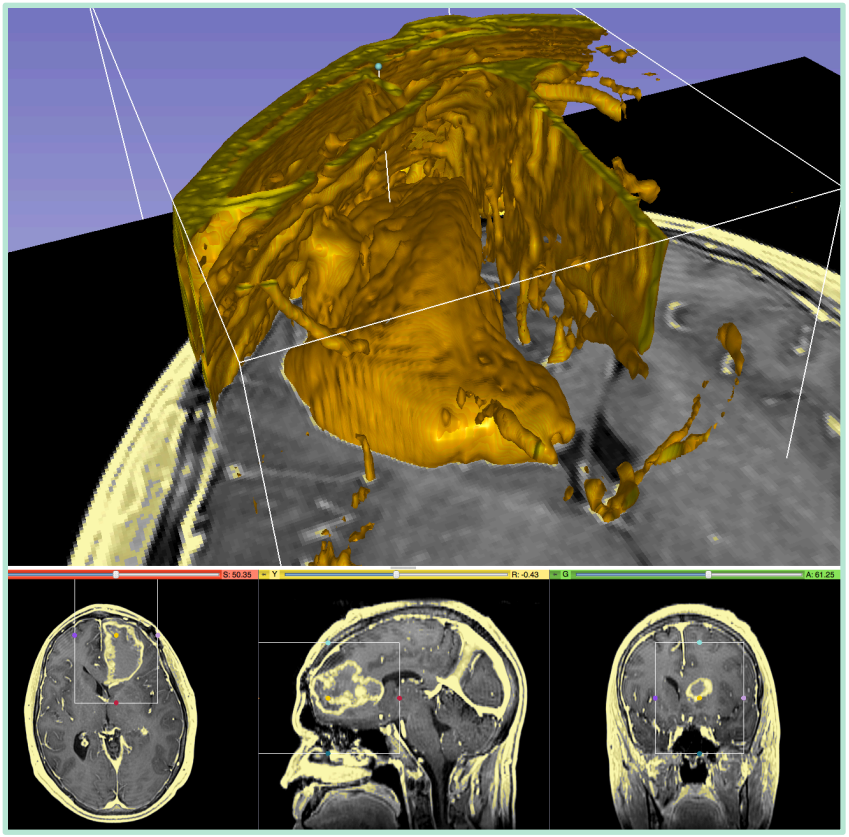
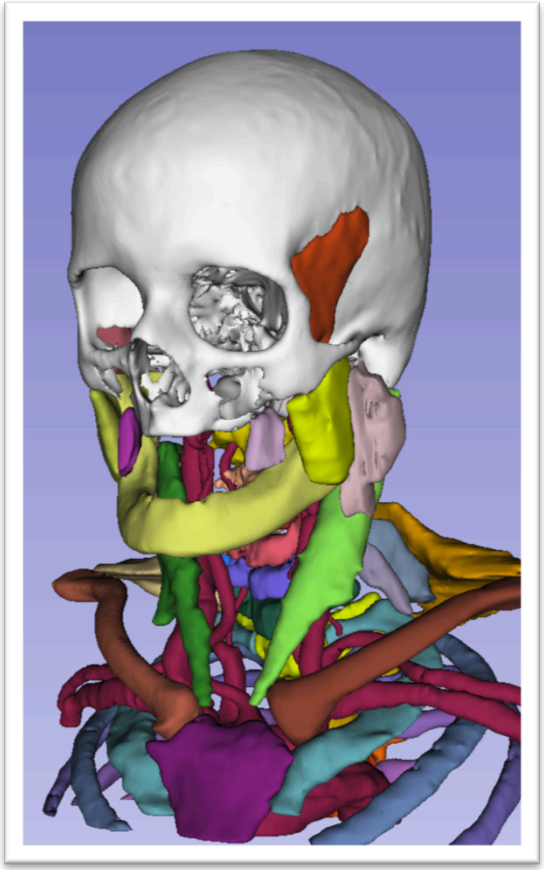


Image provided by R. Kikinis

From Prototypes to Tools

- A **prototype** works for the grad student's thesis
  - Not portable
  - Unstable, no support
- A **tool** works in your environment
  - Easy to install
  - Easy to use
  - Stable, supported
- Significant resources are needed to get from a prototype to a tool

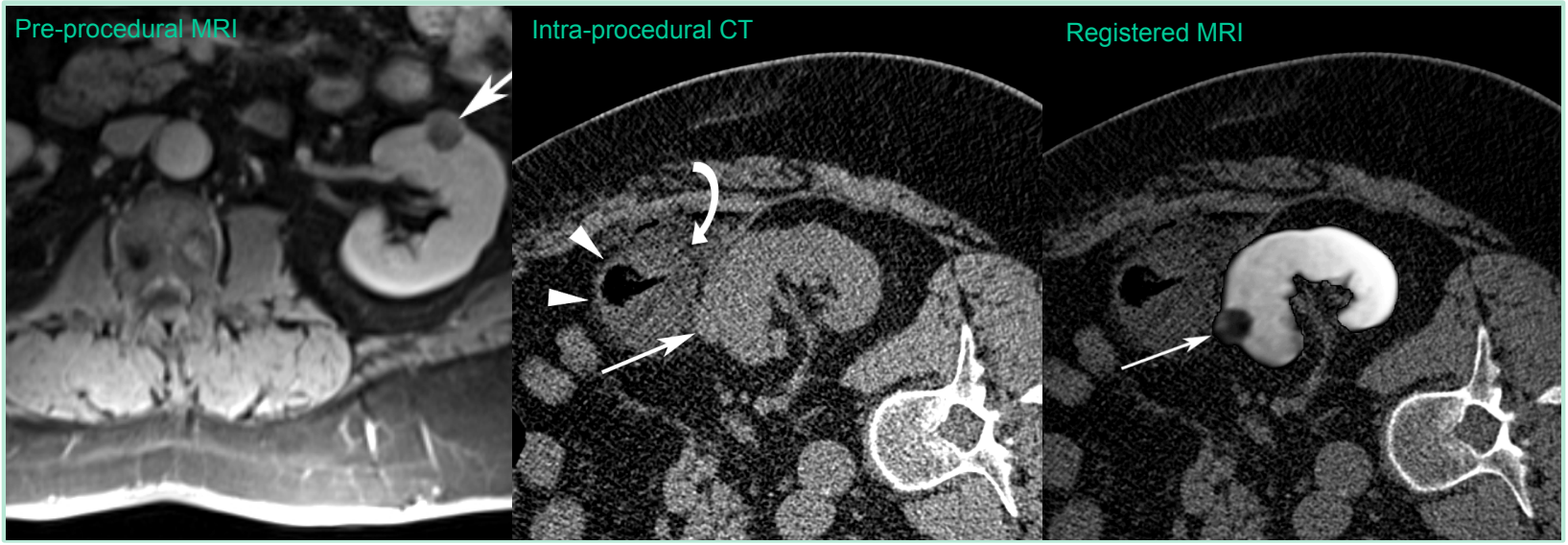


Atlas provided by M. Jakab

The Valley of Death

The translation pipeline is failing to create tools enabling biomedical research

- Scientist: Tools do not help academic promotion
- Funding agencies: Toolmaking is not innovative
- Companies: not proven, it is too risky



Oguro et al, Int J Comput Assist Radiol Surg, 2011
Elhawary et al, Acad Rad, 2010

From Tools to Medical Product

- Open Source facilitates scientific exchange
  - Open Source means **no restriction on use** (i.e. no restriction on commercial use)
- Medical Products are closed source
  - Significant Regulatory Requirements
- How to accomplish the transition?

The Translation Pipeline

Open source

Closed source

3D Slicer

Mevis Lab

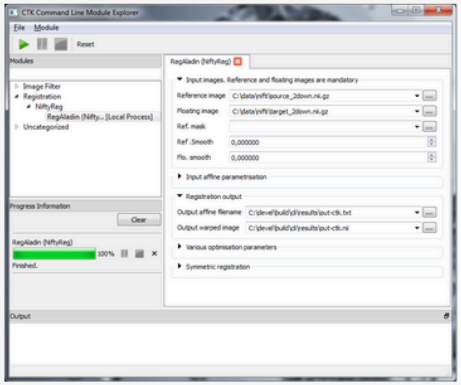
Plug-ins

Syngo Via,
Advantage Windows,
Vitrea

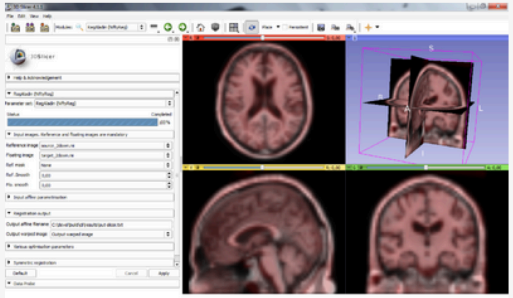
Plug-Ins: The Key for Translation of Software

- Example: CTK plug-ins

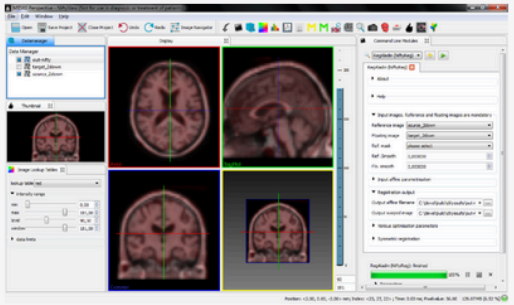
niftyreg on the different platforms



CTK command line module explorer

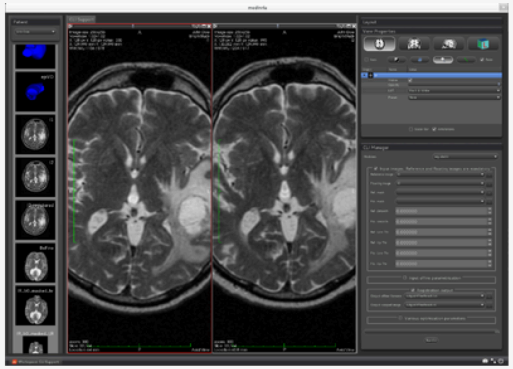


3D Slicer



NiftyView

GIMIAS



MedInria

Across the Atlantic

Translation is a challenge

- US:
  - NIH focuses on innovation, slowly beginning to acknowledge need for engineering
  - Companies are risk averse. Software offers little IP protections
  - SBIR program is aimed at start-ups
- Europe:
  - Fragmented system
  - In general, funding is available for commercialization, less for translation
  - There are exceptions. E.G.: German Fraunhofer targets translation

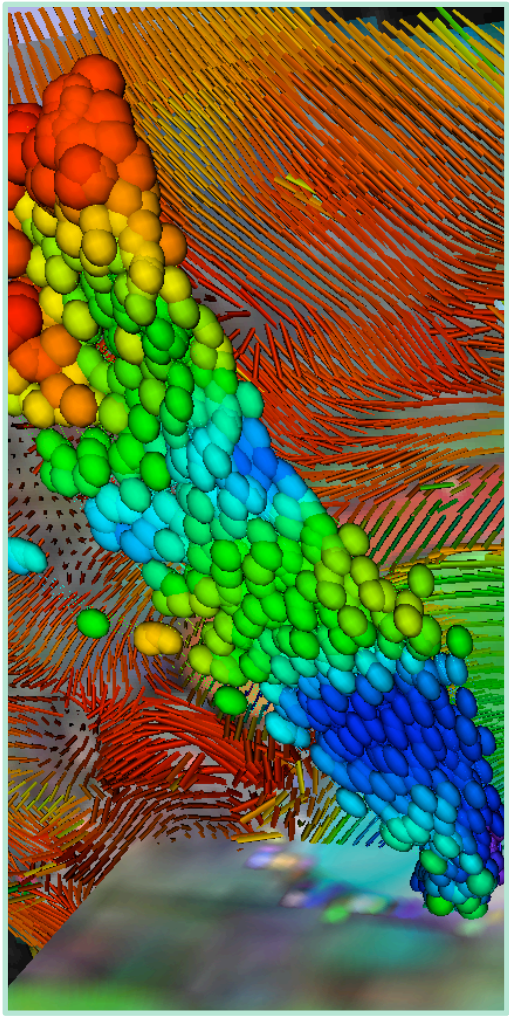


Image provided by Kikinis

Different Styles of Research

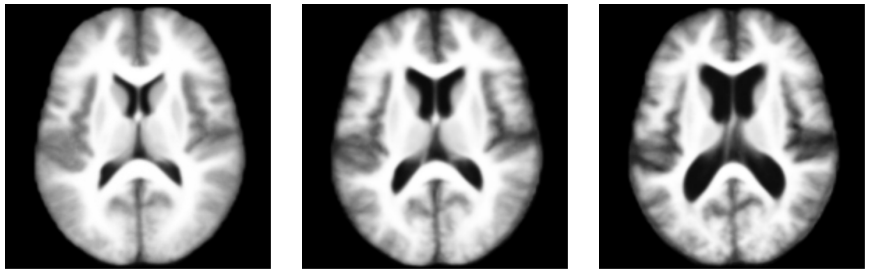
- Group Comparisons
- Subject Specific Analysis (SSA)

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

Group Comparisons

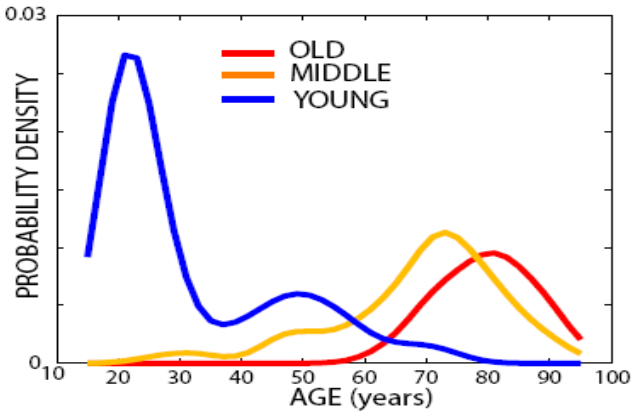
- Often used in basic imaging research
- Targets normal appearing structures. Questions: What is the….
  - Typical appearance
  - Normal variability
- Extensive resources are deployed: personnel, computational
- Most of our research is of this type, it's the easiest way to get results suitable for publication

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



Group Comparisons

- Clinical Imaging Studies are similar to the basic science paradigm:
  - Large number of subjects
  - Years for the analysis
- Requires fully automated pipelines
- Requires large computational resources
- Lack of quality in the processing pipeline **can** be compensated by adding subjects

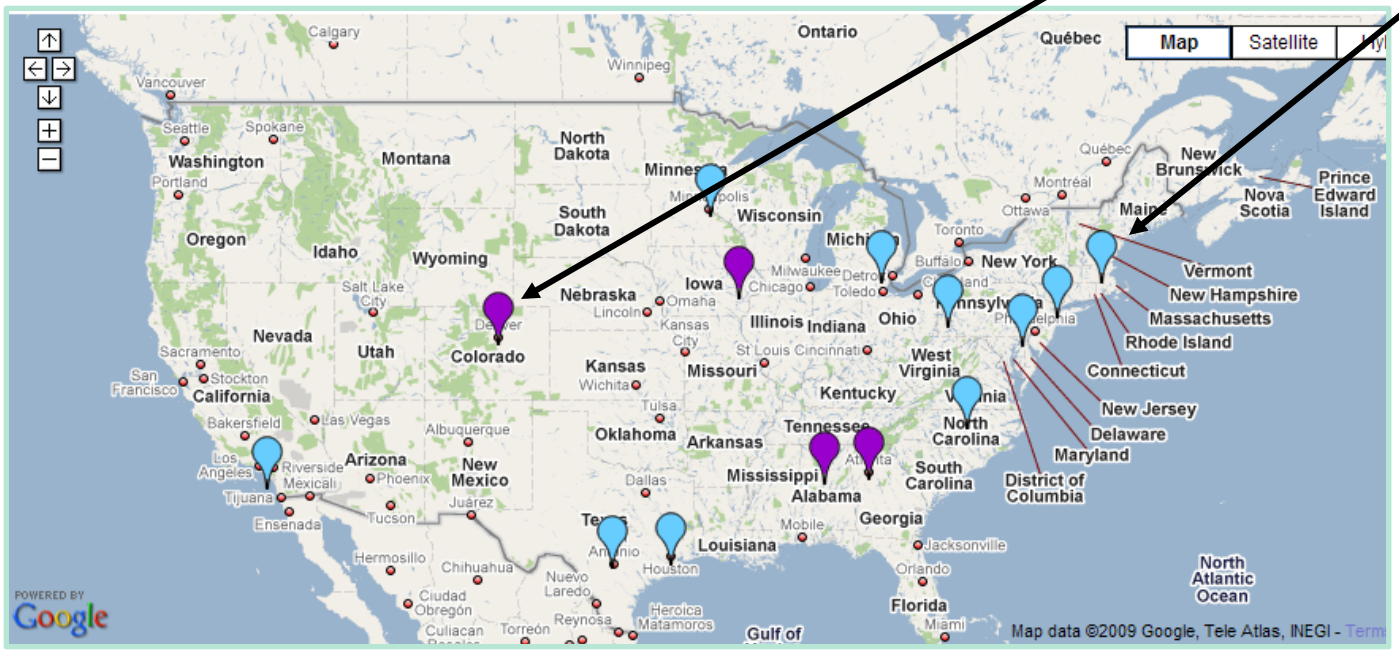
COPDGene

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:

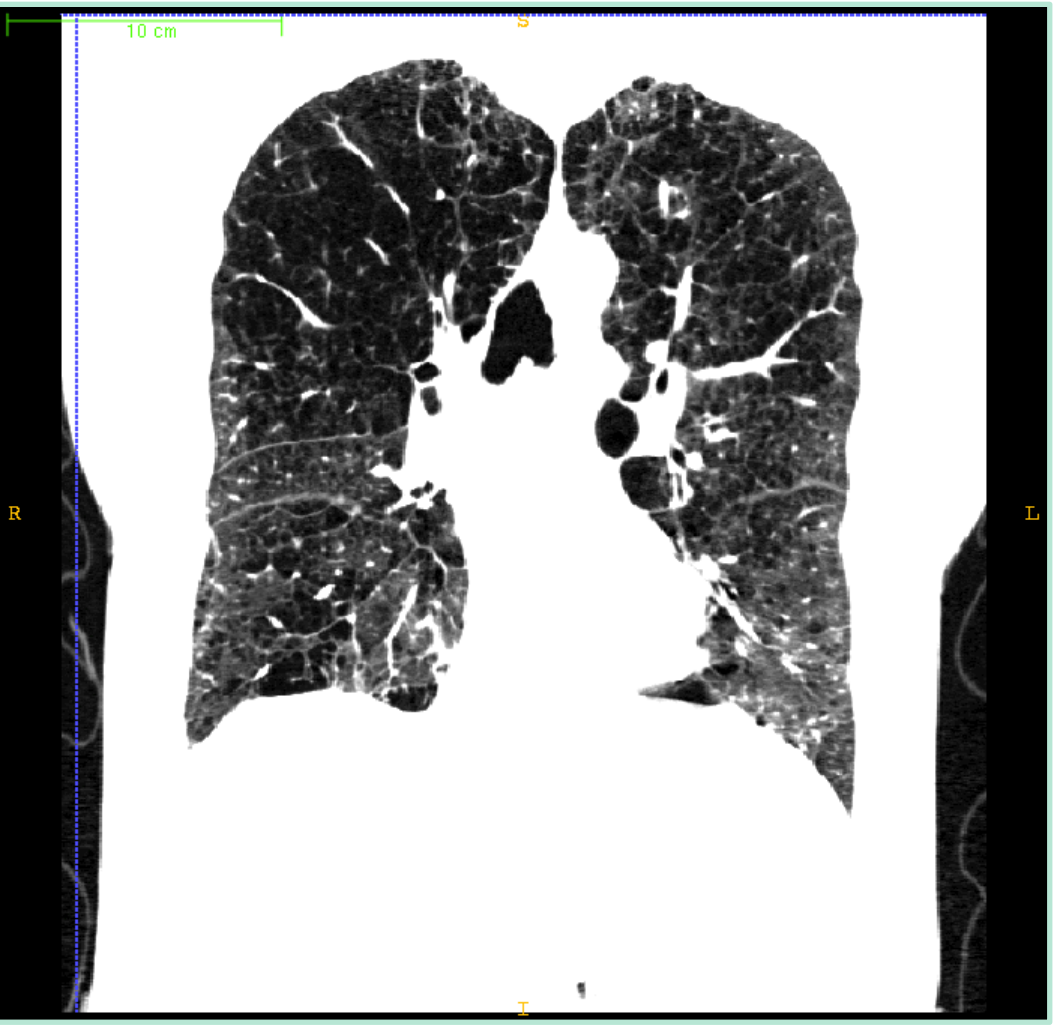
- Denver
- Boston
- Iowa

2 imaging platforms:

- VIDA
- Slicer

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.

Slide courtesy R. San Jose

Phenotype Extraction In The Lung

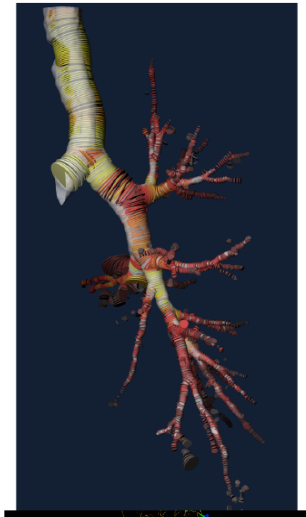
Extraction

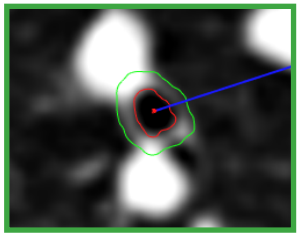
Sizing

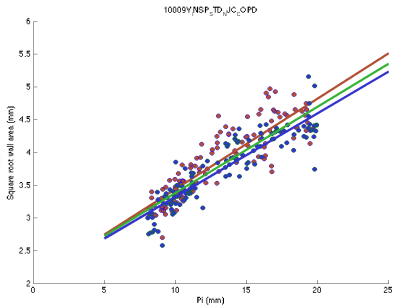
Phenotype

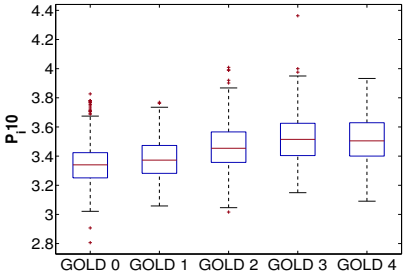
Population Study

Airways







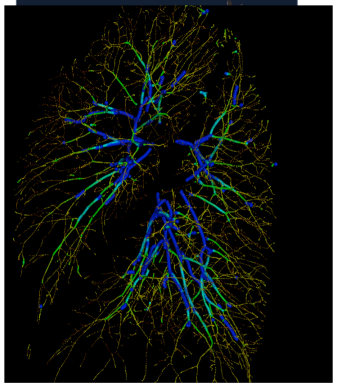


Airway Wall corresponding to a 10 mm internal Perimeter

Smoker Controls → Severe Disease

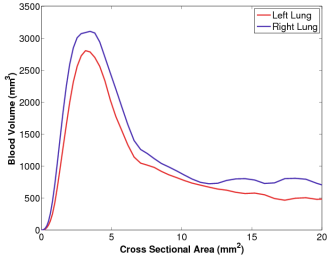
San Jose Estepar R et al, **Automatic Airway Analysis for Genome-Wide Association Studies in COPD,** ISBI 2012

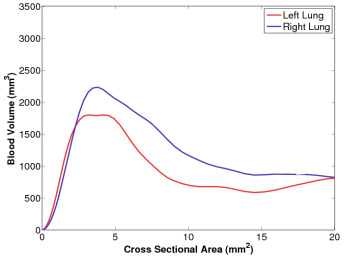
Vessels



Smoker control

Severe disease





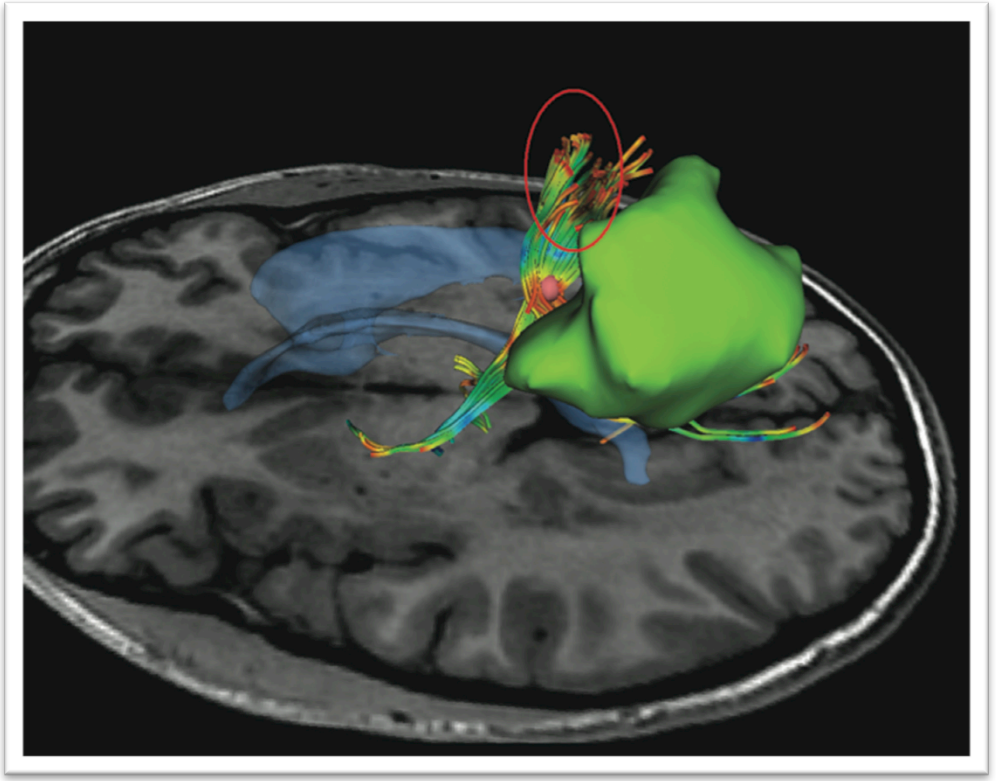
Shift in blood volume per cross sectional area indicating distal pruning and proximal remodeling with disease progression

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

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)

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

- 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.

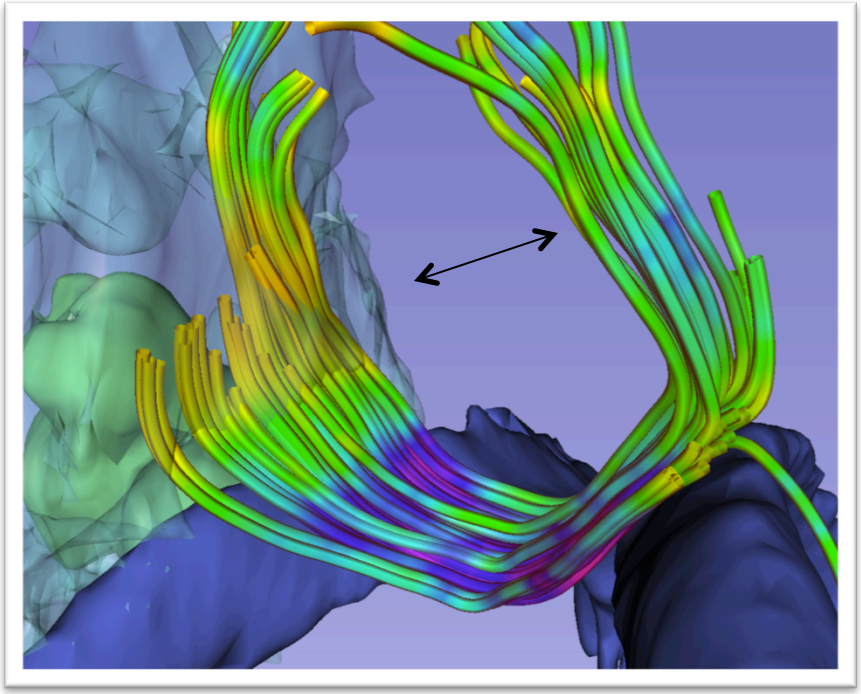
SSA Challenges

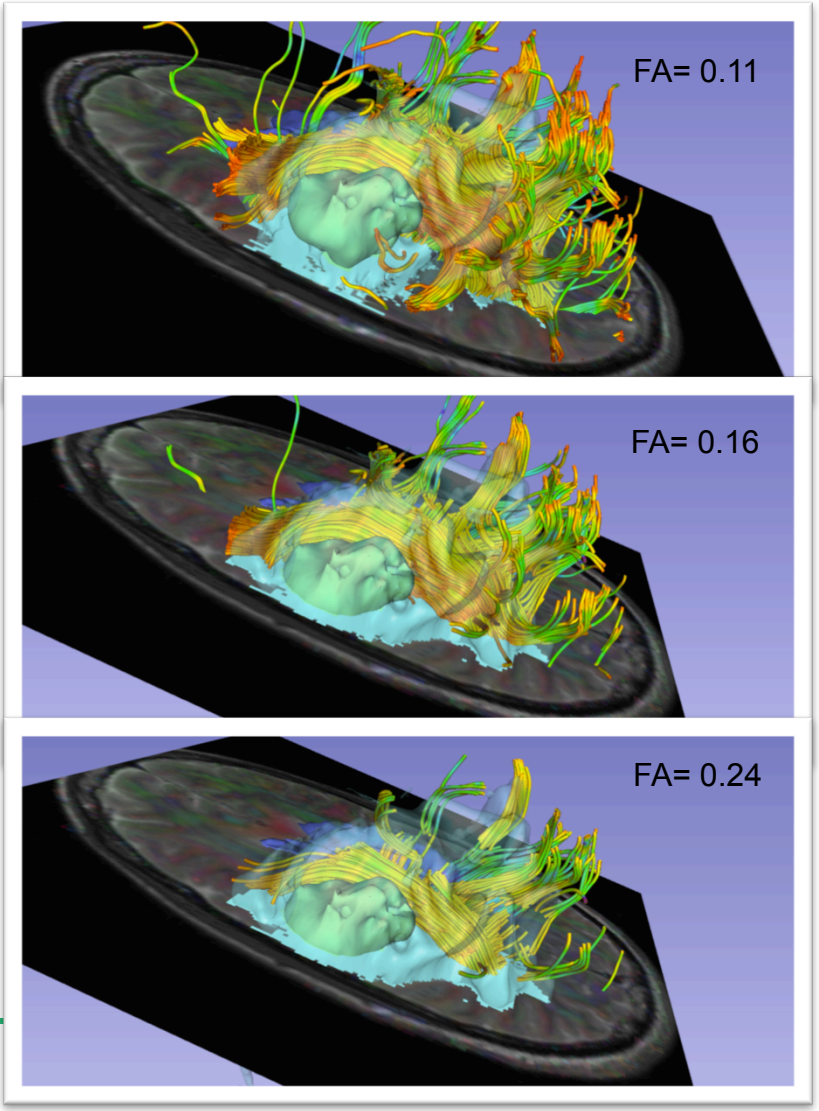
- Many patients have visible pathology. Most MIC technology was developed for analysis of healthy looking subjects
- Tools need to be robust, easy to learn, and quick
- Due to the “valley of death”, very little technology has made it from research into clinical devices

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.

FA Changes Around a Tumor

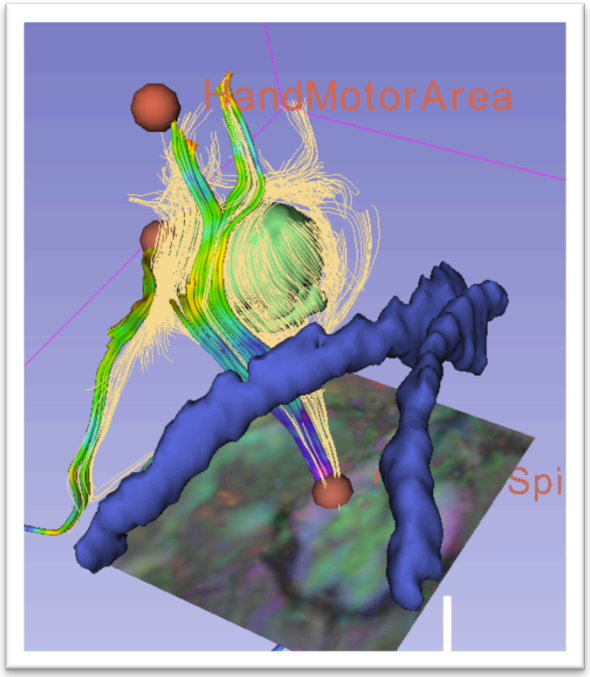


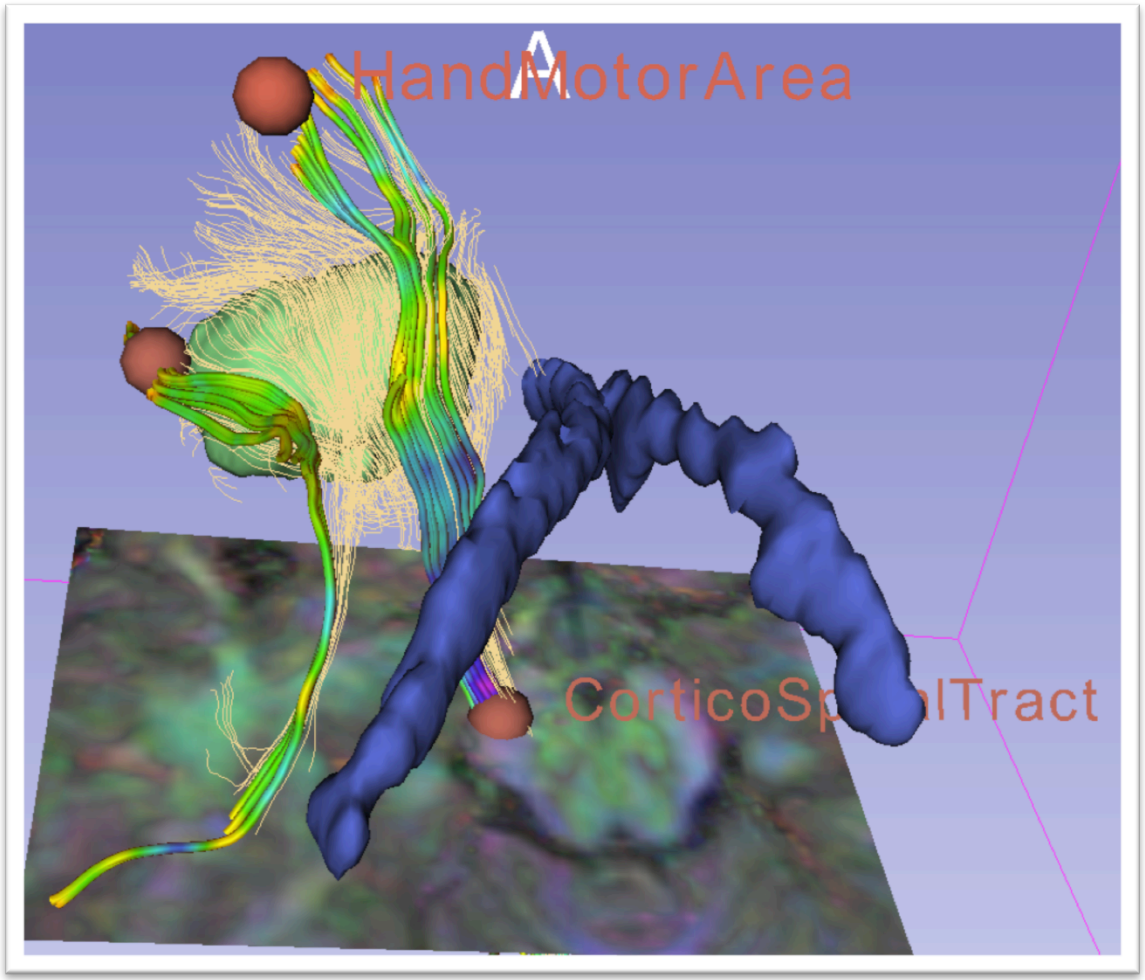


- Asymmetric colorization of the corpus callosum inside the peritumoral edema indicates reduction in FA

Dislocation of Normal Anatomy

The cortico-spinal tract is moved backwards, not toward the midline



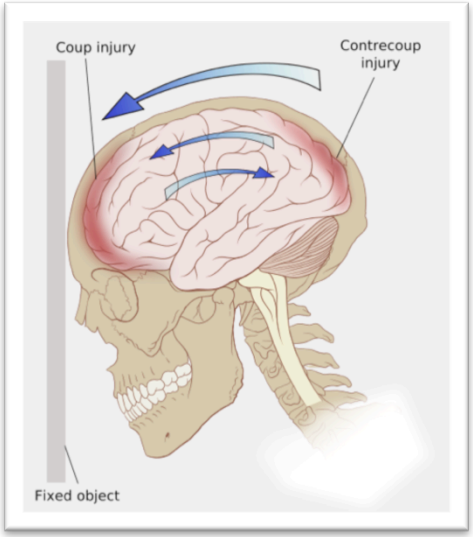


SSA Example

- NA-MIC collaboration between UCLA, Utah, Kitware: Perform Neuroimage Analysis in TBI
- Make segmentation and registration work on TBI subjects. Then parcellate the grey matter and analyze the diffusion weighted images of the white matter

Traumatic Brain Injury Facts

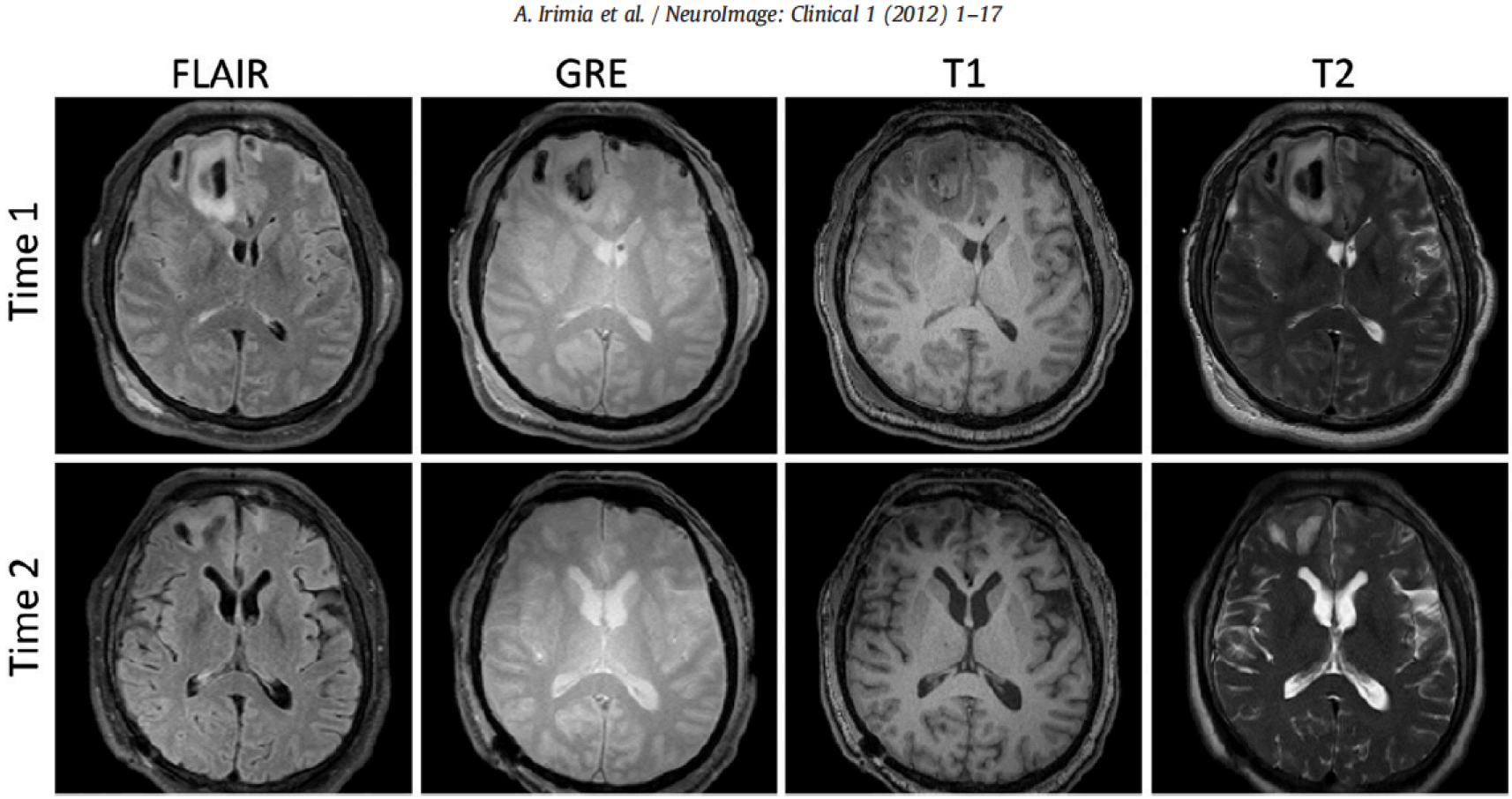
- There are approximately 1.5 million new cases of non-fatal traumatic brain injury (TBI) in the US every year.
- The worldwide incidence of this condition has been estimated to amount to at least 6.8 million TBI cases every year.
- The financial burden of this condition in the USA alone amounts to over $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

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

Traumatic Brain Injury

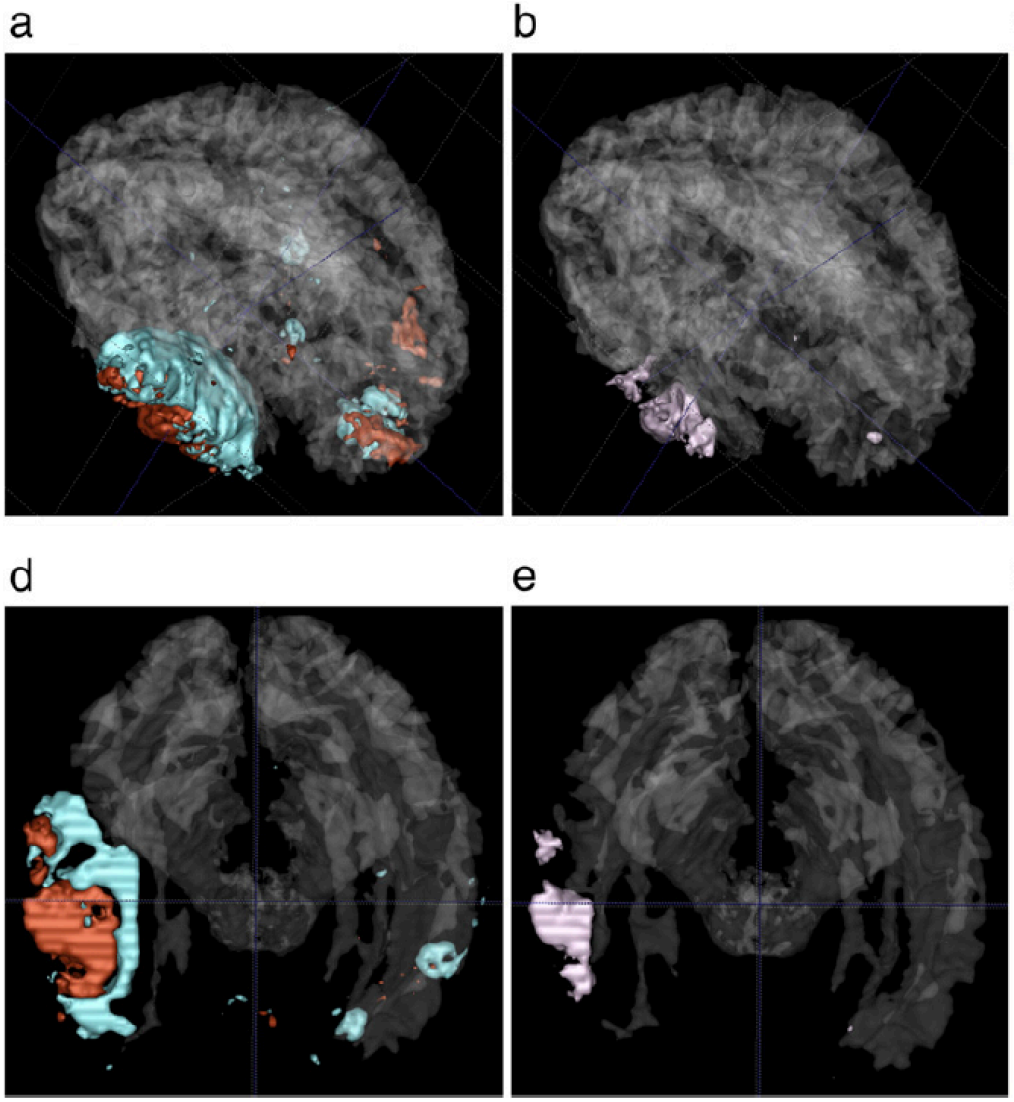


Brain images of patients with traumatic brain injury undergo dramatic changes

Example Traumatic Brain Injury

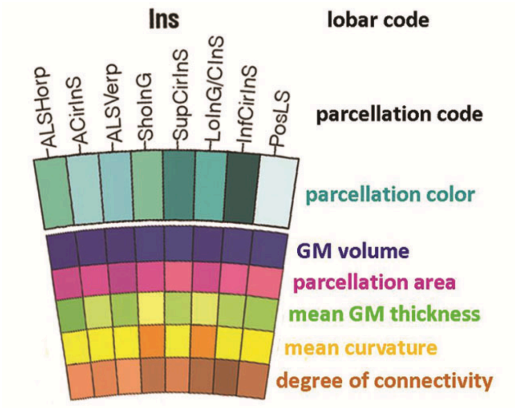
Creation of new algorithms

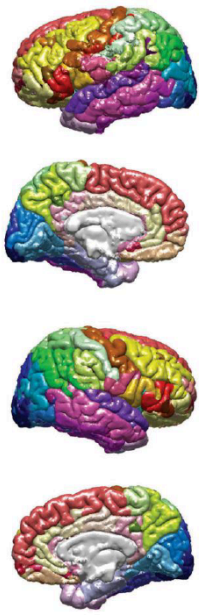
- EM segmenter (Prastawa et al.)
- Non-rigid registration (Pace et al.)

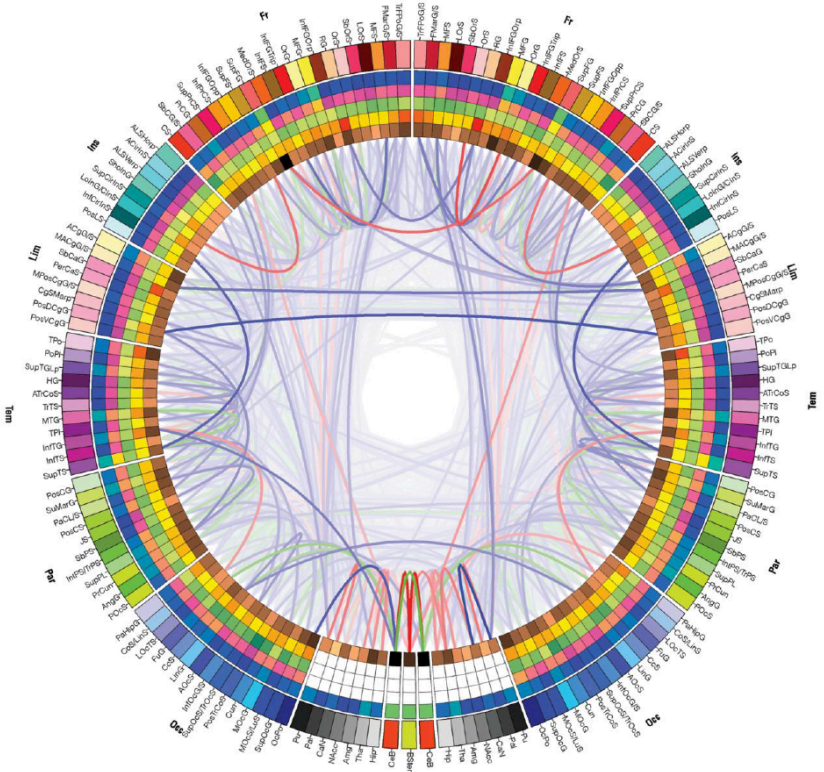


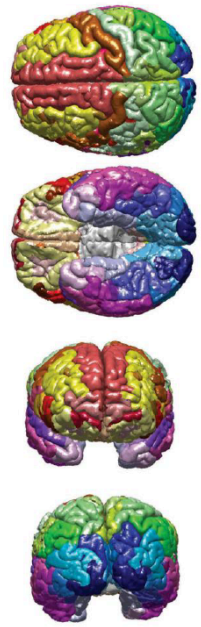
A. Irimia et al. / NeuroImage: Clinical 1 (2012) 1–17

Connectograms





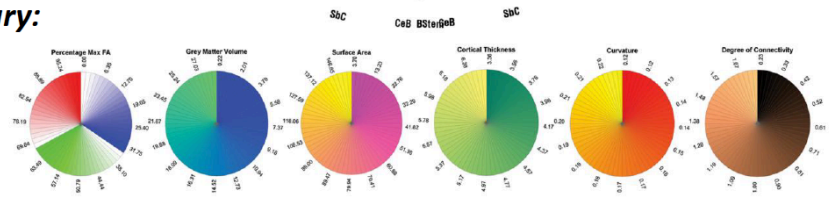




Connectograms use parcellated gray matter regions to analyse the white matter

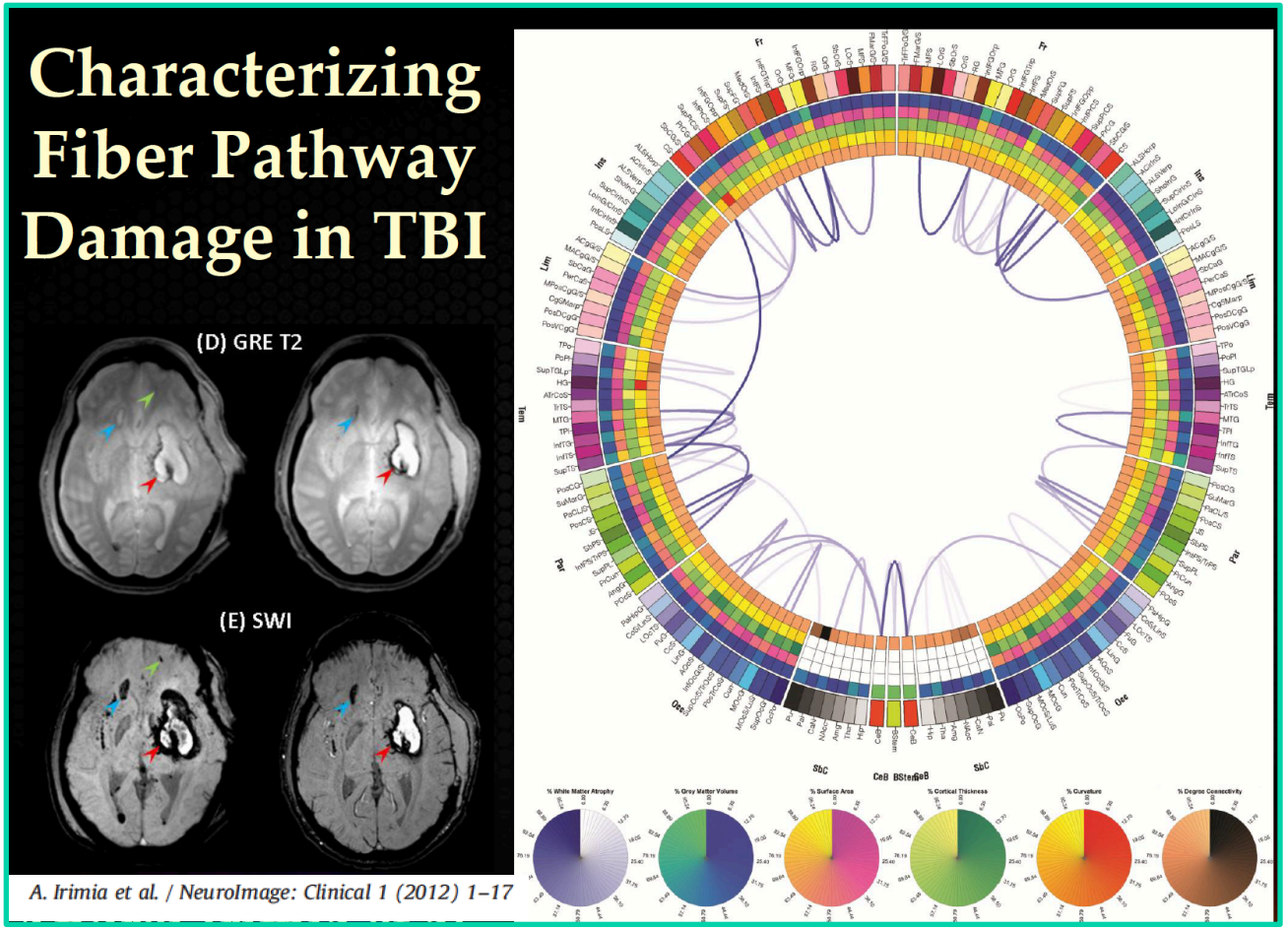
Sample Summary:

N=100
Right handed
Males
25-36 years old



Disease Evolution: Connectomics

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



The Procedure Room

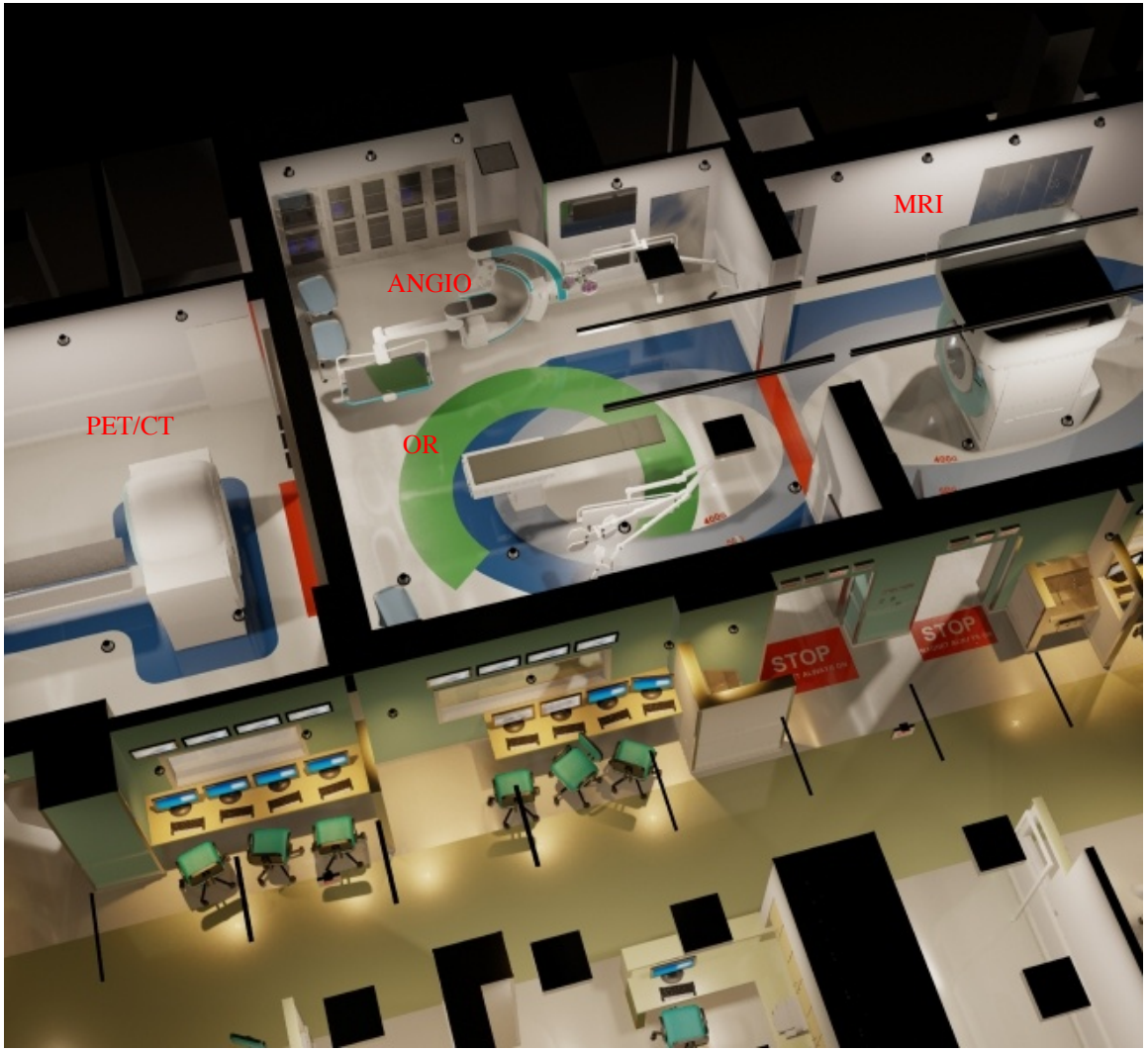
- Procedure rooms such as operating rooms are complex environments
  - Many people in many roles
  - Many devices
- A procedure is like a ballet
  - Every performer has a role
  - The choreography has to be practiced to perfection

Innovation in the Procedure Room

- Introducing a new element into a procedure changes the choreography
- This has to be done carefully and under consideration of impact on the patient
- While bench-top experimentation is necessary, it can not replace work in the procedure room

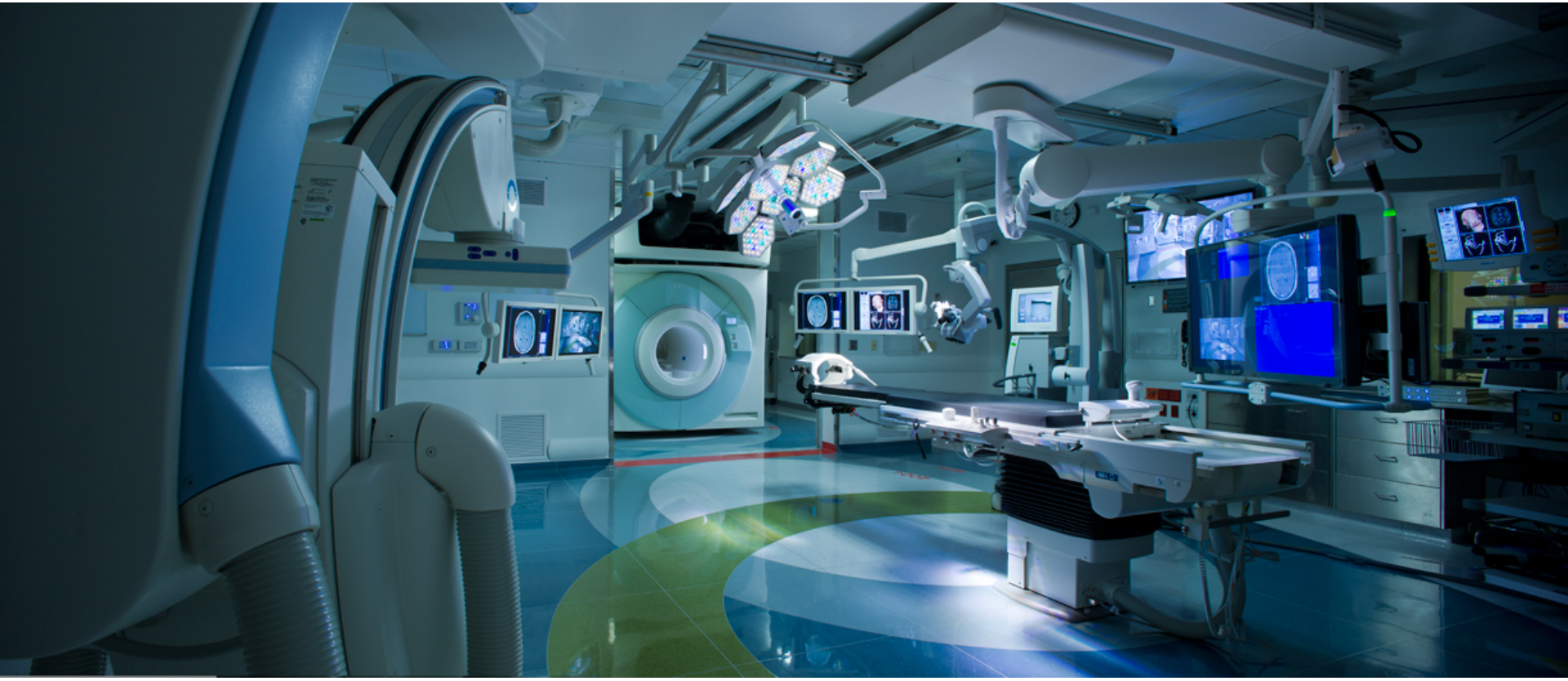
It's a Suite, Not a Room

- Image Guidance procedure rooms are surrounded by support space for imaging and surgery
- Products from a multitude of vendors are present
- Compliance with regulatory requirements provide a dis-incentive for integration across vendors



Rendering courtesy Balasz Lengyel, BWH

Amigo: Environment for IGT Research



Advanced Multimodality Image Guided Operating (AMIGO) Suite

P41 RR019703 – National Center for Image Guided Therapy (NCIGT) 2005-2015

Ferenc Jolesz, MD Clare Tempany, MD

AMIGO : 20 years in the making


Photo by J. D. Levine Photography

AMIGO represents the latest step in IGT research at BWH started in the early 1990's

1991
- BWH Image-guided Therapy program founded by Ferenc Jolesz
- Introduction of world's first inter-operative MR magnet: MRT 'double-donut'

1994
- BWH develops first MR-guided Focused Ultrasound (MRgFUS) system

2005
- Creation of NIH-funded National Center for Image Guided Therapy
- IGT applications expand to other advanced imaging modalities

2011
- AMIGO: First suite to offer the full array of advanced imaging modalities in one operating theater (MRI, PET/CT, 3D US, Fluoro, Angio)

MRT

MRgFUS

NCIGT

NATIONAL CENTER FOR IMAGE-GUIDED THERAPY iGT

AMIGO

Since the early/mid-1990's, over 100 interoperative MRIs and close to 100 MRgFUS systems have been installed throughout the world

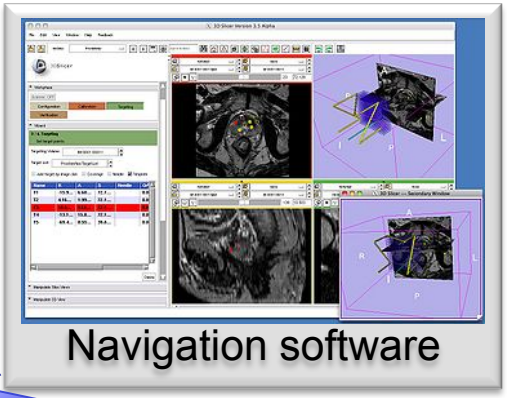
Training and technology dissemination: eg, 3D slicer

A clinical and translational test bed for multi-modal IGT

Slide courtesy T. Kapur

OpenIGTLink: Device API

- Communication protocol for IGT
  - Intraoperative imaging
  - Optical tracking devices
  - Robotic devices
  - More



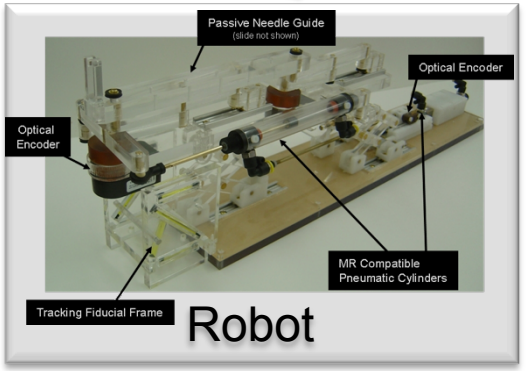
Image

Transform

Status

Command

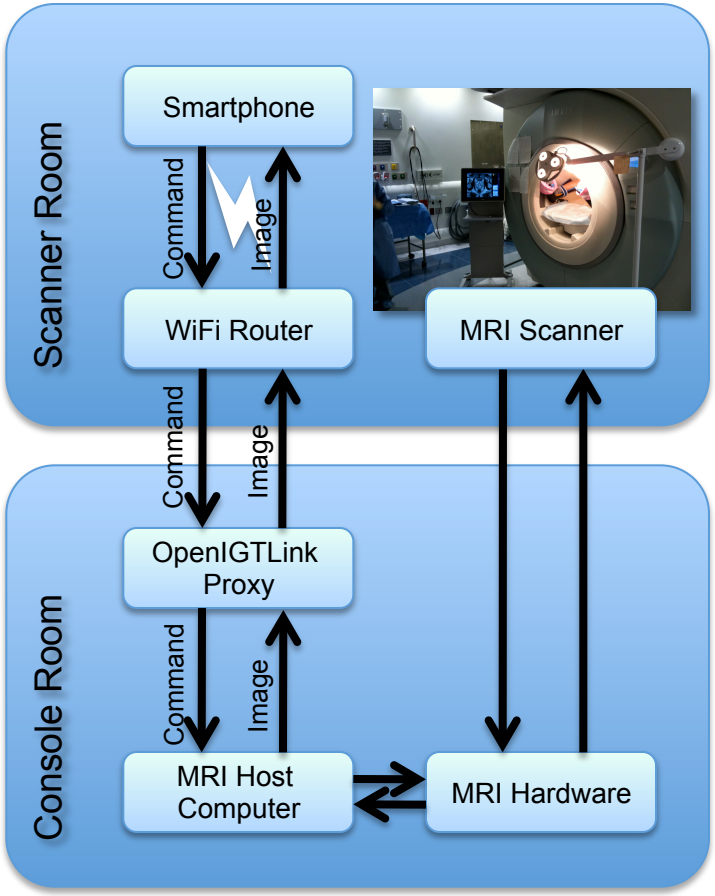
Xenios Papademetris enabled interface to the Brainlab Navigation system using OpenIGTLink



Slide courtesy J. Tokuda

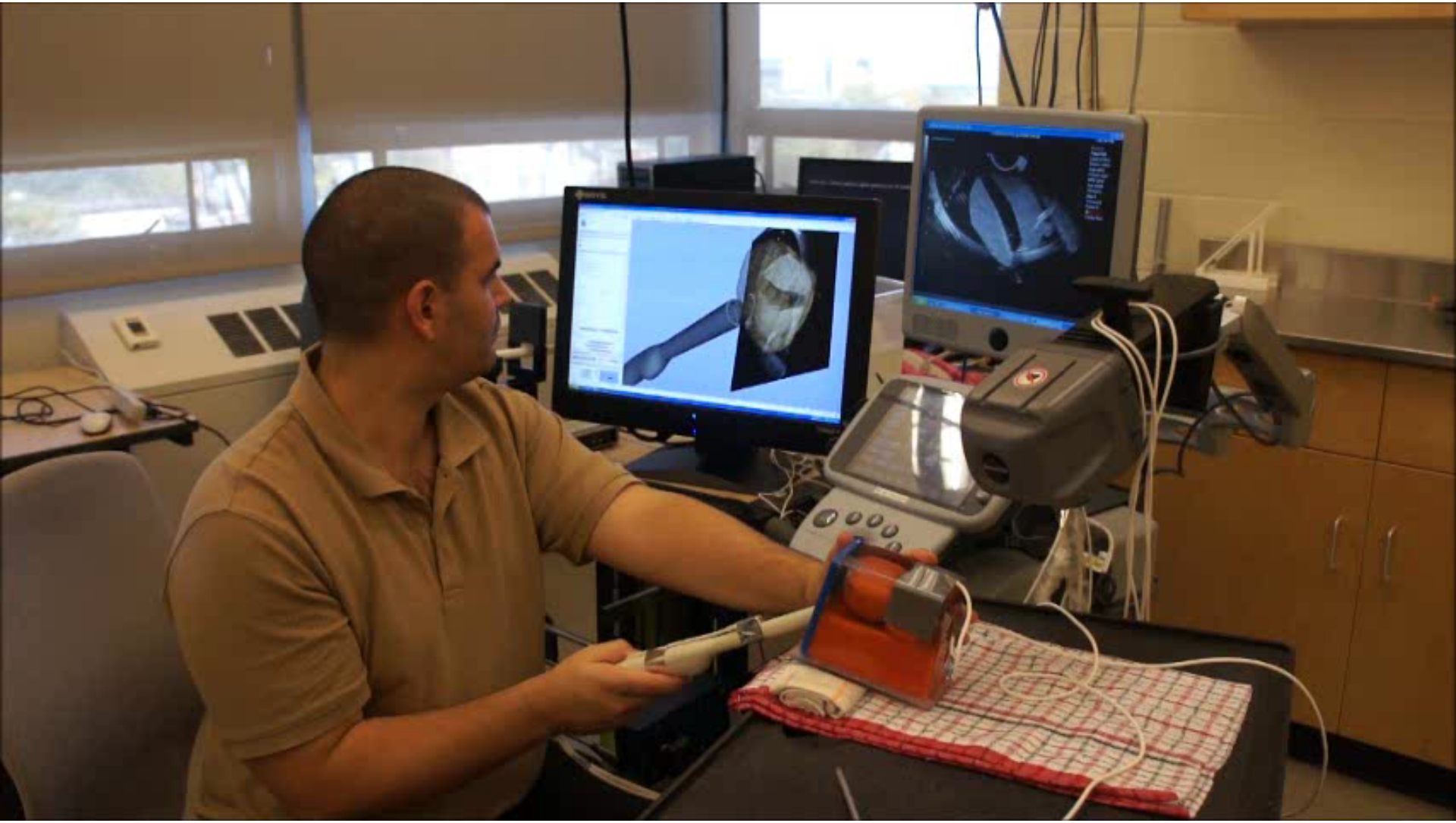
Controlling Devices

Use an iPhone to control scan plane acquisition



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

US Tracking: 2011: Bench

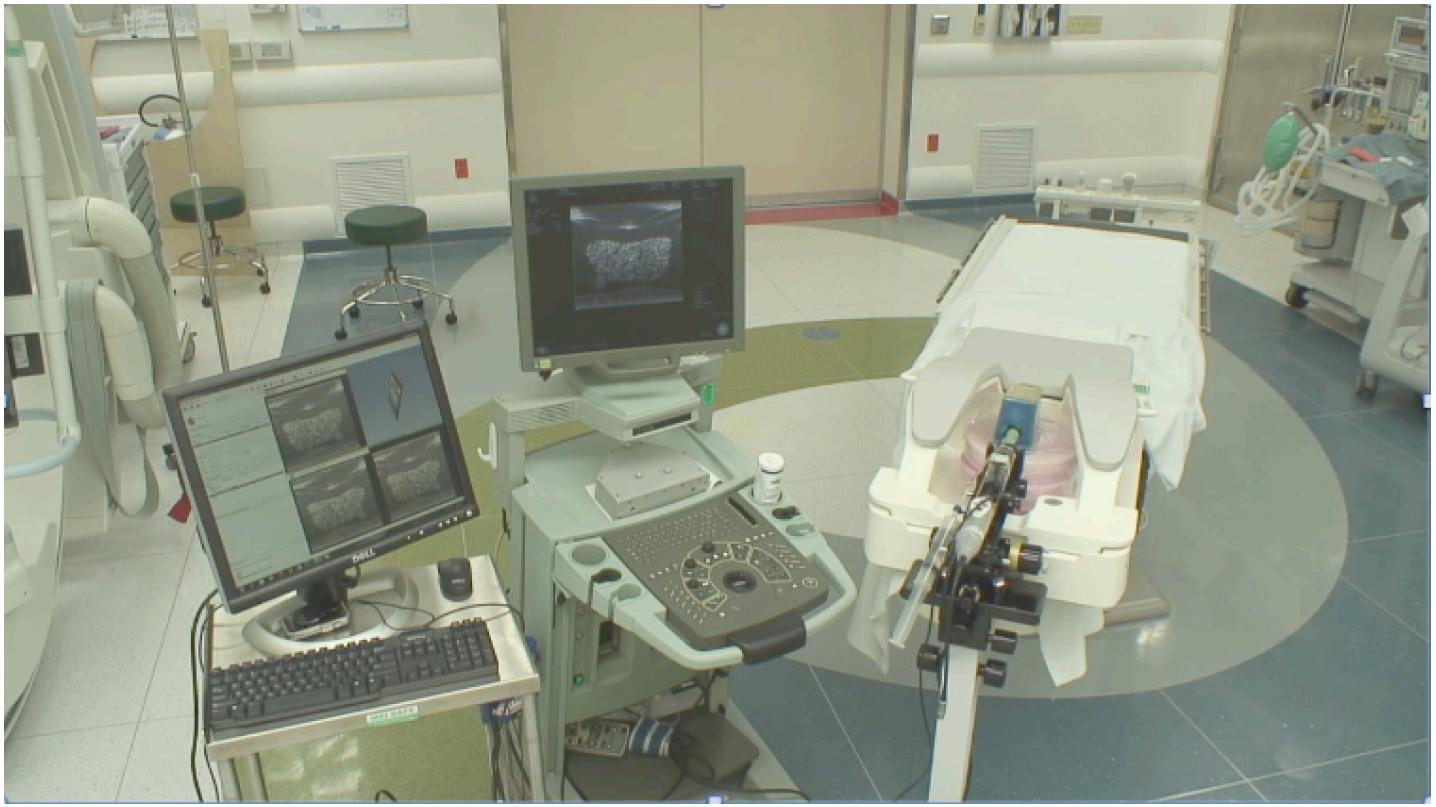


Movie courtesy Ungi, Lasso, Fichtinger

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.



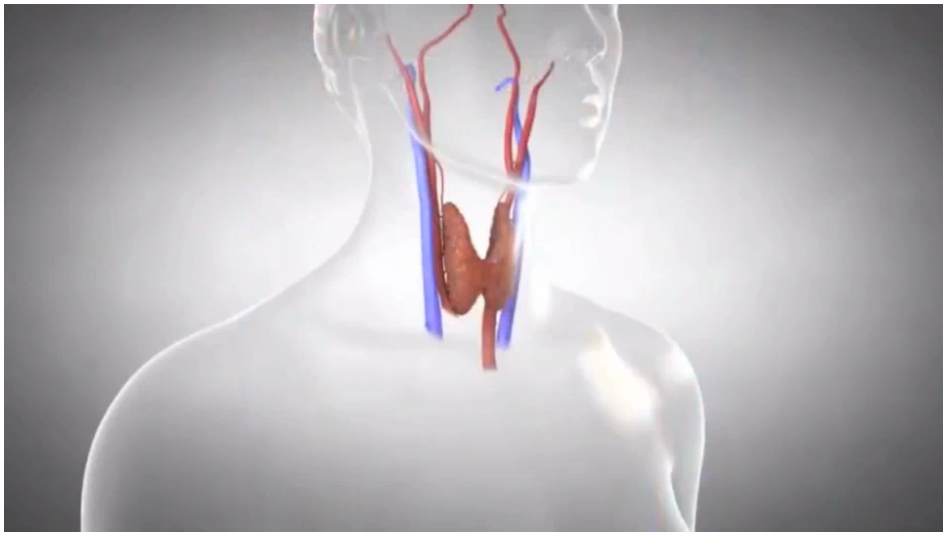
Parathyroidectomy in AMIGO

Image-guided navigation to localize and excise parathyroid adenoma

Slide courtesy of Jayender Jagadeesan

Hyperparathyroidism

- Primary hyperparathyroidism (HPT) affects 0.2 to 0.5% of the population
- 100,000 new cases in the US per year
- Surgery is the only treatment option
- 5-10% of cases are recurrent or persistent HPT after surgery

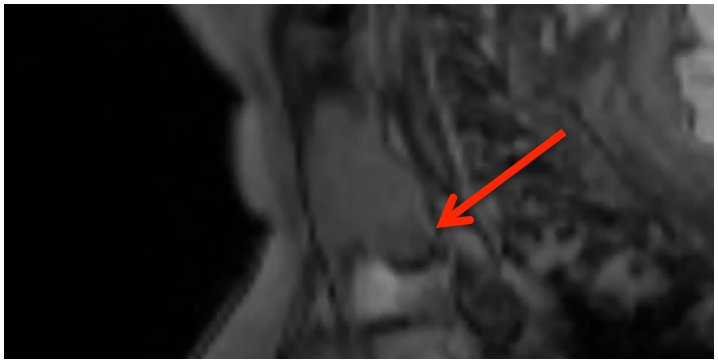


Video: ParathyroidTV.com

Slide courtesy of Jayender Jagadeesan

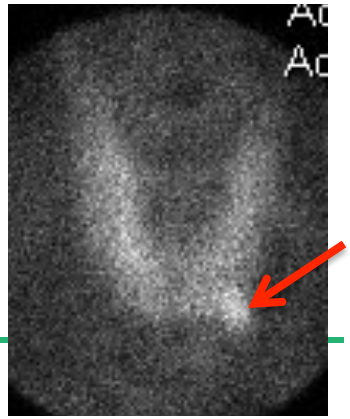
Diagnostic Imaging

DCE MRI



CT

Sestamibi scans



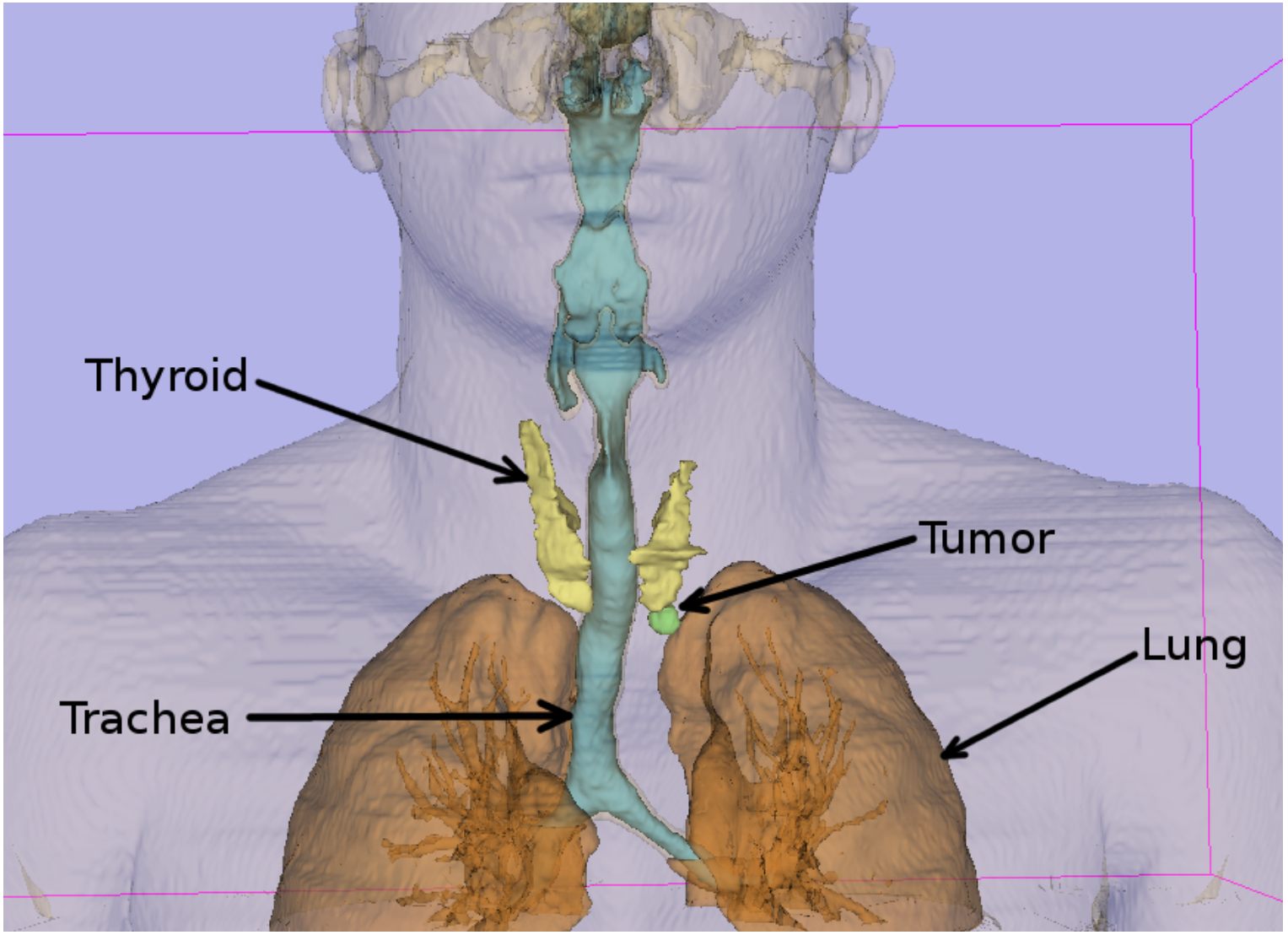
Jayender et. al, Segmentation of parathyroid tumors from DCE-MRI using Linear Dynamic System analysis, ISBI 2013

Intraoperative MRI

- Fiducials placed on the patient for enabling “Patient-to-Image” registration
- A two part IMRIS cardiac coil is utilized for imaging
- Cartridge built to house the cardiac coil and EM flat plate transmitter (red arrow)
- Imaging
  - Gross T1 3mm slices
  - Hi-res T2 images

Images courtesy Jayender Jagadeesan

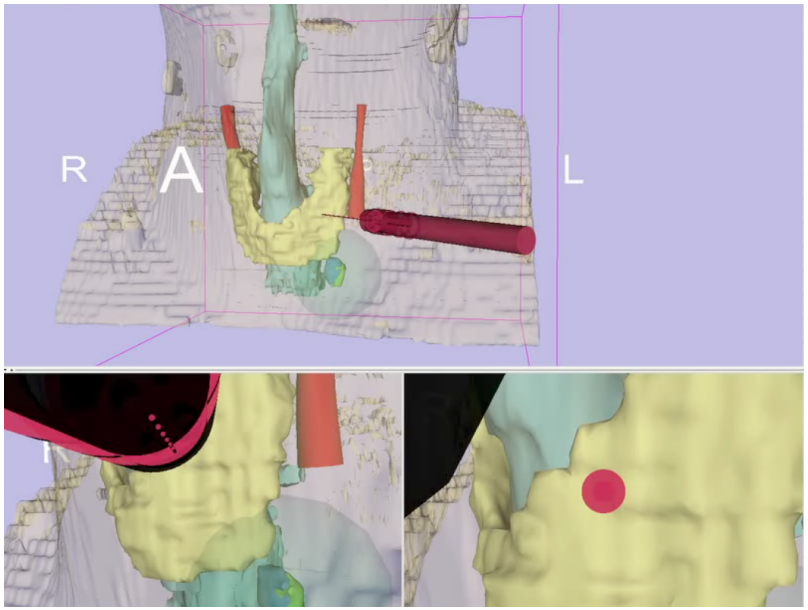
Surgical Planning for Procedure



Slide courtesy of Jayender Jagadeesan

Customized Navigation Display

- Three views
  - Global
  - Wingman's view
  - Virtual Endoscopy
- Deformation sensor
  - Estimate deformation of the tumor and compensate in the virtual reality display
- Visual and Audio tumor proximity feedback
  - Dilated tumor model with 1cm margin
  - Increase beep frequency based on tumor proximity



Slide courtesy of Jayender Jagadeesan

Intraoperative Video

x 2 speed

Slide courtesy of Jayender Jagadeesan

Result of Navigation System

- Registration error = 3.23 mm
  (Rigid = 1.97mm)
- Minimum distance of the instrument to
  - Tumor = 0.48 mm
  - Trachea = 0.20 mm
  - Thyroid gland = 1.81 mm
  - RMS deformation sensor = 2.0 mm
- NASA TLX
  - Physical, Mental demand very low

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

Slide courtesy of Jayender Jagadeesan