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Medical Imaging 101

Randy Gollub,MD,PhD
Harvard Catalyst Imaging Consortium

http://catalyst.harvard.edu

November 5, 2009

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Imaging Consortium Team

Massachusetts General Hospital	**Bruce Rosen, Director** **Randy Gollub, Co-Director** **Gordon J. Harris, Consultant** **William Hanlon, Consultant**
Beth Israel Deaconess Medical Center	**Robert Lenkinski, Consultant** **Neil Rofsky, Consultant**
Brigham and Women's Hospital, A Teaching Affiliate of Harvard Medical School	**Clare Tempany, Consultant** **Ron Kikinis, Consultant** **Charles Guttmann, Consultant** **Todd Perlstein, Consultant** **Gordon Williams, PI for CTSC Translational Technologies**
Children's Hospital Boston, The Hospital for Children	**Stephan Voss, Consultant** **Simon Warfield, Consultant**
Dana-Farber Cancer Institute	**Annick D. Van den Abbeele, Consultant** **Jeff Yap, Consultant, Director of Education**
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Imaging Consortium Consultation Service

http://catalyst.harvard.edu/services/imagingconsulting.html

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MedscapeWire

MRI and CT Ranked the Top Medical Innovations by Physicians

October 11, 2001

New York - Physicians surveyed about the most important innovations of the last 25 years ranked interventions for cardiovascular disease and high-tech scanning devices such as magnetic resonance imaging (MRI) and computed tomography (CT) among the most important. They ranked bone marrow transplantation and the erectile dysfunction drug sildenafil among the least important innovations.

The ranking of the 30 medical innovations in the study are as follows:

1. MRI and CT
2. ACE inhibitors
3. Balloon angioplasty
4. Statins
5. Mammography
6. Coronary artery bypass graft
7. Proton pump inhibitors and H2 blockers
8. Selective serotonin reuptake inhibitors (SSRIs) and new non-SSRI antidepressants
9. Cataract extraction and lens implant
10. Hip and knee replacement
11. Ultrasonography and echocardiography
12. Gastrointestinal endoscopy
13. Inhaled steroids for asthma
14. Laparoscopic surgery
15. Nonsteroidal anti-inflammatory drugs and COX-2 inhibitors
16. Cardiac enzymes
17. Fluoroquinolones
18. New hypoglycemic agents
19. HIV testing and treatment
20. Tamoxifen
21. Prostate-specific antigen testing
22. Long-acting and local opioid anesthetics
23. *Helicobacter pylori* testing and treatment
24. Bone densitometry
25. Third-generation cephalosporins
26. Calcium channel blockers
27. Intravenous conscious sedation
28. Sildenafil (Viagra)
29. Nonsedating antihistamines
30. Bone marrow transplant

Fuchs and Sox, Health Affairs 2001 20(5):30-43

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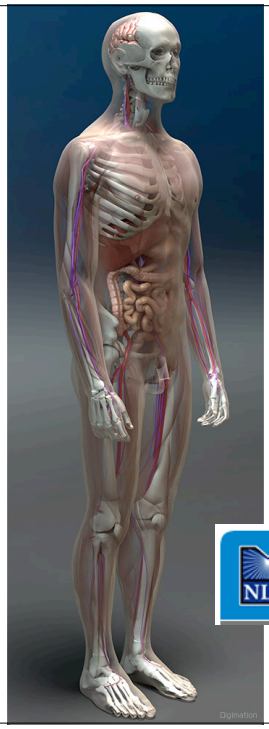

Your patient?

United States National Library of Medicine
National Institutes of Health

The Visible Human Project®
http://www.nlm.nih.gov/research/visible/

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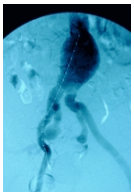
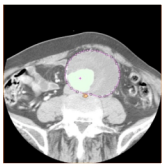
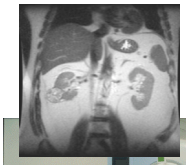
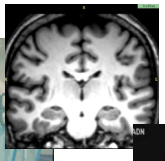
X-Ray Fluoroscopy

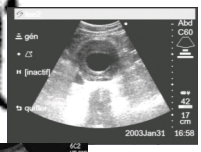
Computed Tomography

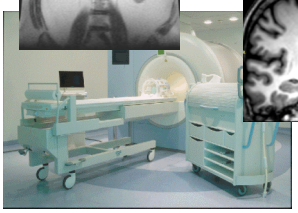


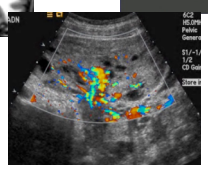












Magnetic Resonance Imaging

Ultrasound Imaging

Advances in Structural MRI Acquisition

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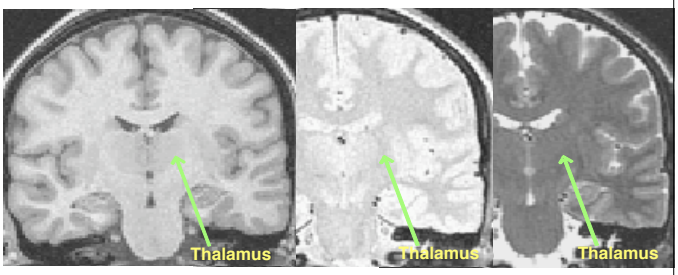
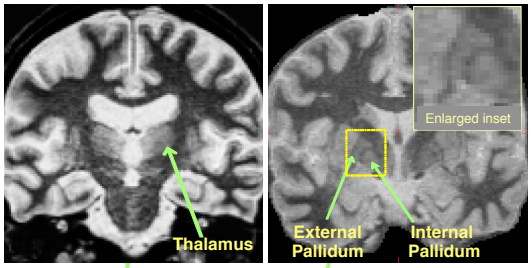
- Traditional pulse sequences

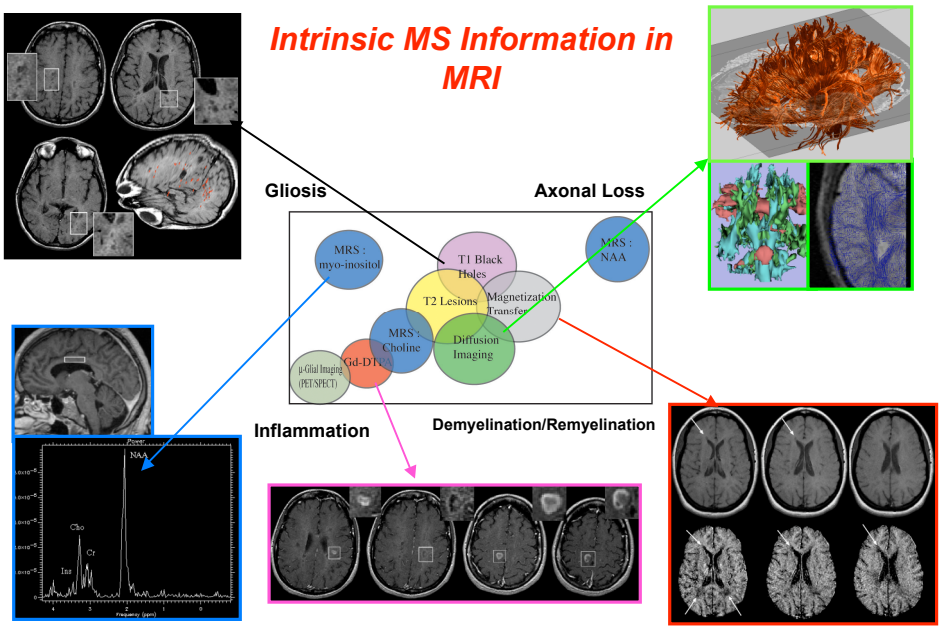


- Novel pulse sequence improves subcortical region



Fischl et al., 2006

Intrinsic MS Information in MRI



Dominik Meier, Wing Wu, Charles Guttmann, Center for Neurological Imaging, BWH

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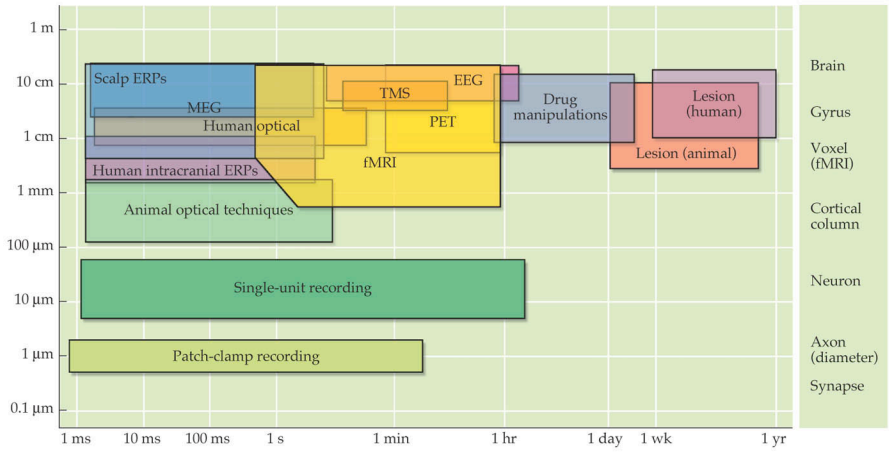
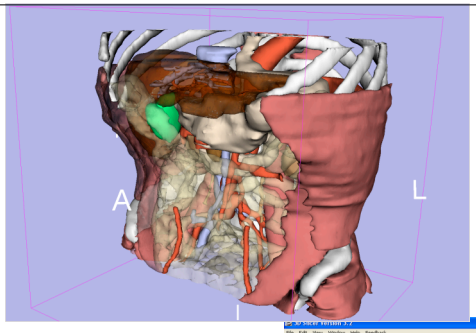
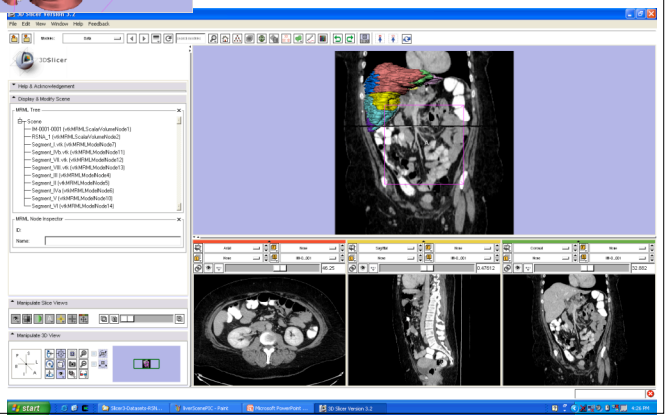
Scale in studying the nervous system





Interact in 3D to enhance data interpretation



Slicer Workshop
November 23, 12 pm
Countway

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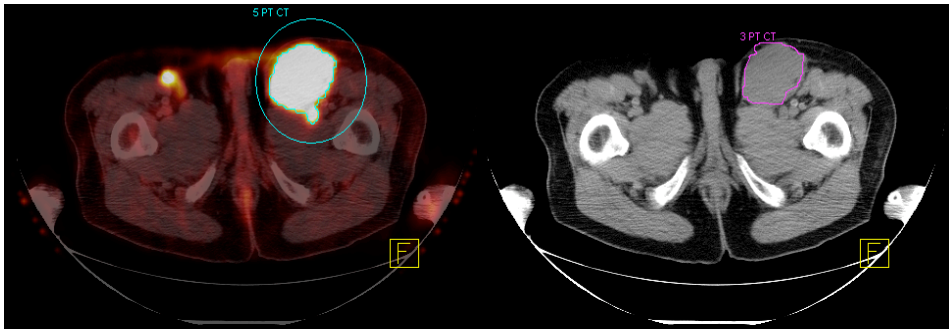
Matching Image Acquisition to Target Biomarker



Primary outcome measures determine details of acquisition and analysis

All acquisitions must be standardized within &/or across site and time

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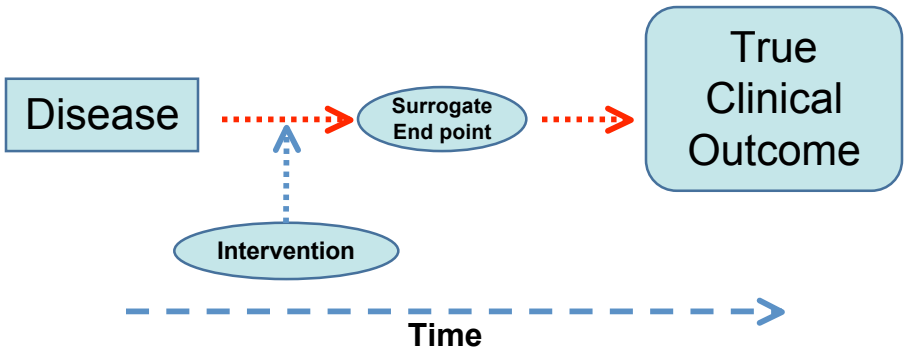
Definition of a biomarker

- "A characteristic that is objectively measured and evaluated as an indicator of normal biologic processes, pathogenic processes, or pharmacologic responses to a therapeutic intervention."

** Biomarkers Definitions Working Group. Biomarkers and surrogate endpoints: Preferred definitions and conceptual framework. Clin Pharmacol Ther. 2001;69:89–95.*

Ideal relationship between intervention, disease and surrogate endpoint

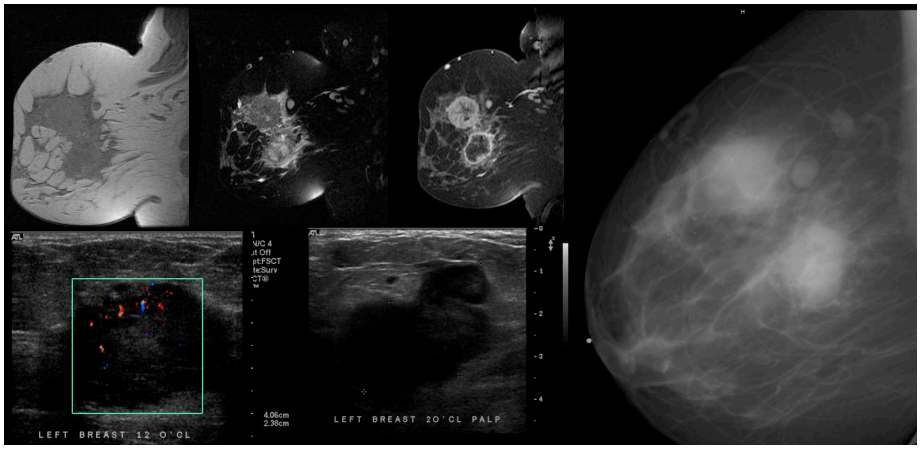
- Surrogate is in the only causal pathway of disease and intervention's entire effect on true clinical outcome is mediated through its effect on the surrogate



Fleming, et al. Ann Intern Med. 1996; 125:605

What is quantitative imaging?

- Extracting quantitative measurements from medical imaging



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Which imaging parameters are quantitative?

- Morphology
  - Volume, 3D techniques
  - Cellularity/density/composition of tissues
- Function
  - Perfusion (DCE-MRI)
  - Metabolic activity (PET)
  - Metabolite concentration (H1 spectroscopy, Na23)
  - Molecule movement, e.g. water molecule (DWI)

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Why QI qualifies as a biomarker?

- An ideal biomarker should give a specific and continuous indication of the disease and be quantifiable by using a readily obtainable matrix
- Imaging provides quantifiable parameters noninvasively

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Alzheimer's Disease Neuroimaging Initiative

- ADNI Imaging Goals:
  - Link all data at each time point and share data with public
  - Develop technical standards for imaging in longitudinal studies
  - Optimize acquisition and analysis
  - Validate imaging and biomarker data with psychometric and clinical assessments
  - Improve clinical trial methods

from The Alzheimer's Disease Neuroimaging Initiative (ADNI): MRI Methods. Jack CR et al. JMRI 27:685-691 (2008).

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ADNI – Biomarkers for AD

- A longitudinal multisite study of elderly people with either mild cognitive impairment (MCI, N=400), Alzheimer's Disease (AD, N=200) or normal cognition (N=200).
- Data was collected at 55 sites.
- Half of the subjects were imaged using FDG positron emission tomography (PET). All were imaged using MRI on a 1.5T scanner with a structural imaging protocol.

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ADNI – Technical Issues

- While humans can make sense of images with minor artifacts, this is not usually true of automated processing pipelines.

Therefore:

1. use larger fields-of view and many slices
2. no parallel imaging
3. no partial k-space imaging
4. correct for chemical shift artifacts
5. correct for intensity inhomogeneity

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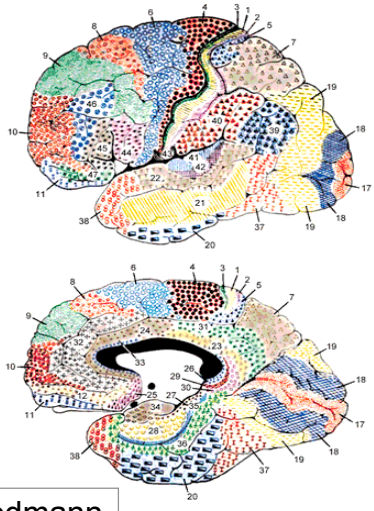
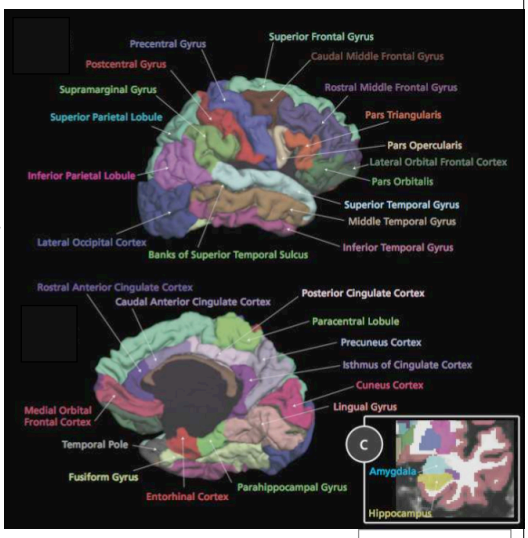
Structural localization of function



Brodmann 1909



Desikan 2009

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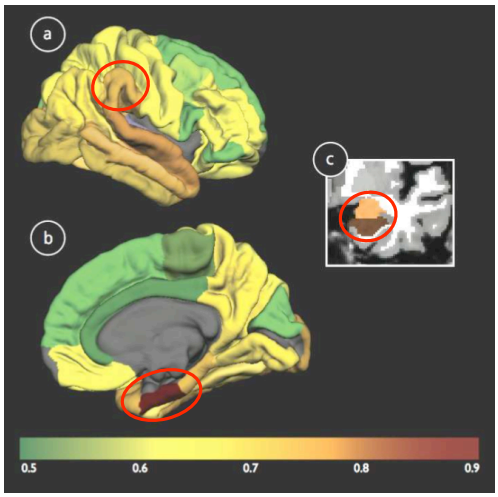
Automated Freesurfer segmentation output predicts MCI



- Entorhinal cortical thickness
- Hippocampal volume
- Supermarginal gyrus thickness

Desikan, et al Brain, 2009

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Clinical Research with vascular ultrasound

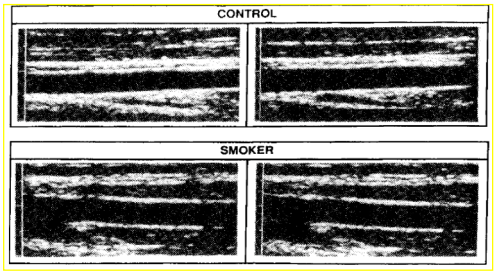
Todd Perlstein

Brigham and Women's Hospital

Ultrasound assessed flow mediated vasodilation is an effective means of measuring endothelium-derived nitric oxide

- Endothelium-derived relaxing factor (EDRF) identified 1980
- Nitric oxide (NO) identified as being EDRF in 1986
- NO now recognized as principal determinant of endothelial function and vascular homeostasis
- NO half-life of seconds prevents direct quantification in humans

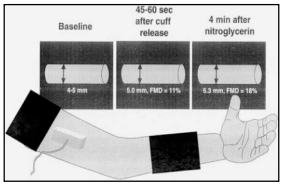
Vanhoutte PM. ATVB 2009.



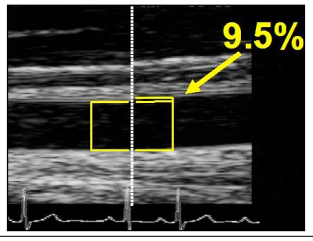
- Ultrasound measurement of brachial artery flow-mediated dilation (FMD) described in 1992. Celermajer DS. Lancet.
- Demonstration that FMD is NO-dependent in 1996. Lieberman EH. AJC.

Ultrasound assessed flow mediated vasodilation is an effective means of measuring endothelium-derived NO

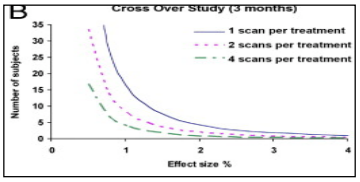
Standardized protocol completed in < 1 hour



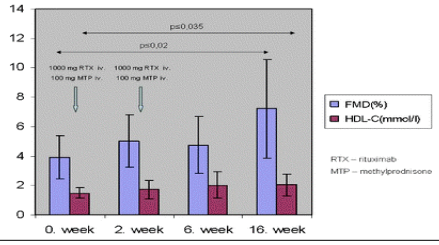
High-resolution ultrasound achieves excellent endothelial imaging



Precise measurement enables small sample size. Donald AE. JACC 2008

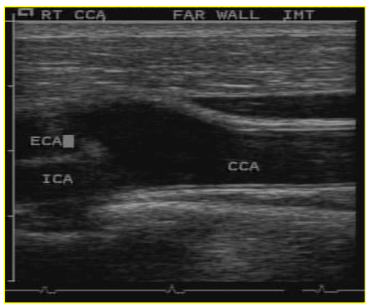


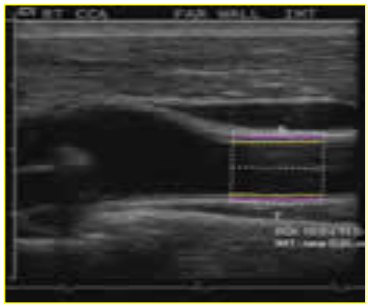
FMD improves with Rituximab therapy in Rheumatoid Arthritis. Kerekes G. Clin Rheum 2009



Non-invasive determination of atherosclerosis burden: carotid intima-media thickness

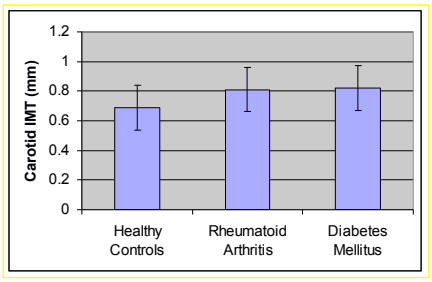
- High-resolution ultrasound measurement of carotid IMT described in 1991. Salonen R. Ultrasound Med Biol.
- Carotid IMT strongly correlates with CV risk factors
- Carotid IMT independently predicts CV events. Lorenz. Circulation 2007.
- Standardized protocol completed in < 20 min





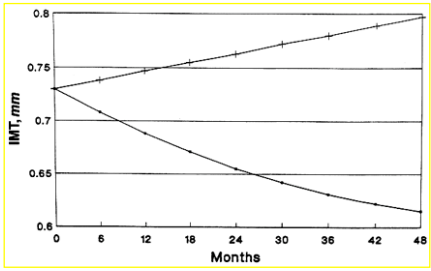
Non-invasive determination of atherosclerosis burden: carotid intima-media thickness

Carotid IMT can demonstrate accelerated atherosclerosis in chronic inflammatory diseases



Stamatelopoulos et al. ATVB 2009.

Carotid IMT progression documents benefit of lipid-lowering therapy in patients with coronary artery disease



Hodis et al. Ann Intern Med 1996.

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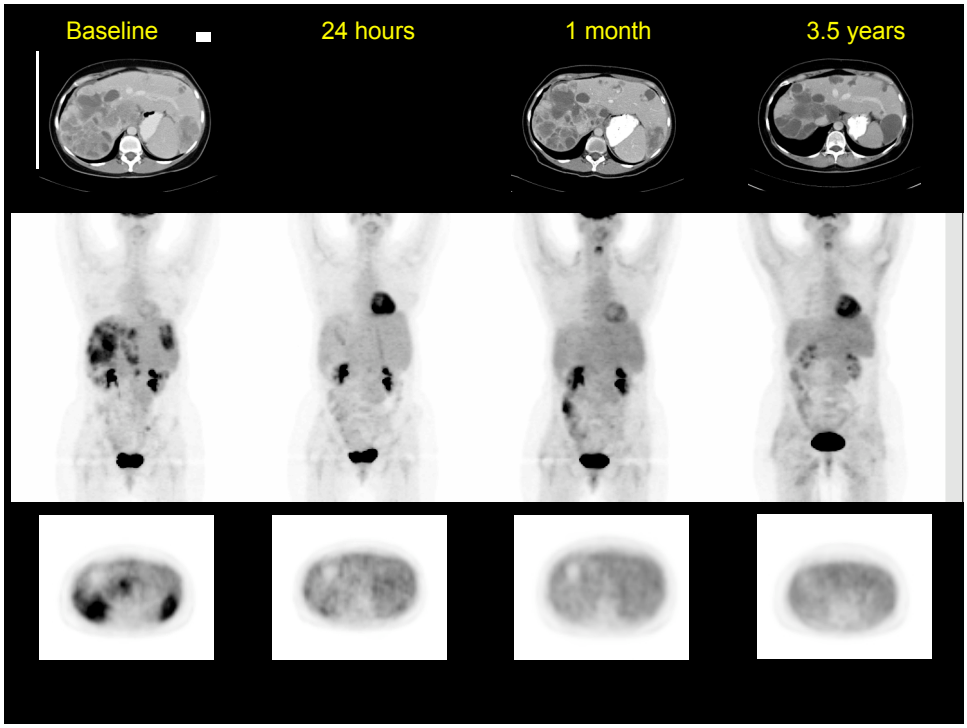
FDG-PET as an imaging biomarker of metabolic response to Gleevec in GIST patients

Jeffrey Yap, Annick Van den Abbeele

Dana Farber Cancer Institute



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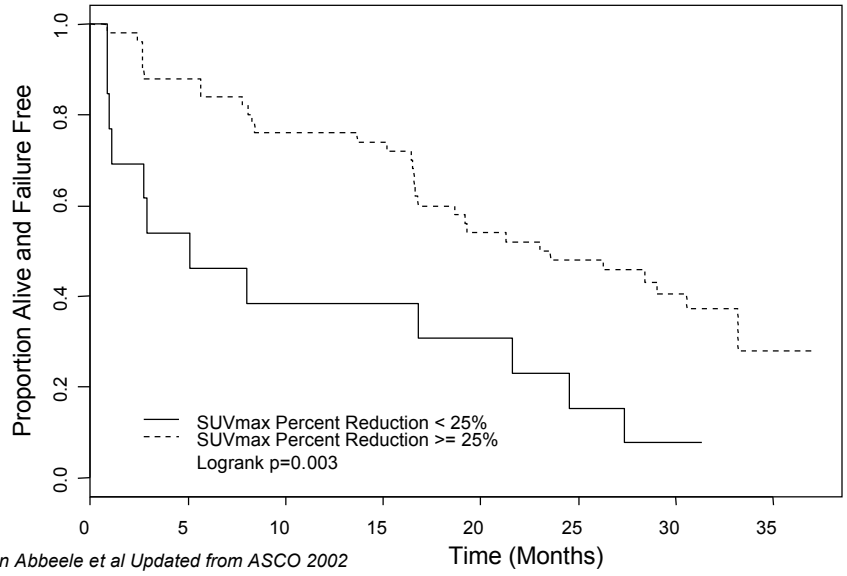
Time to Treatment Failure by SUVmax Percent Reduction



Van den Abbeele et al Updated from ASCO 2002

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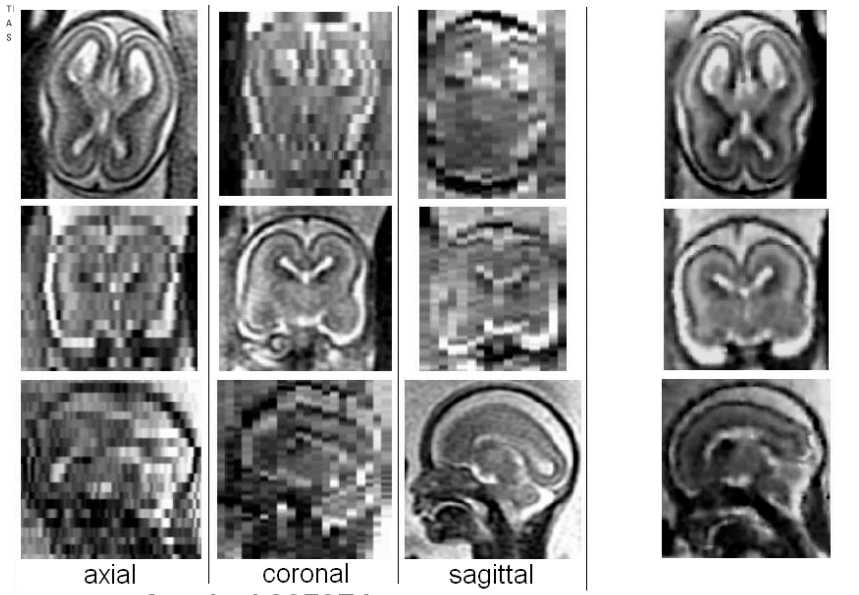
Volumetric Fetal Brain MRI Reconstruction and Processing

Ali Gholipour, Neil I. Weisenfeld, Simon K. Warfield
Computational Radiology Laboratory

Judy A. Estroff, Carol E. Barnewolt, Ellen Grant
Advanced Fetal Care Center

Children's Hospital Boston

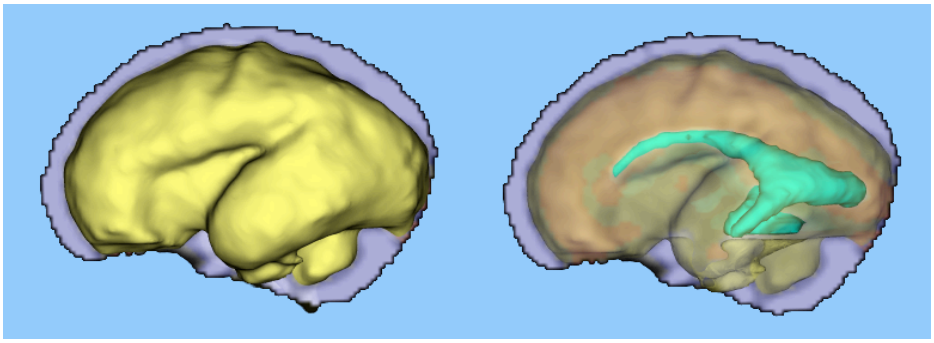
Volumetric Fetal Brain MRI Reconstruction



Acquired SSFSE images **3D Reconstruction**

Reconstructed fetal brain MR image segmentation and visualization

- Left: pial surface model of a reconstructed fetal brain image; and right: 3D model of tissue segmentations with ventricles highlighted in green



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High Leadcount EEG Source Localization for Pediatric Epilepsy Surgical Planning

Damon Hyde, Simon K. Warfield
Computational Radiology Laboratory

Children's Hospital Boston

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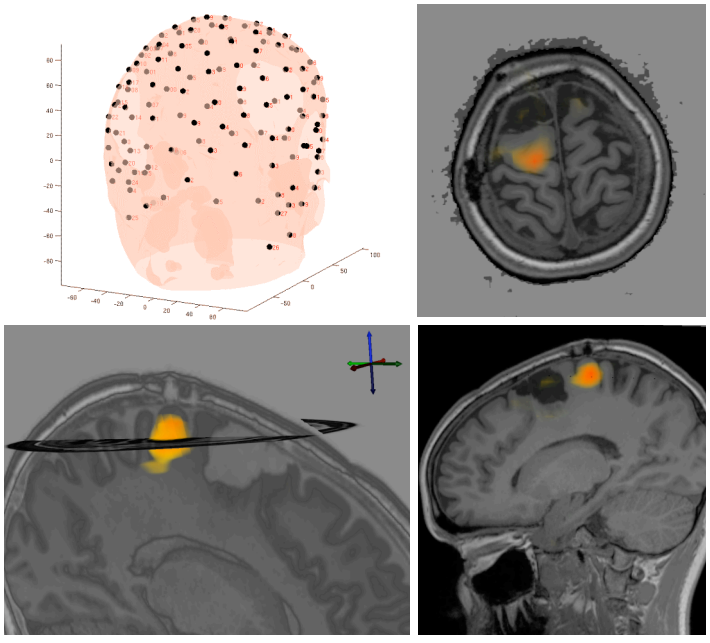

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Detection of DTI White Matter Abnormalities in Multiple Sclerosis Patients

O. Commowick, P. Fillard, O. Clatz, S.K. Warfield

Children's Hospital Boston

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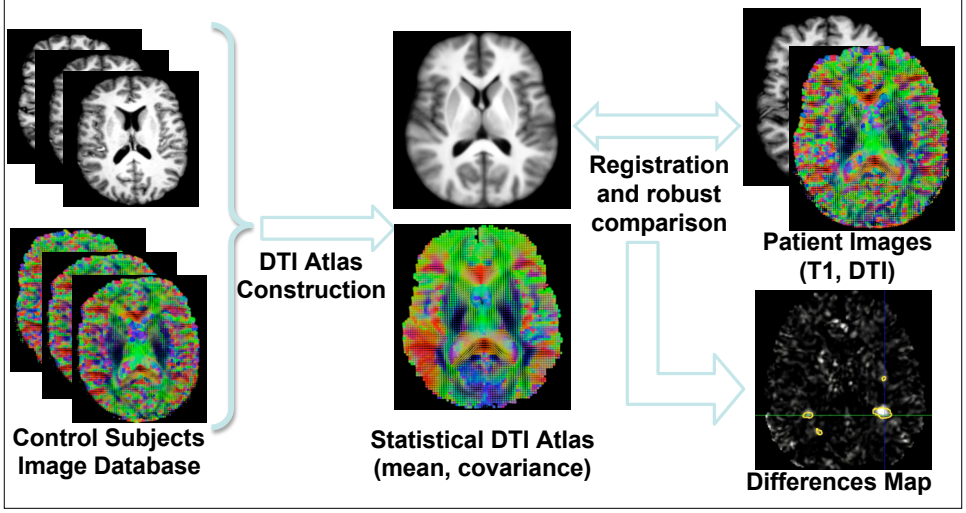
Objective: Detect local and remote damages to the white matter due to MS
Method: Build a reference standard to be compared locally to patients
Results: Abnormalities detected both inside the lesions and around them



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3D MR volumetric analysis of prostate cancer : treatment response

Clare Tempany

Brigham and Women's Hospital

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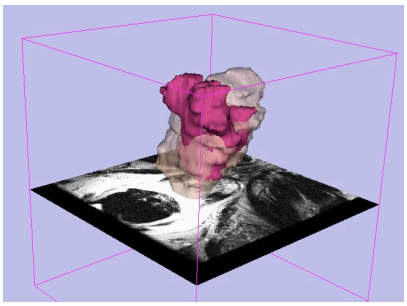
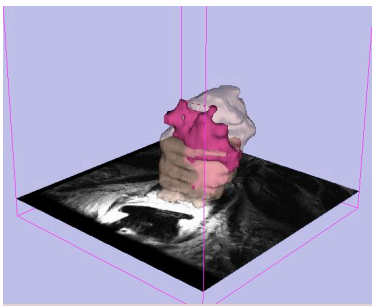
CALGB Study Protocol

Baseline MRI

2 Months Total Androgen Suppression
LHRH Agonist (Lupron)
Anti Androgen (Flutamide)



TUMOR VOLUME 17.84 cc



TUMOR VOLUME 7.8 cc

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Dynamic contrast enhanced MRI of prostate cancer

Clare Tempany

Brigham and Women's Hospital

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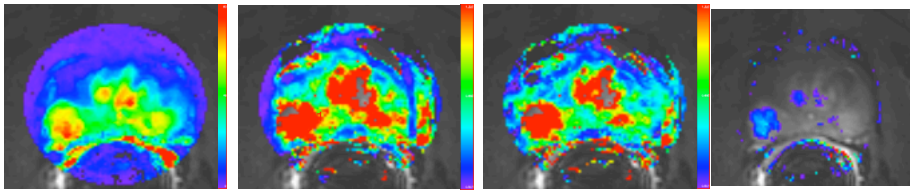
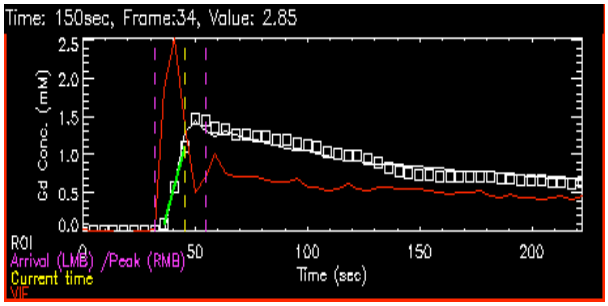
Dynamic contrast enhanced MRI of prostate cancer



MaxSlope **Ktrans** **Kep** **Washout**



AIF and tumor kinetic curve

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Imaging Consortium Consultation Service

http://catalyst.harvard.edu/services/imagingconsulting.html

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Imaging Consortium wiki

www.na-mic.org/Wiki/index.php/Collaboration:Harvard_CTSC

- Medical imaging education and training
- Medical image acquisition, analysis and visualization resources