Multimodality Imaging in Radiation Oncology

Joint ICTP-IAEA International Workshop on the Implementation of Image Guided Radiotherapy (IGRT)
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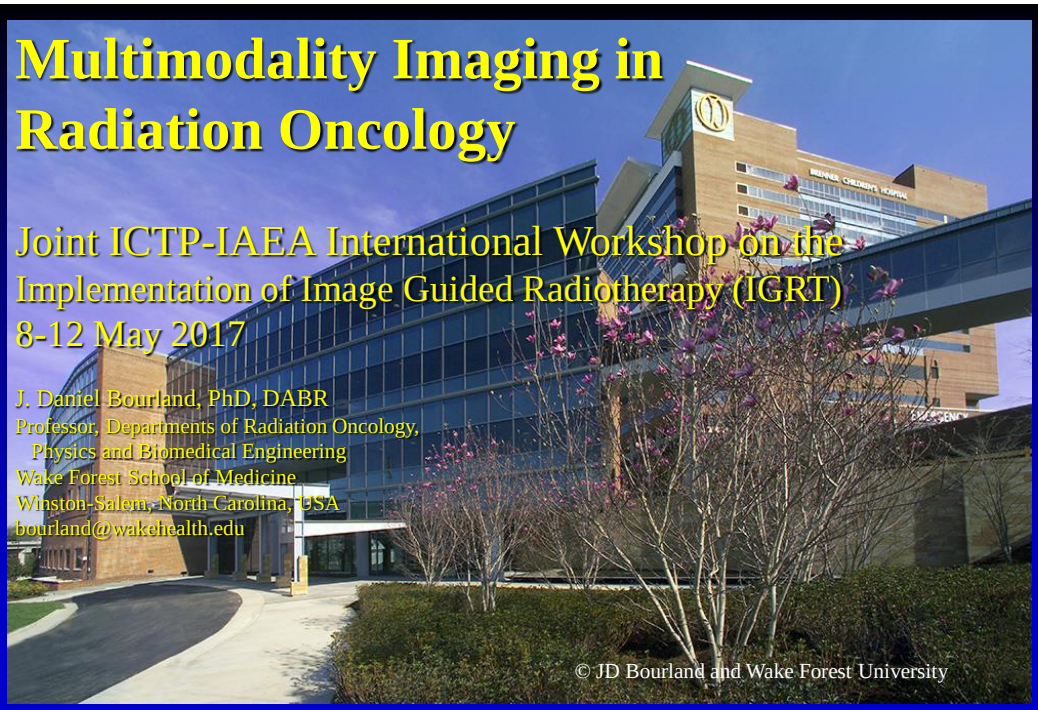

Outline

- Digital imaging and image interpretation
- Molecular and biological images
- Target delineation – the threshold
- Biologically-matched dose
- Research opportunities

The Digital Imaging Process

• Acquisition Mode/Device	• MR (MR MRs, pMR, fMR); PET (FDG, hypoxia, perfusion, proliferation); SPECT; Optical (in vivo microscopy, tomography)
• Post Acquisition Processing	• Reconstruction, Transfer
• Manipulation/Application	• Classification, Localization, Registration, Segmentation, Measurement [spatial, intensity], Physical and Biological Models
• Secondary Image Generation	• DRRs, Composite Images
• Display	• Observation, Evaluation

Digital Imaging and RTP

Image Content and Pixel Meaning

Images provide 3D and 4D information. The challenge is to extract the morphologic, pathologic, biologic, physiologic, or metabolic "meaning" of the image numbers.

CT: electron density (attenuation, dose)
MR: proton density, magnetic moment (?)
PET: radionuclide distribution (physiology?)
SPECT: radionuclide distribution (physiology ?)
Other: What does a pixel mean?

Imaging Science Tasks

Classification/Estimation
Hypothesis of data, (tumor, kidney)
Sample object
→ image: SNR, contrast, …

Imaging Science Tasks

Four outcomes

- True positive (TP); Sensitivity (TPF)
- False positive (FP); Specificity (1 - FPF)
- True negative (TN)
- False negative (FN)

Anatomical Imaging

- CT
- MR

Biological Imaging

- PET/SPECT
- MR Spectroscopy
- Functional MR
- Receptors
- Optical Imaging
- EEG, ...

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Molecular and Conventional Imaging

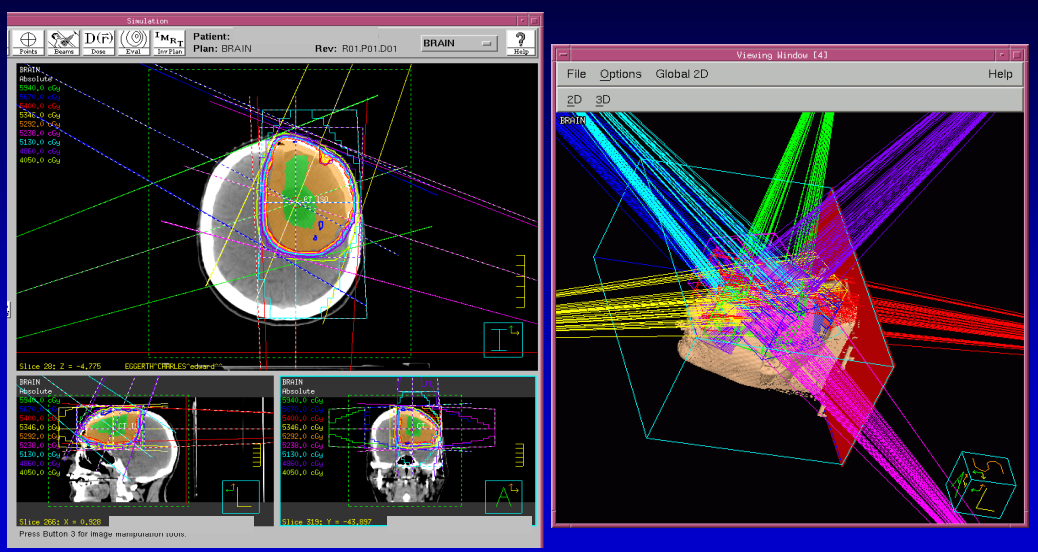
- Molecular Imaging: When the image source or signal is a specific molecule
  - Protein, large/small, endogenous/exogenous
  - Indicator of anatomy, physiology, function or process
  - Magnetic resonance, radioisotopes, optical approaches
- Conventional Imaging: When the image source or signal is bulk (macro?) physio-chemical entity
  - e- density, acoustic interface, T1/T2 relaxation, etc

A matter of scales and signal origin

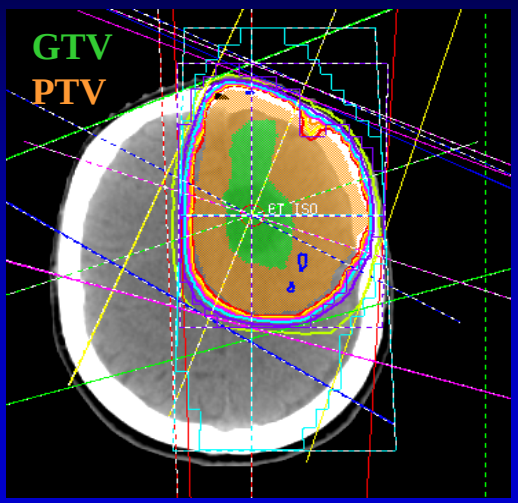
Typical Brain Tumor Radiation Treatment Plan

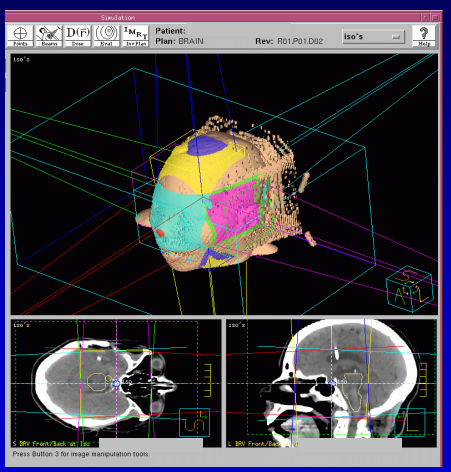
- CT simulation of patient in treatment position
- GTV defined: MR[CT] contrast enhanced
- CTV defined: MR[CT] edema (microscopic disease)
- Normal structures, eloquent areas defined
- Multiple treatment beams
  - Co-planar, non-coplanar; 3D-CRT or IMRT

Typical Brain Tumor Radiation Treatment Plan



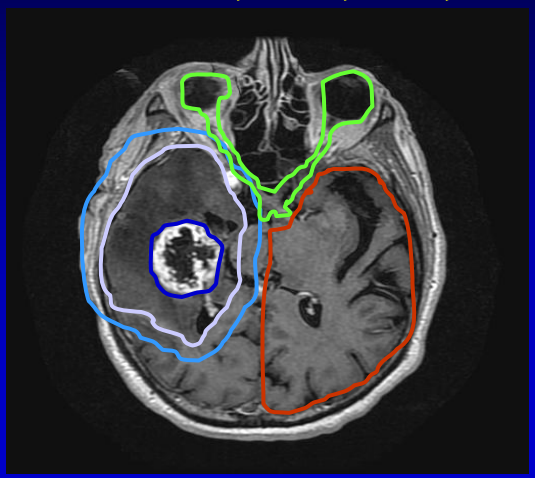
Typical Brain Tumor Radiation Treatment Plan





Role of MR Imaging Excellent Soft Tissue Contrast

Anatomic GTV, CTV, PTV, and Normal Structures

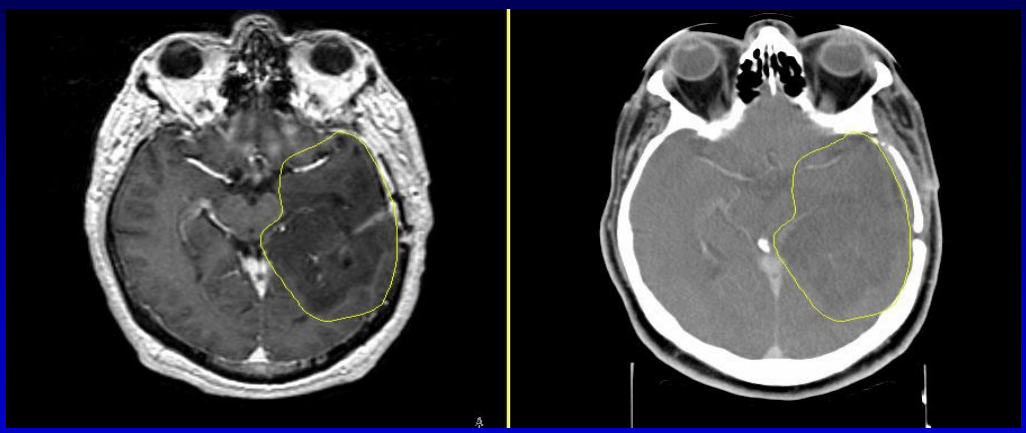


Key:

- **GTV – Contrast Enhanced**
- **CTV - Edema**
- **PTV - +Margin**
- **Normal tissue (eyes/ optic chiasm)**
- **Normal tissue (contralateral brain)**

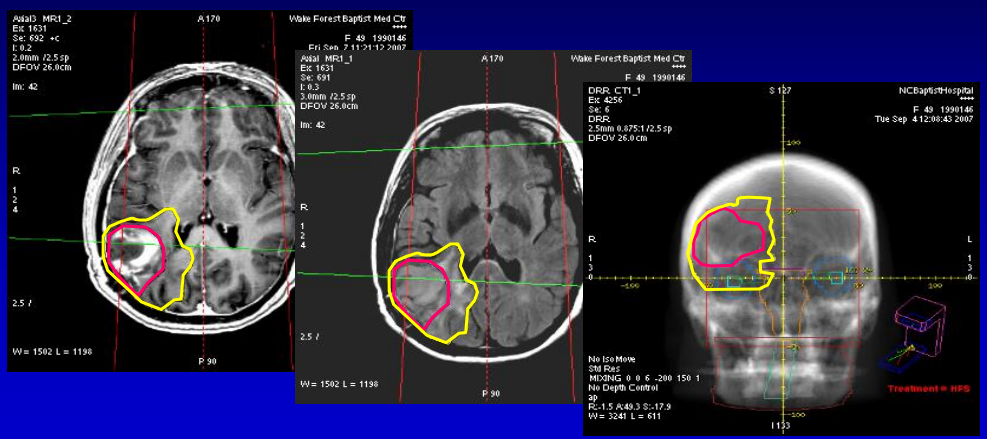
Courtesy EG Shaw, MD

Multi-Modality Image Registration
MRI to CT Registration



Contouring in one modality with simultaneous reproduction in the co-registered space of the other image set.

Virtual Simulation
Registration of MR with CT



Courtesy EG Shaw, MD

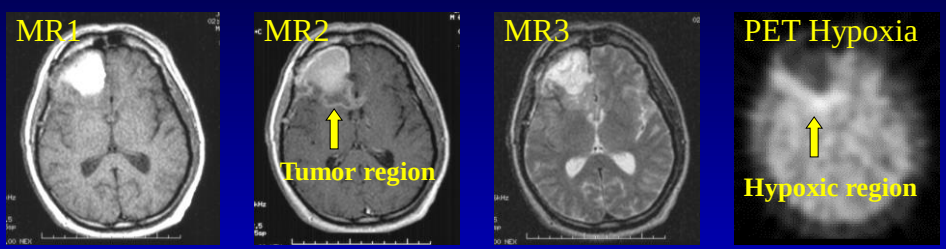
Advanced Brain Tumor Imaging

- Perfusion-weighted MRI: vascularity
  - DCE, DSC, ASL
- MR Spectroscopy: metabolite concentration
- Diffusion-weighted MRI: material transport
- fMRI: functional/processing regions
- Non-FDG PET: proliferation, hypoxia
- MEG: functional/processing regions

Bourland: Bioanatomic Treatment Planning

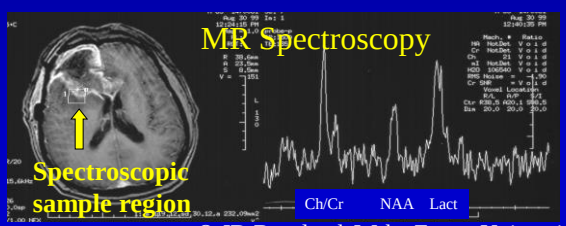
Patient 2: Bioanatomic Imaging

F18 Misonidazole PET and MRI Spectroscopy



Applications

- 3D RTP (IMRT)
- "Biologically targeted" therapy
- Response assessment



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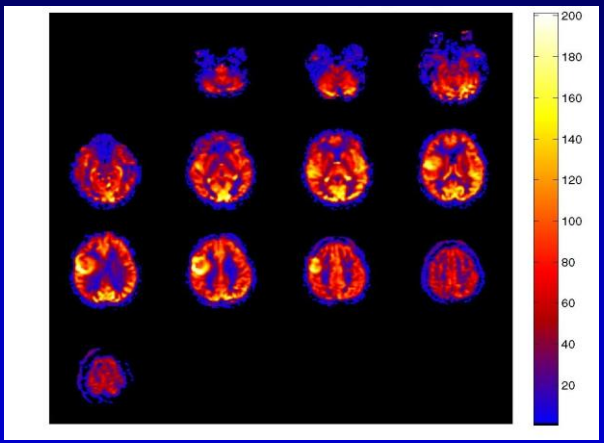
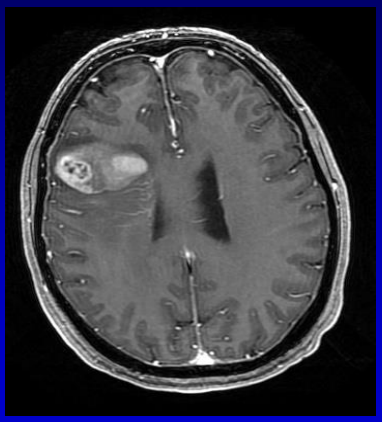
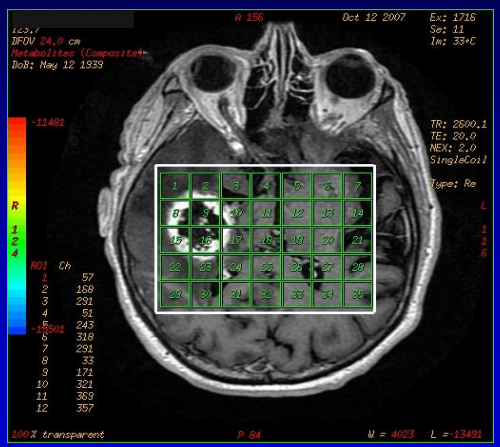
Biological Imaging
Dynamic Contrast MRI

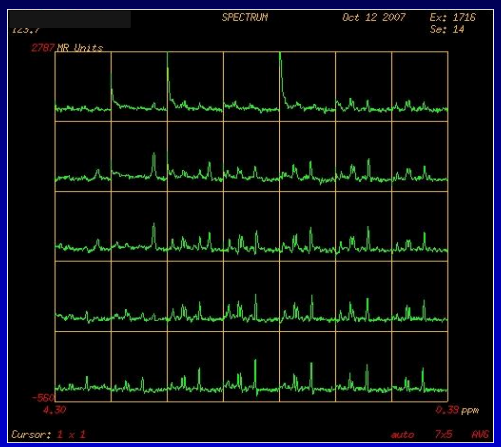




Courtesy EG Shaw, MD

Biological Imaging
MR Spectroscopy

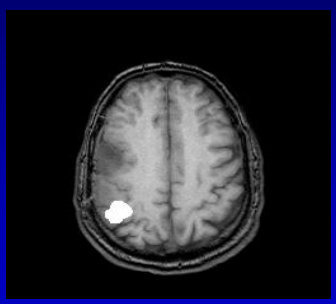




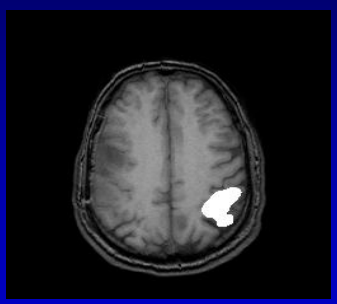
Courtesy EG Shaw, MD

Biological Imaging
Functional MRI – Areas of Avoidance

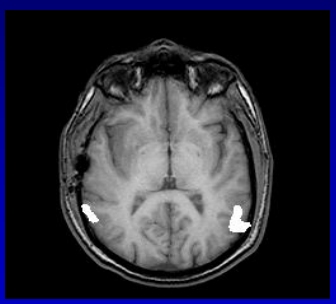
(ANSIR Group, J Maldjian, MD)



Left Motor



Right Motor



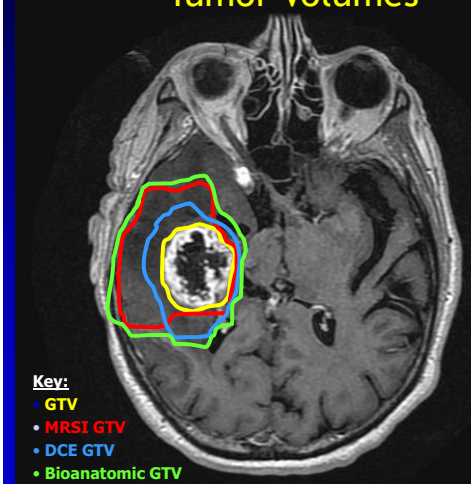
Language

Courtesy EG Shaw, MD

Imaging and Technology in Brain Tumor Clinical Care and Research

Bioanatomic Imaging in Practice

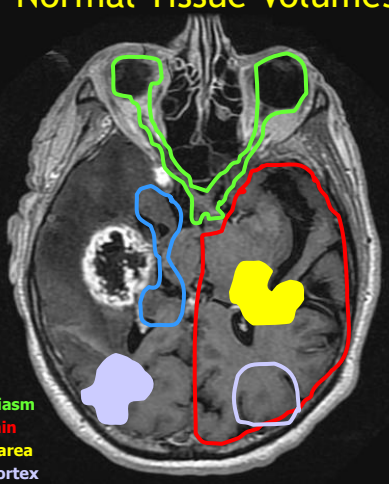
Tumor Volumes



Key:
- GTV
- MRSI GTV
- DCE GTV
- Bioanatomic GTV

(images courtesy EG Shaw, MD)

Normal Tissue Volumes



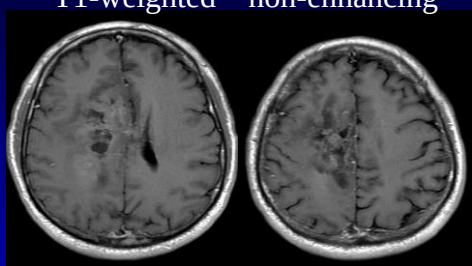
Key:
- Eyes/ optic chiasm
- Contra- lat brain
- fMRI: Broca's area
- fMRI: motor cortex
- DTI: internal capsule

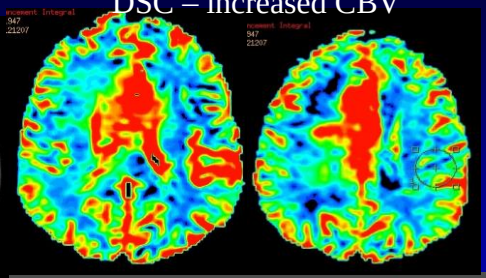
Current Practice: MR for Brain Tumors

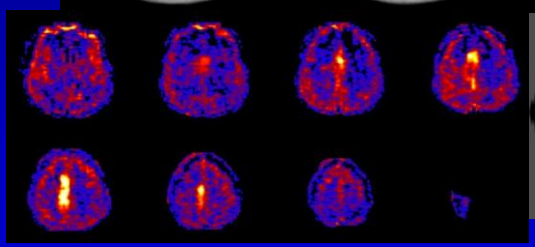
consistent with high grade glioma: pathology → anaplastic astrocytoma

T1-weighted – non-enhancing

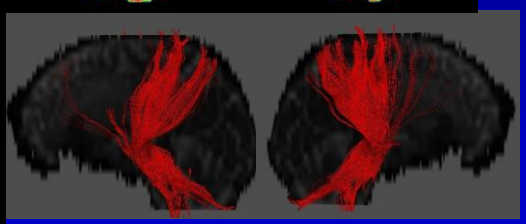
DSC – increased CBV







ASL – increased CBF

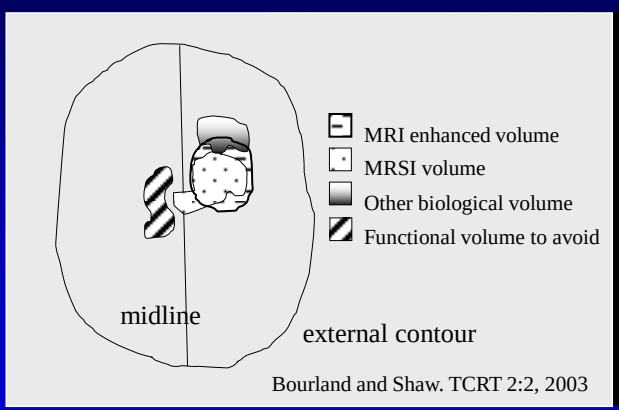


DTI – disrupted corticospinal tracts

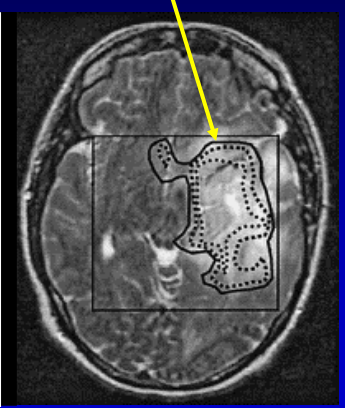
Courtesy A Johnson, MD

The Bioanatomic Target Volume

Choline:N-Acetyl-Aspertate index (CNI) > 2:1 +



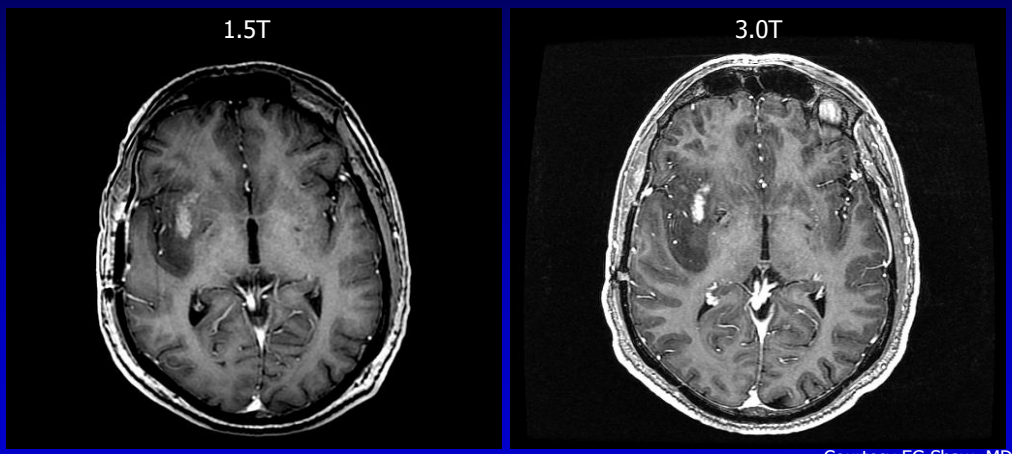
Bourland and Shaw. TCRT 2:2, 2003



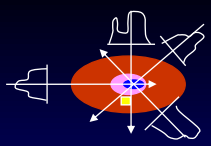
Pirzkall et al., UCSF

Topic: MR Field Strength

Advantages at 3.0T: edges, contrast – not significant?

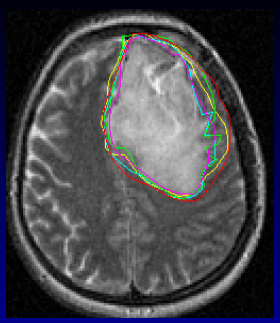


Courtesy EG Shaw, MD

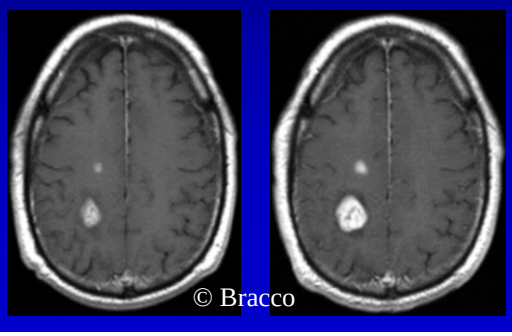


Other

- Biological targeting – clinical trials
- Other advanced MRI: multi-nuclear
- Hypoxia, proliferation
- Contrast agents, NSF
- Whole-head imaging
  - Metastases
- Observer variability

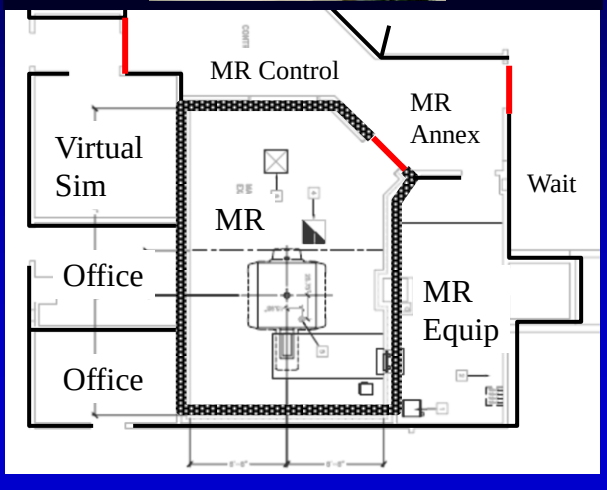


Gd-DTPA Gd-BOPTA



3.0T MR

- Adjacent control, view window, scanner, plus annex
- RF- and B-Field shielding – 5 gauss line containment
- Shared Virtual Simulation
- Laser marking system (work)
- Med gases, port for monitoring
- Equipment is very stable, excellent field homogeneity, meets ACR accreditation criteria for 3.0T
- Examining MRSI stability
- Automated PACS archive, selective push to TPS
- Postings per magnetic field in English and Spanish
- All entry points carded for security

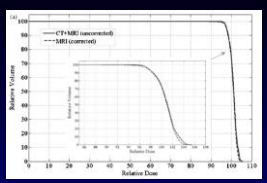


IOP Publishing — Physics in Medicine and Biology

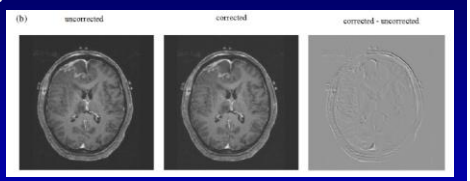
Phys. Med. Biol. **53** (2008) 3579–3593 doi:10.1088/0031-9155/53/13/013

A study on the magnetic resonance imaging (MRI)-based radiation treatment planning of intracranial lesions

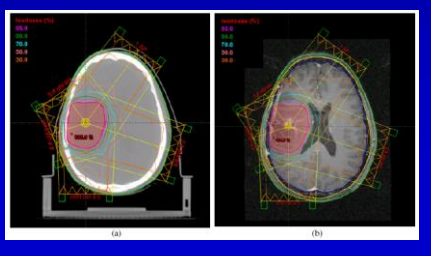
T Stanescu[1,2], H-S Jans[3], N Pervez[1], P Stavrev[3] and B G Fallone[1,2,3]



- Goal: MRI-based RTP procedures for brain tumors
- 3D distortion correction of MR images
- Auto-segmentation of head anatomy
- Bulk electron density assignments to MR regions
- Compare: CT+MR plan to MR-only plan
- No significant difference: MRI-based RTP suitable



- 3T MR: T1, T2
- Phantom-based distortion correction ~ 2 mm
- Contour shift ~ 1.5 mm
- MatLab auto-seg
- Bulk CT values (e-density) ~ 1%
- DVHs, dose statistics: excellent agreement



PHYSICS CONTRIBUTION

EVIDENCE THAT MR DIFFUSION TENSOR IMAGING (TRACTOGRAPHY) PREDICTS THE NATURAL HISTORY OF REGIONAL PROGRESSION IN PATIENTS IRRADIATED CONFORMALLY FOR PRIMARY BRAIN TUMORS

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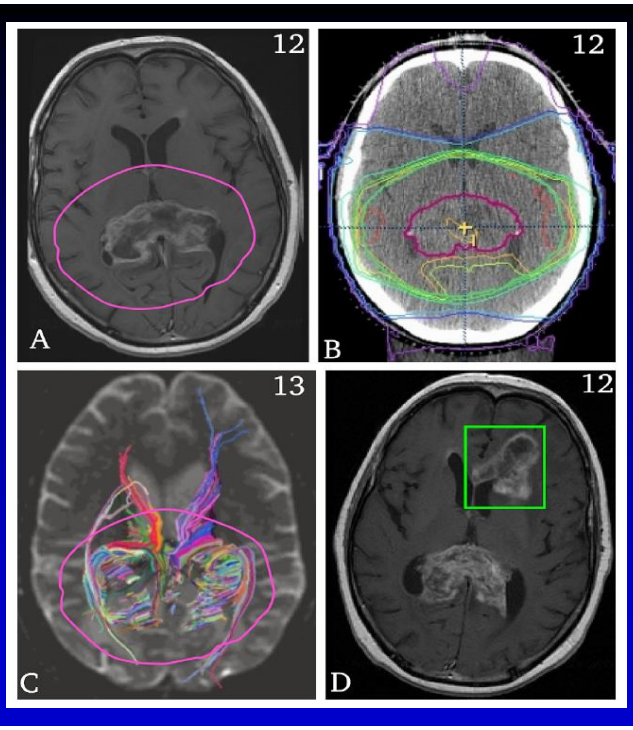
Departments of *Biomedical Engineering, †Radiation Oncology, and ‡Imaging Sciences, University of Rochester, Rochester, NY

Int. J. Radiation Oncology Biol. Phys., Vol. 71, No. 5, pp. 1553–1562, 2008

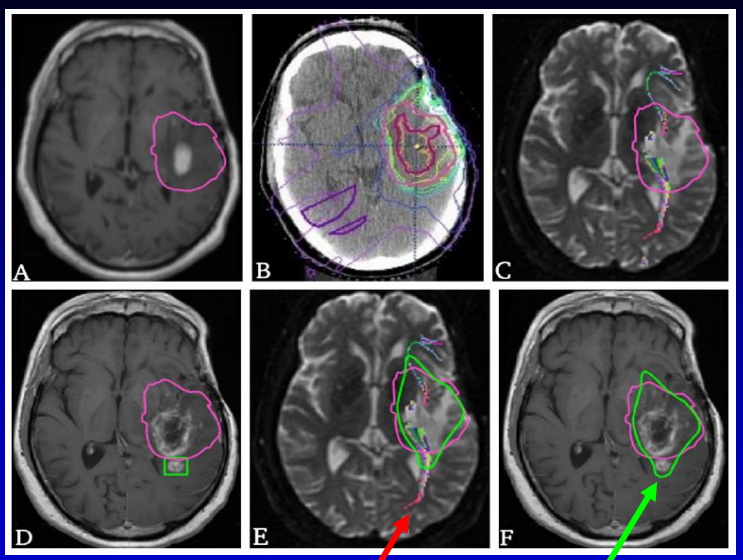
- Diffusion Tensor Imaging (DTI)
- Hypothesis: "migrating brain cancer cells follow paths of least resistance" – DTI will show paths
- 1.5T: T1, T2, DTI: pre- and post-SRT
- Patients grouped by distance of secondary tumor
- Post-SRT MRI obtained until progression
- Analysis of pre-SRT and post-SRT imaging
- No intervention based on DTI findings

- GBM
- Two fiber tracts
- Disease @ > 2cm

Krishnan et al. 2008

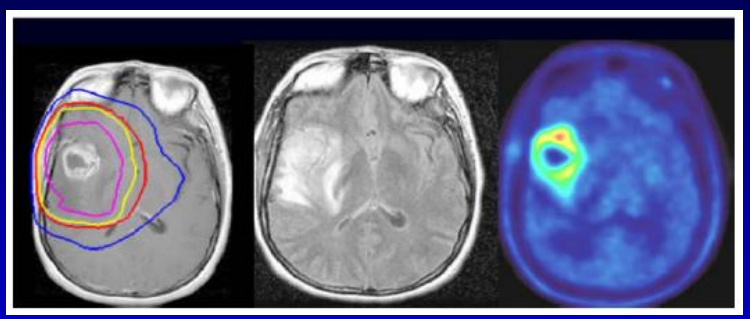


- Anaplastic astrocytoma
- Hypothetical target volume (green outline) that follows extension of diffusion path (red arrow)



Krishnan et al. 2008

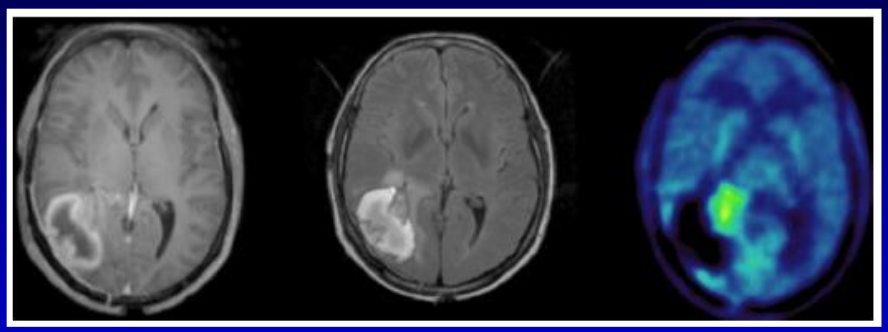
Non-Surgical, Pre-Radiation Treatment T1-MR, T2-FLAIR, and ^{11}C-MET PET



T1 + C	FLAIR	^{11}C-MET PET
Typical RTP	Edema, CTV	Prolif, BTV

Tsien CI, Cao Y, Lawrence TS. Functional and Metabolic Magnetic Resonance Imaging and Positron Emission Tomography for Tumor Volume Definition in High-Grade Gliomas. Semin Radiat Oncol 19:155-162, 2009.

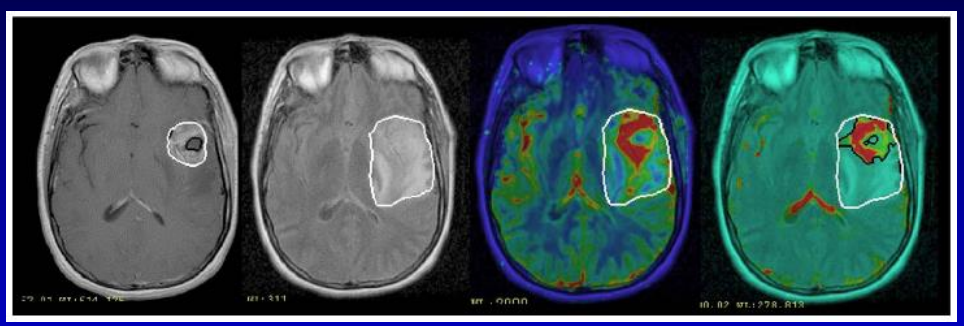
Post-Surgical, Pre-Radiation Treatment T1-MR, T2-FLAIR, and ^{11}C-MET PET



T1 + C	FLAIR	^{11}C-MET PET
GTV	Edema, CTV	Prolif, BTV

Tsien CI, Cao Y, Lawrence TS. Functional and Metabolic Magnetic Resonance Imaging and Positron Emission Tomography for Tumor Volume Definition in High-Grade Gliomas. Semin Radiat Oncol 19:155-162, 2009.

Pre-Radiation Treatment Advanced MR



T1 + C	FLAIR	CBV Map	CVP Map
GTV	Edema, CTV	BTV	BTV

Tsien CI, Cao Y, Lawrence TS. Functional and Metabolic Magnetic Resonance Imaging and Positron Emission Tomography for Tumor Volume Definition in High-Grade Gliomas. Semin Radiat Oncol 19:155-162, 2009.

EXPERT REVIEWS

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MRI for identification of progression in brain tumors: from morphology to function

Expert Rev. Neurother. 8(10), 1507–1525 (2008)

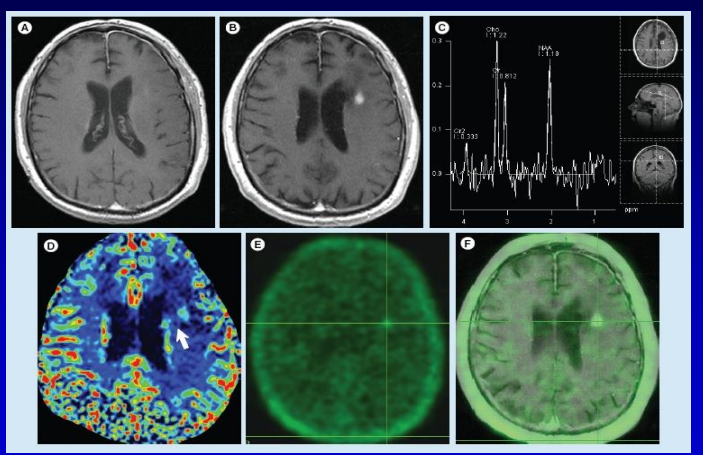
- Main MRI predictor of response is tumor size
- Consistency in imaging parameters across time
- MRSI most practicable approach for radionecrosis
- Anti-angiogenesis response imaging developing
- DWI surrogate for tumor cellularity/heterogeneity
- DTI may show infiltration patterns
- Functional MRI → guide therapeutic choice
- Methods are complementary

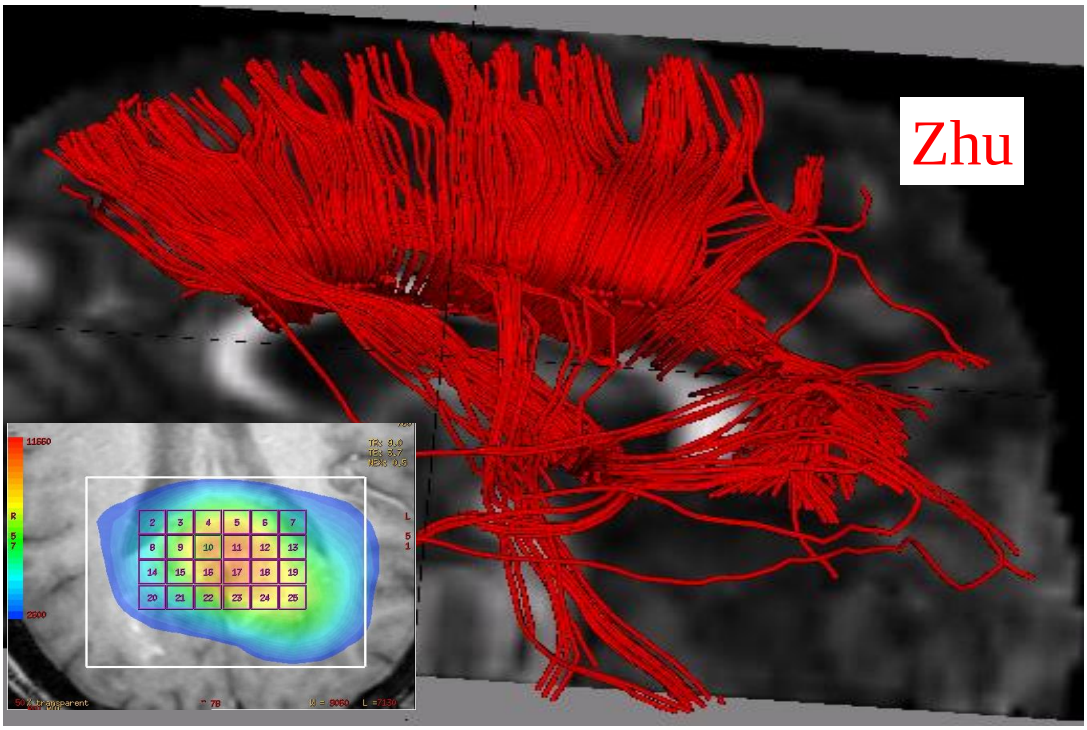
Necrosis vs Recurrence

- T1 (A, B)
- MRSI +choline (C)
- Higher CBF (D)
- 18FLT PET + proliferation (E)
- Image fusion

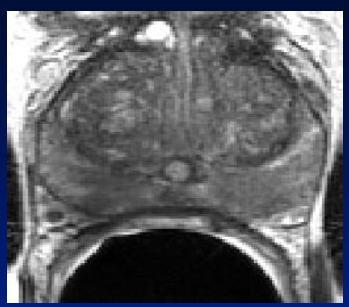
- Recurrent tumor

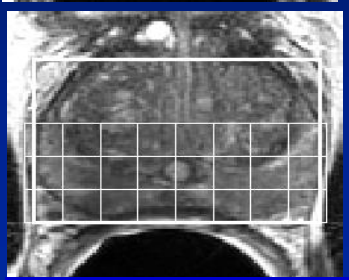
Weber et al. 2008

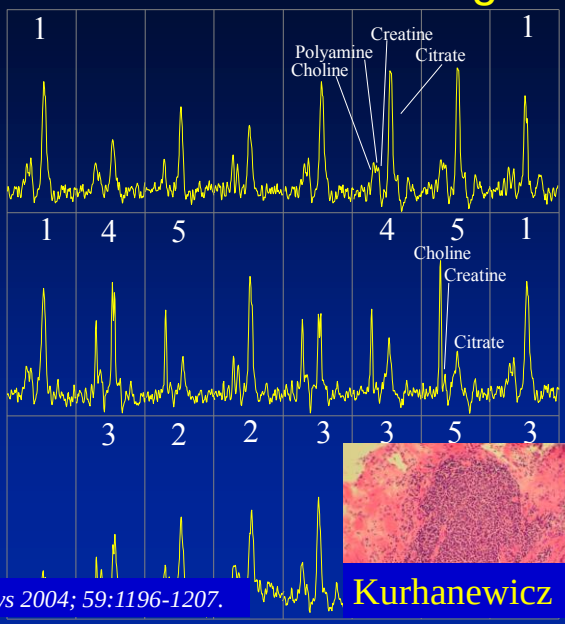




MRI/MRSI-Based Radiation Planning



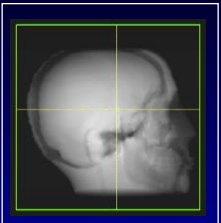




Pouliet, Int J Radiat Oncol Biol Phys 2004; 59:1196-1207.

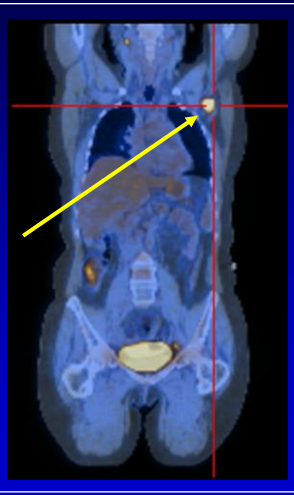
Kurhanewicz

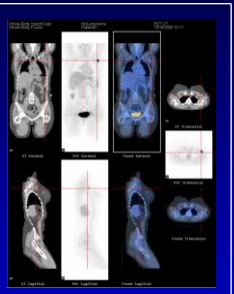
Why PET?
A Picture of the Patient



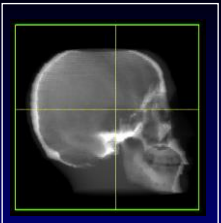
MR "Radiograph"

PET-avid tumor registered with CT obtained at the same time





CT-PET Hybrid Imaging for Tumor Diagnosis and Treatment Planning: (Courtesy General Electric Healthcare)

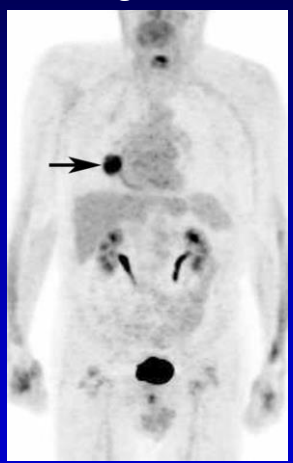


MR "Radiograph" with bone added - the MR is changed into a CT-like radiograph

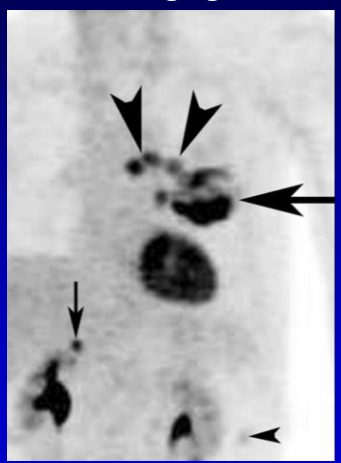
WAKE FOREST UNIVERSITY
SCHOOL of MEDICINE
THE BOWMAN GRAY CAMPUS

PET: Non-Small Cell Lung Cancer

Diagnosis



Staging



Re-Staging

From Rohren, Turkington, Coleman: Radiology 2004; 231:305-332

PET in Oncology

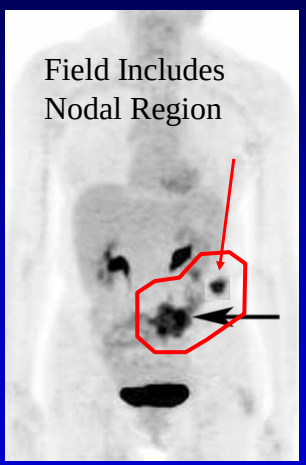
Colon Cancer: Possible Treatment Fields

PET in Oncology

- Diagnosis – less common
- **Staging - yes**
- Target Definition
  - Radiation treatment
  - Other "targeted" therapy
- Re-staging – yes
- Treatment Evaluation

Node Negative

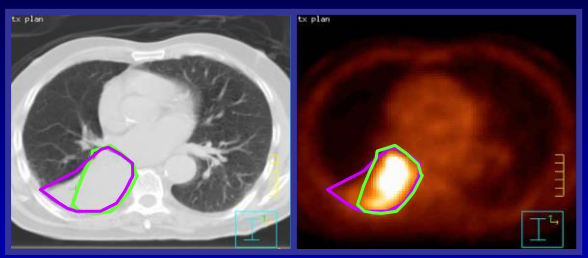
Node Positive



Adapted from Rohren, Turkington, Coleman: Radiology 2004; 231:305-332

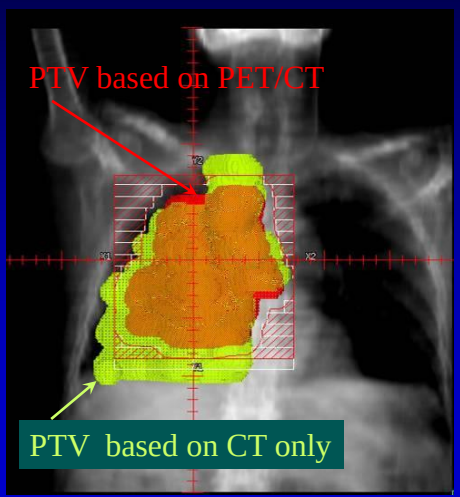
Secondary Impact: Target Definition

PET may decrease or increase target volumes compared to CT-only



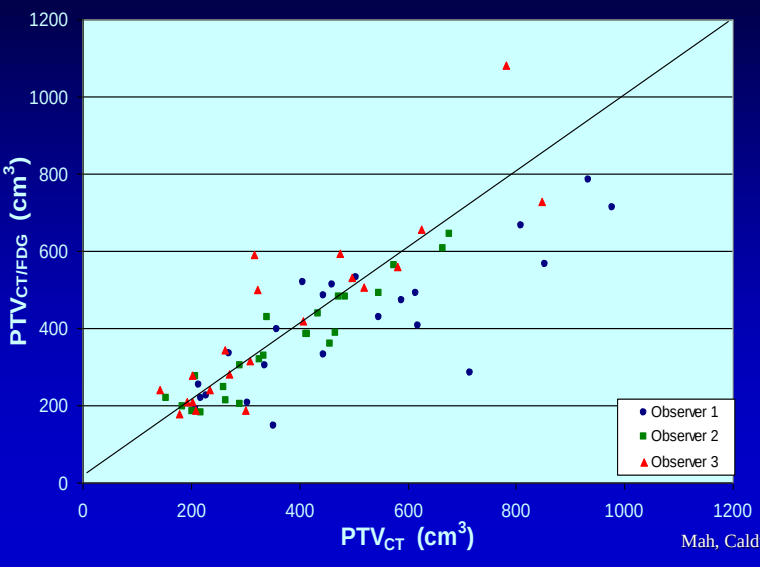
CT: Purple PET/CT: Green

Changes in target outline translate to reduced treatment field size



Courtesy of K Mah, Univ Toronto, Sunnybrook

Impact on size of PTV: CT vs PET/CT



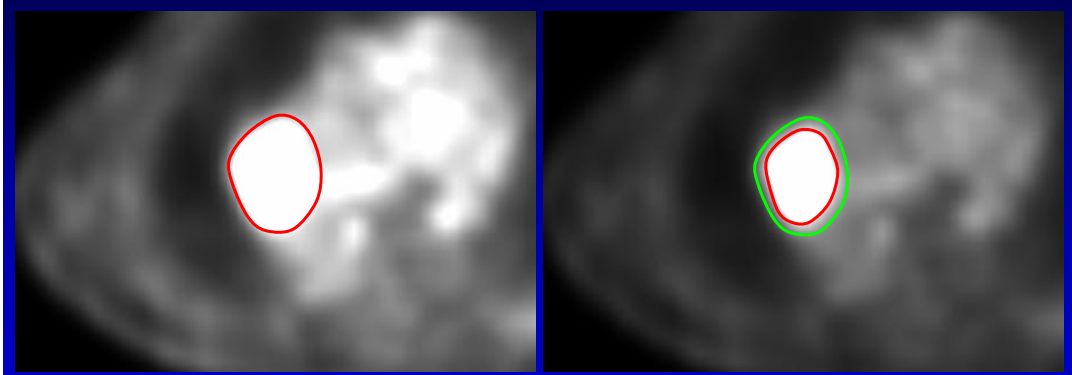
- Relative changes ranged from 0.40 to 1.86
- In 5 of 23 cases, new FDG nodes detected that increased PTV

Mah, Caldwell, Ung et al. IJROBP 52, 2002

Radiation Treatment Planning with PET

Target Definition

Same patient image: different window and level!



Washington University in St. Louis
School of Medicine
MIR Mallinckrodt Institute of Radiology

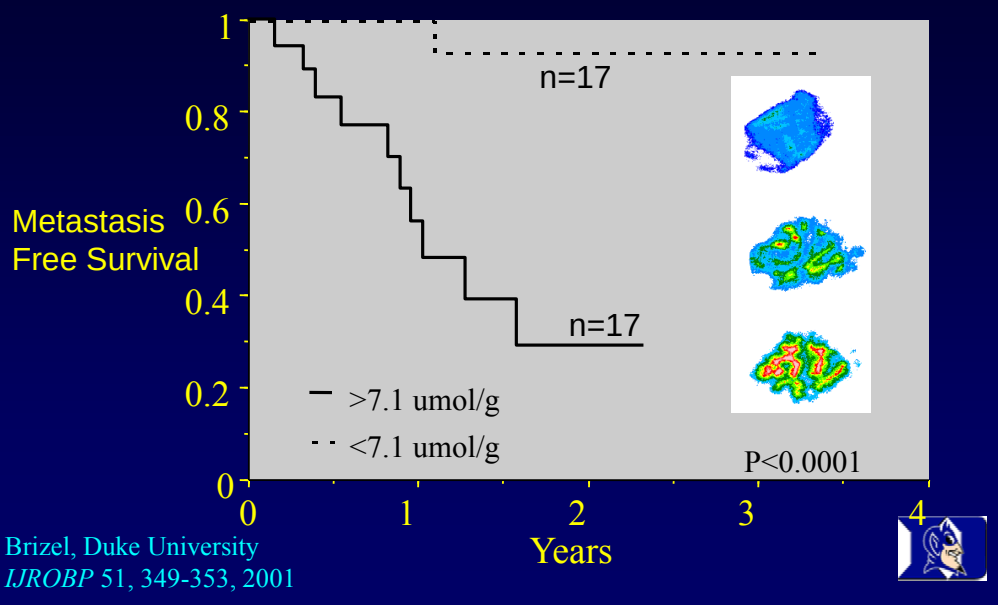
In this example, Lt target is larger than Rt target by factor of 1.2 (Lt v Rt), and shape is slightly different

Approaches to PET-Target Definition

- 40-50% of peak intensity (above background?)
- Standardized Uptake Value (SUV) of ROI
  - ie, SUV > 2.5 indicates positive for cancer
- Region determined by PET, extent by CT
- Calibrated method for scanner?

In common – digital image with voxel intensities

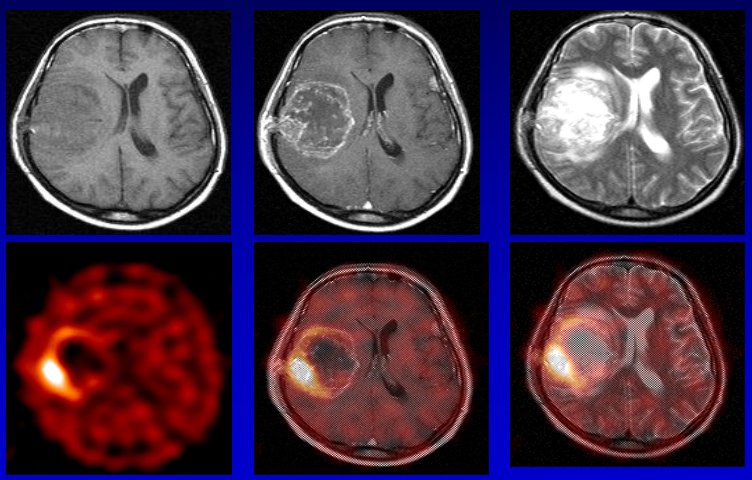
↑Tumor Lactate→More Metastases



Brizel, Duke University
IJROBP 51, 349-353, 2001

IMT (Thymidine)-SPECT/MRI: GBM Proliferation

(from Grosu, Weber et al, Technical University of Munich)



4D PET/CT: Respiratory gated PET and CT

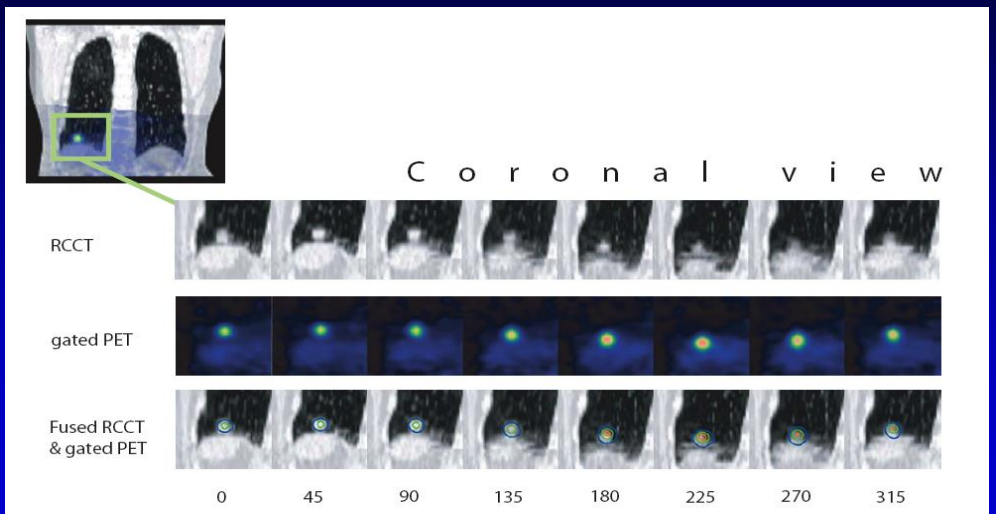


Image from Wolthaus et al. Phys Med Bio 50, 2005

4D PET-CT: Liver

Courtesy of WT Kearns, Wake Forest Univ

Target to Background Ratios

Advanced Imaging Methods and Systems across Multiple Scales: Tom Budinger, PhD

"Its Physics, but the key is Chemistry"

TARGET DETECTION

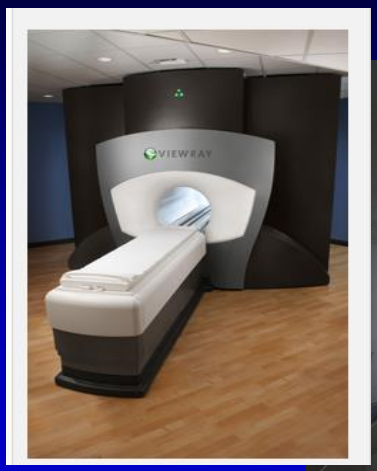
1. Detector coverage, materials, design
2. Reduced error propagation
3. Increase in specific activity by factors of 100
4. Ligand design for good affinity
5. Amplification through chemical sequestration.

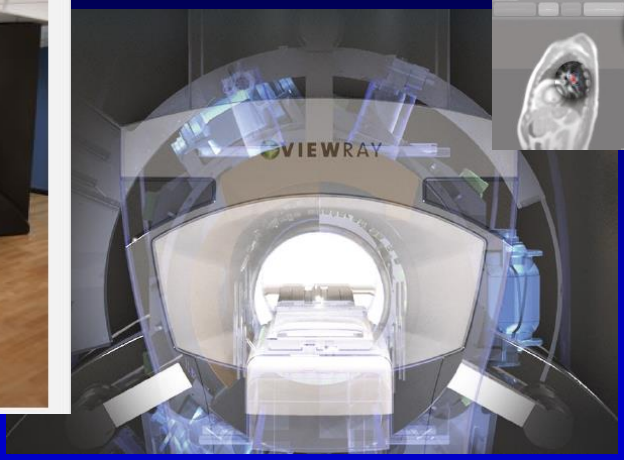
BACKGROUND MINIMIZATION

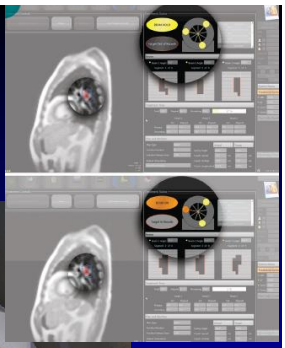
1. Scatter/noise reduction designs
2. Increase in specific activity to avoid saturation
3. Ligands with poor affinity for the background
4. Biodistribution strategies

* Expect factors of 10 – 100.

Gamma + MRI



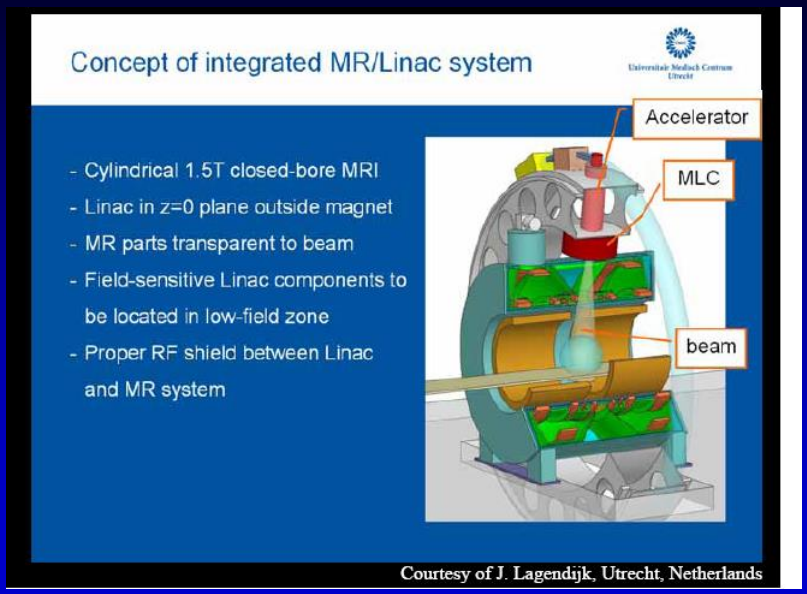




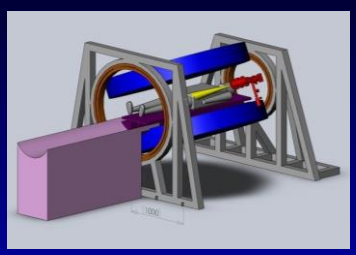
Courtesy Viewray, Inc

MR + Linear Acclerator

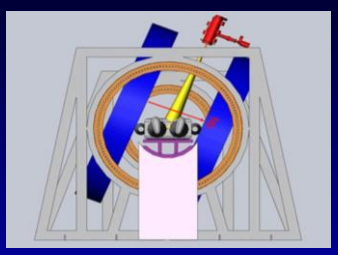
MR + Linear Acclerator

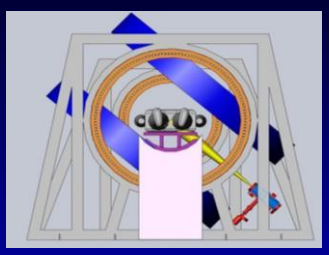


MR + Linear Acclerator

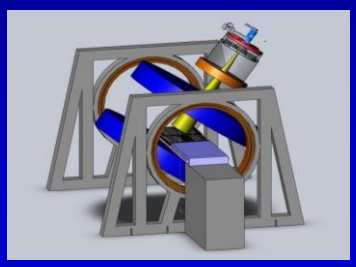


Longitudinal Orientation

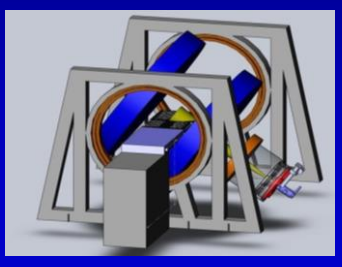


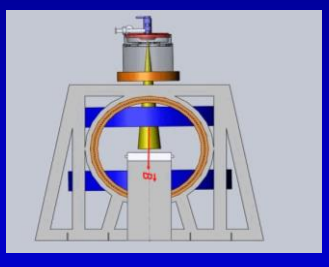


Courtesy of University of Alberta, Canada



Transverse Orientation





Courtesy of University of Alberta, Canada

Hybrid IGRT Technologies

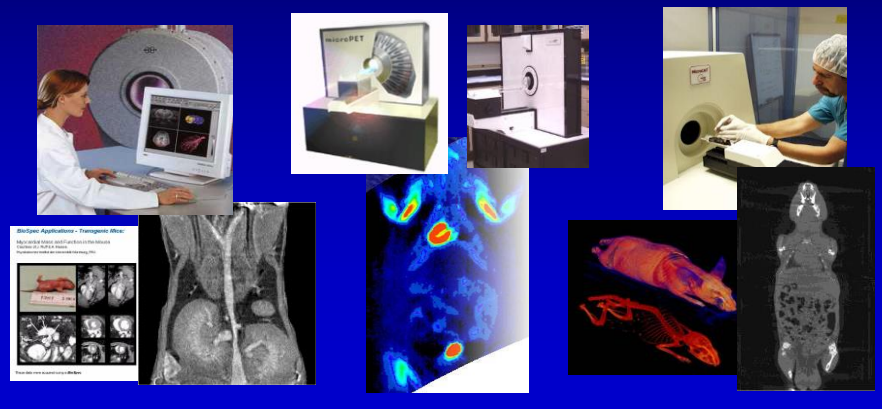
Treatment Device →

Imaging Device ↓

	Gamma RadSurg	MV x rays Linac	MV x rays robotic	Brachy	HiFUS
US		X	?		
Optical		X	X		
Remote Send		X	X		
Fiducial Markers		X	X	X	
CT		X		?	
PET-CT		X			
MV FBCT		X			
kV CBCT	X	X		X	
MV CBCT		X			
Stereo XR		X	X	X	
MRI	X	X		X	X
SPECT/NM		X			

Small animal imaging (small size/features) micro Imaging: MR, PET, CT

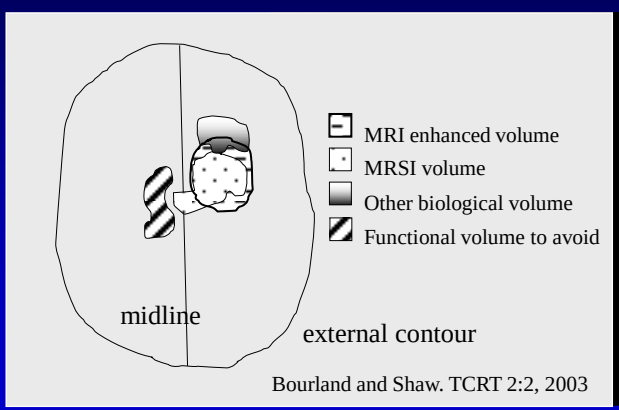
- Small animals (rodents, other mammals) present challenges
  - Small size and features
  - Small signal
- Imaging devices: small bore units
  - microPET
  - microMR
  - microCT



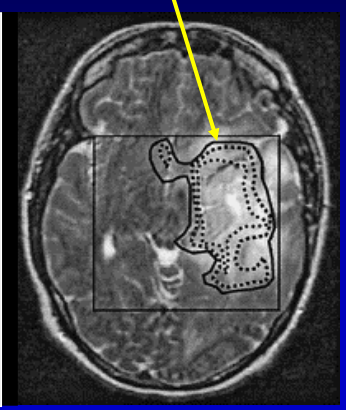
The Oncologic Target

Example: The Bioanatomic Target Volume?

Choline:N-Acetyl-Aspertate index (CNI) > 2:1 +



Bourland and Shaw. TCRT 2:2, 2003

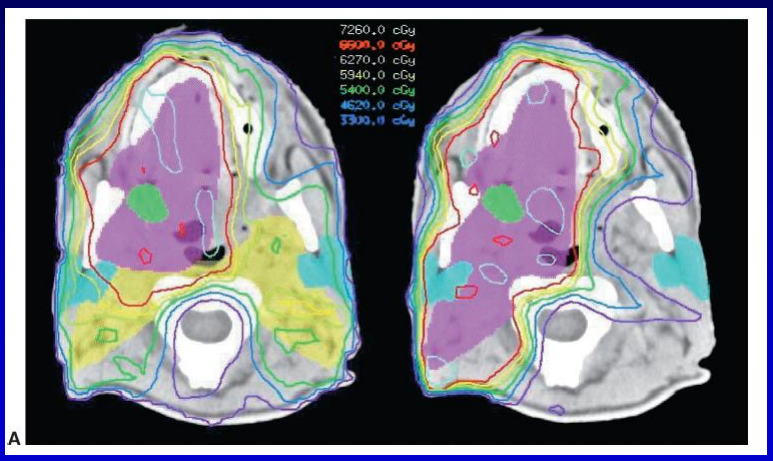


Pirzkall et al., UCSF

GTV: CT v PET-CT

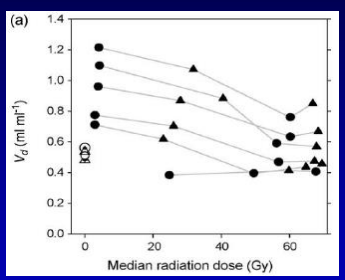
Use of PET-CT may **reduce** GTV/CTV

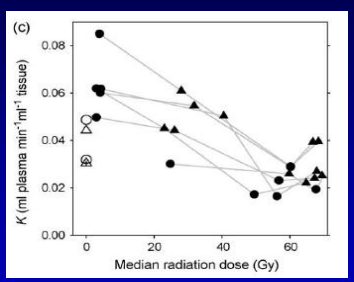
GTV-CT GTV-PET-CT

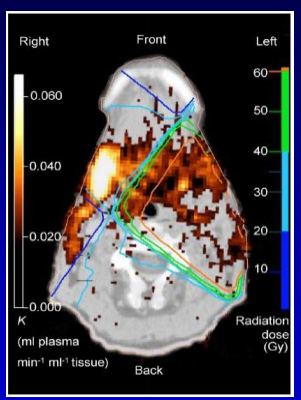


From Schwartz, Ford, Rajendran, et al., Head & Neck 27(6): 478-487, 2005.

11C-Methionine PET
Regional Salivary Gland Function







a) Volume of distribution of 11C-methionine

b) K, the net metabolic clearance of 11C-methionine

Washington University in St. Louis
School of Medicine
MIR Mallinckrodt Institute of Radiology

Buus *et al*, Radiotherapy and Oncology 73:289-296, (2004).

The Radiation Targeting Issue

See
then
Treat
then
See
then
Treat
(and so on …)

- See
  - How well – target localization?
    - Specificity/sensitivity?
    - Modality?
    - Anatomy, biology?
  - How often?
    - Once, weekly?
    - Per fraction?
- Treat
  - Verification of target hit?
  - Matched to imaging?
    - Static, dynamic, contrast?
  - Readily interpretable?

The Radiation Targeting Issue

- Target localization: confidence of target boundary

  This is the greatest unknown and challenge!
- Target motion: respiration (cardiac, other)
- Target shape: patient shape changes (weight, position, motion), treatment response

"to know is to treat"

Wake Forest Baptist Medical Center