Multimodality Imaging in Radiation Oncology

Joint ICTP-IAEA International Workshop on the Implementation of Image Guided Radiotherapy (IGRT)
8-12 May 2017

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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, ...

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

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)
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

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

Biological Imaging
MR Spectroscopy
Current Practice: MR for Brain Tumors

consistent with high grade glioma: pathology $\rightarrow$ anaplastic astrocytoma

- T1-weighted – non-enhancing
- DSC – increased CBV
- ASL – increased CBF
- DTI – disrupted corticospinal tracts

The Bioanatomic Target Volume

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

MRI enhanced volume
MRSI volume
Other biological volume
Functional volume to avoid

midline
external contour

Bourland and Shaw. TCRT 2:2, 2003

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Pirzkall et al., UCSF
Topic: MR Field Strength

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

Other

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

Courtesy EG Shaw, MD

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

- 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
• 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

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

T1 + C
GTV

FLAIR
Edema, CTV

$^{11}$C-MET PET
Prolif, BTV


Pre-Radiation Treatment Advanced MR

T1 + C
GTV

FLAIR
Edema, CTV

CBV Map
BTV

CVP Map
BTV

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

- 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


Kurhanewicz
Why PET?
A Picture of the Patient

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)

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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

Node Negative

Simple Field

Node Positive

Field Includes Nodal Region

PET in Oncology

- Diagnosis – less common
- Staging - yes
- Target Definition
  - Radiation treatment
  - Other “targeted” therapy
- Restaging – yes
- Treatment Evaluation

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

PTV based on PET/CT
PTV based on CT only

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

Radiation Treatment Planning with PET

Target Definition

Same patient image: different window and level!

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

![Graph showing association between tumor lactate and metastases](image-url)

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
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

First Images March 2009

MR imaging without 6 MV irradiation

MR imaging during 6 MV irradiation of object imaged (no FF)

Courtesy of G. Fallone, Cross Cancer Institute, Edmonton, Canada
MR + Linear Accelerator

Concept of integrated MR/Linac system

- Cylindrical 1.5T closed-bore MRI
- Linac in z=0 plane outside magnet
- MR parts transparent to beam
- Field-sensitive Linac components to be located in low-field zone
- Proper RF shield between Linac and MR system

Courtesy of J. Lagendijk, Utrecht, Netherlands
Hybrid IGRT Technologies

<table>
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<th>MV x rays robotic</th>
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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-Aspartate index (CNI) > 2:1 +

Bourland and Shaw. TCRT 2:2, 2003

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

GTV-CT | GTV-PET-CT


11C-Methionine PET
Regional Salivary Gland Function

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

The Radiation Targeting Issue

See then Treat
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