Use of imaging systems for patient modeling - PET and SPECT

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Nuclear Medicine Imaging in RT

• The goal is to accurately delineate and biologically characterize an individual tumor, select an appropriate course of therapy, and to predict the response at the earliest possible time.

• Image information can be categorized as:
  – Anatomical
  – Biological
    » Metabolic
    » Functional
    » Physiological
    » Genotypic
    » Phenotypic
The potential of Nuclear Medicine Imaging in RT

• **Detection** – Possibly better and earlier detection
  – Current imaging of disease is based on anatomic or physiologic changes that are a late manifestation of molecular changes that underlie the disease

• **Staging** - Improved staging and patient selection
  – Improved staging can define a more appropriate course of therapy
Lymph Node Status

n = 256

Fig 1. Kaplan-Meier progression-free survival estimates based on pelvic lymph node status (P = .001) (n = 101).

Fig 2. Kaplan-Meier progression-free survival estimates based on paraaortic lymph node status (P = .0001) (n = 101).

P.W. Grigsby et al, JCO, 2001
The potential of imaging in RT

- **Target definition**
  - Improved target identification can significantly alter current treatment volumes
  - The true extent of the disease may extend beyond anatomically defined volumes
  - Anatomically defined volumes may contain regions of increased importance - Biological target volume (BTV)


Cu(II)-diacetyl-bis (N<sub>4</sub>-methylthiosemicarbazone) (⁶⁰Cu-ATSM) PET - used to detect regions of tumor hypoxia
The potential of multimodality-imaging in RT

- **Target definition** – Biological target volume

The potential of multimodality-imaging in RT

- **Dose distribution**
  - Treatment plans can be designed to deliver escalated doses to BTV
  - With IMRT the concept of “dose painting” can be implemented
  - The question becomes how much paint should be used

Cu(II)-diacetyl-bis (N⁴-methylthiosemicarbazone) (⁶⁰Cu-ATSM) PET - used to detect regions of tumor hypoxia
Altered/Escalated Dose Distributions

$^{60}\text{Cu-ATSM (Hypoxia)}$ - Guided IMRT

- 80 Gy in 35 fractions to the hypoxic tumor sub-volume as judged by Cu-ATSM PET (red)
- GTV (blue) simultaneously receives 70 Gy in 35 fractions
- Clinical target volume (yellow) receives 60 Gy
- More than half of the parotid glands (green) are spared to less than 30 Gy.

60Cu-ATSM-PET

Normoxic  Hypoxic

Cervical Cancer

$^{60}$Cu-ATSM-PET  

FDG-PET

Pre-therapy

T/M = 2.3

$^{60}\text{Cu-ATSM-PET}$

$^{18}$Fluorodeoxyglucose-positron emission tomography (FDG-PET)

Pre-therapy

T/M = 5.1

Results

- 6/15 pt’s tumors were characterized as hypoxic.
- All pts with hypoxic tumors developed recurrent disease (p=0.0005).
- 8/9 pts disease free (follow-up 6.1-13.9 months).
- All 6/6 pts with hypoxia had pelvic LN vs. 3/9 without hypoxic tumors (p =0.03).

ATSM T/M ratio >3.5

\[ p = 0.0078 \]
PET imaging for RT

C-11 acetate      F-18 FDG      Prostascint      CT

The potential of multimodality-imaging in RT

- **Treatment planning- continued**
  - Tumor biology (phenotype) and therapy selection –
    - Intermodality and intramodality changes
    - Radiation or chemotherapy sensitivity
    - Incorporate biological response models to maximize the therapeutic ratio
    - Indicator for more aggressive therapy in certain patients
  - New treatment techniques
    - Revised target volumes and desired dose distributions will require reevaluation of current treatment techniques
FDG-PET Guided IMRT
Dose escalation to PALN

**Rationale**
- The survival of cervical cancer patients with para-aortic lymph node (PALN) metastasis is poor
- Results of RTOG-7920 suggest 45 Gy para-aortic lymph node irradiation (PALNI) is associated with better survival - *Rotman et al JAMA 274:387-393 (1995)*
- PALN dose is limited by bladder, rectum, colon, kidney, small intestine, and spinal cord radiation tolerances

**Objective**
- Dose escalation to PALN while maintaining or even reducing dose to the surrounding critical organs using IMRT
- Use of PET to delineate target volume

Process

- PET and CT scans are acquired in treatment position with PET/CT scanner
- Positive PALN are identified on PET and contours are related to CT
- Treatment plans are created to escalate dose to positive PALN
Dose Distribution
First protocol patient - treatment start date 11-3-2003

50 Gy to PALN bed
60 Gy to positive PALN
Altered/Escalated Dose Distributions
PET Guided GYN Brachytherapy Implants

- Tandem and colpostat applicator inserted in the OR
  - Applicator design and mode of delivery (HDR or LDR) not important
- Foley catheter placed in the urinary bladder
- Patient taken to the PET scanner where 555 MBq (15 mCi) $^{18}$F-FDG ($^{18}$F-fluorodeoxyglucose) is intravenously administered
- Three small tubes containing $^{18}$F-FDG inserted into the applicator
- Whole pelvis scan obtained and images transferred to the treatment planning system (XiO, CMS, St. Louis, MO)
- 3D treatment plan created with target and normal structure DVHs
Anatomy
PET Guided GYN Brachytherapy Implants

- Bladder
- Foley Catheter Displacement
- Rt. Colpostat
- Tandem
- Lt. Colpostat
- Rectum
Treatment planning
PET Guided GYN Brachytherapy Implants

- Applicators, critical structures and tumor contoured
- Software places sources at predefined positions with respect to applicator tips
- Source strengths and treatments times optimized
- Alternatively, deliver conventional dose distributions
Conventional Dose Distributions

PET Guided GYN Brachytherapy Implants
Optimized Dose Distributions
PET Guided GYN Brachytherapy Implants

- Same Integrated Reference Air Kerma (IRAK) strength used for both plans
- Dwell positions rearranged to conform dose distribution
The potential of multimodality-imaging in RT

• **Normal Tissue Sparing**
  – Functional properties of normal structures are used for guidance in organ sparing
  – Highly functioning portions of critical structures are given priority
  – Potentially can simplify delivery and improve tumor dose distribution
SPECT Guided Bone Marrow Sparing

Tc-99m sulfur colloid

SPECT Guided Bone Marrow Sparing

Blue lines identify active bone marrow

PET, SPECT and CT Imaging during Radiation Treatment Planning

FDG PET grayscale

MAA SPECT grayscale

Courtesy: MT Munley, MUSC
Dose-Function Histogram (DFH)

- Similar to the dose-volume histogram (DVH), but displaying the percent relative function of a structure versus dose.
- Uses the value of each voxel element:
  - Targets: F-18 FDG PET (metabolism)
    - F-18 Misonidazole PET (hypoxia)
  - Normal: Tc-99m MAA SPECT (lung perfusion)

Courtesy: MT Munley, MUSC
Beam Orientation as a Function of Lung Function

Comparison of Beam Orientations using the DVH

Lung Cumulative DVH

- AP/PA pair
- Oblique pair

Comparison of Beam Orientations using the DFH

Lung Cumulative DFH

- AP/PA Pair
- Oblique Pair

Percent Perfusion (function)

Percent Isocenter Dose

Courtesy: MT Munley, MUSC

The potential of PET-imaging in RT

- **Evaluation** - Therapy response and follow-up
  - Tumor control
    - Image at a molecular level
    - Evaluate response shortly after initiation of therapy
    - Possibly modify the planned course of therapy based on the initial response
  - Normal tissue function
FDG-PET
Ilb Cx Only—Pre & Post RT

P.W. Grigsby et al
Follow-up FDG-PET
Overall Survival

P.W. Grigsby et al
Pre Treatment

First Implant

Third Implant

Lin et al, IJROBP 63 (2005) 1494-1501
Lin et al, IJROBP 63 (2005) 1494-1501
11C-methionine PET measuring regional salivary gland function

Right-mean dose 30Gy       Left-mean dose 57 Gy

11C-methionine PET measuring regional salivary gland function

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

*Buus et al, Radiotherapy and Oncology 73:289-296, (2004).*
11C-methionine PET measuring regional salivary gland function

RT Treatment Planning with PET/SPECT

Setup reproducibility the primary concern

Poor setup reproducibility may require deformable image registration

These can be separate units or a combined CT/PET or CT/SPECT machine
Fusion/Image Registration

- Lack of anatomical definition makes a registration with CT image a necessity
- Due to the same lack of anatomical definition, CT and PET or SPECT study registration is somewhat challenging
- Combined scanners can simplify the process
Multimodality Image Registration

- Registration Techniques:
  - Surface-based Registration
    - Internal
    - External
  - Image-based Registration
  - Point-based Registration
  - Automatic and semiautomatic computer assisted methods
Patient positioning and immobilization

Flat Tabletop

Immobilization Device
Fiducial Markers

- 0.5 cm diameter, 3.5 cm long, 0.25 ml, plastic, disposable microcentrifuge tubes
- VWRbrand Disposable Microcentrifuge Tubes, VWR Scientific Products, West Chester, PA
- CT, MR, and PET compatible
  - CT - Aluminum
  - MR - 4 mM CuNO₃
  - PET - ^{18}F-deoxyglucose
  - SPECT - 1 µCi of Tc-99M SC
Fiducial Markers

- CT/PET compatible metallic copper markers
- Cu-64

Fiducial Markers

- For face mask patients, markers are attached to the mask
- For body mould patients, markers are attached to the skin
Fiducial Markers
**PET/CT scanner combined unit**

- Multislice CT scanner mated to a PET scanner
- Possibly three scans acquired during procedure
  - Attenuation correction CT
  - PET
  - Treatment planning CT, with contrast if necessary
PET/CT Scanner
SPECT/CT Scanner
PET/CT scanner combined unit
Patient Motion
Patient Motion
RT Treatment Planning with PET
TARGET DEFINITION

- Depending on image window and level setting, target volume can easily change by 50%
- SUV not a part of DICOM data
- SUV utility unclear
Conclusions

• The role of nuclear medicine imaging in radiation therapy and its impact needs further evaluation.

• For several treatment sites it has already been shown that PET studies have a strong potential to improve staging, outcome prognosis, therapy selection, treatment planning, and follow-up.

• Understanding PET and SPECT limitations is imperative for implementation in the treatment planning process.

• The combined PET/CT and SPECT/CT scanner will simplify the treatment planning process.