Positron Emission Tomography for Radiation Treatment

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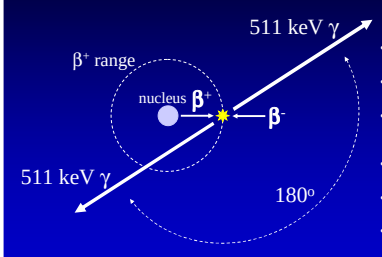
Outline: Part 1

- Physics of PET and PET-CT
- Oncology Imaging with FDG PET
- PET and Radiation Treatment Planning
- Summary

Work supported in part by research grants from North Carolina Baptist Hospital, Varian Medical Systems, and GE Healthcare

Positron Annihilation



- Coincidence detection of two 0.511 MeV photons
- Annihilation radiation from positron-electron pair
- Photon directions at 180o at annihilation point -different from decay point → range of positron
- Positron emitters with biological compatibility
- Low Z (typically), proton rich, short half-lives
- "Local" production with a cyclotron

Physics of PET and PET-CT

- **CE-Imaging: The Physics and Technology of Radionuclide Imaging – III**
  Wednesday, 7:30:00 AM - 9:25:00 AM, Room: L100J
  - **7:30 AM** WE-SAMS-L100J-1**Basic Physics of PET and PET/CT** - F. Fahey*
  - **8:25 AM** WE-SAMS-L100J-2**PET/CT Performance Evaluation Techniques and Quality Assurance** - B. Kemp*
- **PET-CT Workshop**
- Wednesday, 4:00:00 PM - 5:30:00 PM, Room: L100E
  WE-E-L100E-1 **PET CT Workshop - PET/CT Scanner Offering From Different Manufacturers** - J. Anderson*, O. Mawlawi*, M. Georgiou*

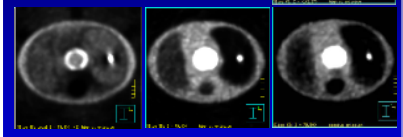
PET Radionuclides

biologically compatible, short half-life

Radionuclide	Half-Life	"run" speed
Fluorine 18 (^{18}F)	110 min	fast
Carbon 11 (^{11}C)	20 min	
Nitrogen 13 (^{13}N)	10 min	
Oxygen 15 (^{15}O)	122 sec	
Rubidium 82 (^{82}Ru) (cardiac)	75 sec	very fast

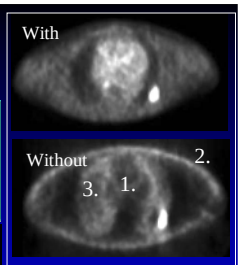
With and Without Attenuation Correction

Phantom with 'normal' uptake except left lung that has air and one spherical 'hot tumor'



Non-corrected PET | CT-attenuated corrected | Cs-attenuated corrected

Courtesy of K Mah, Univ Toronto, Sunnybrook



1. Intensities under-estimated at depth
2. Intensities over-estimated on surface
3. Intensities over-estimated for low density objects (lung)

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

FDG PET Imaging

PET Imaging

- Activity distribution is imaged
  - Physiology, function, biology
- Complementary to (~anatomic) CT and MR
- Increased sensitivity compared to CT alone
- Most indications approved for reimbursement are oncology

PET Imaging in Oncology

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

2-[^{18}F]-fluoro-2-deoxy-D-glucose (FDG)

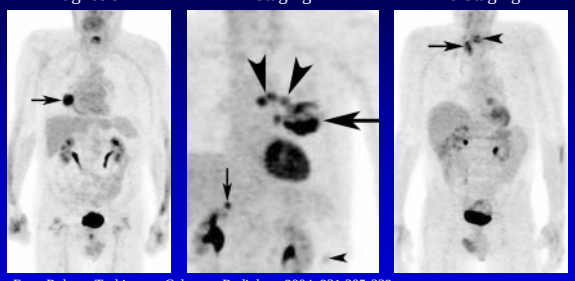
- ^{18}Fluorine-FDG is most common tracer
- Malignant tissues may have increased glycolysis and increased FDG uptake
- FDG-PET images are maps of glucose metabolism – non-specific imaging
- Difficulties with small tumors (< 3 – 10 mm diameter)
- Use increasing – 200 PET-CT scanners in 2 years*
- PET-CT hybrid scanners: registration solved

Courtesy of K Mah, Univ Toronto, Sunnybrook

*From Bradley, Thorstad, Mutic, et al., IJROBP 59(1):78-86, 2004.

Example: Non-Small Cell Lung Cancer

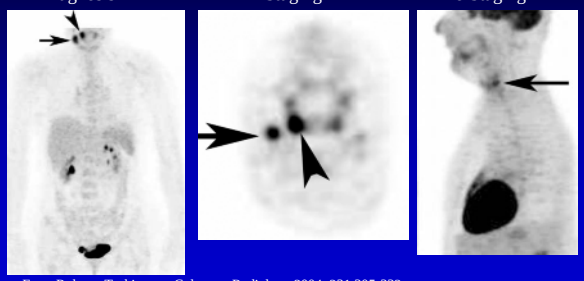
Diagnosis | Staging | Re-Staging



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

Example: Head & Neck Cancer

Diagnosis | Staging | Re-Staging



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

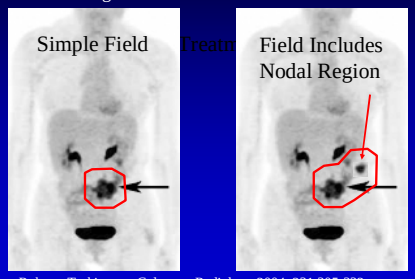
PET and Radiation Treatment Planning

- Main contribution – Staging: Target Localization
  - Very important: stage determines treatment approach
  - Binary results: presence/absence of disease, metastasis
- Dramatic differences possible
  - Treatment mode: reamo, chemo, beamo (EG Shaw)
    - none, one, all three? 10-30% NSCLC patients stage changes
  - Radiation treatment fields: ie, inclusion of nodes
    - Estimation – better coverage of target with PET in 30 – 60% of patients receiving definitive radiation treatment*

*From Bradley, Thorstad, Mutic, et al., IJROBP 59(1):78-86, 2004.

Colon Cancer: Possible Treatment Fields

Node Negative | Node Positive



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

FDG PET and Staging, Localization

Change in stage before and after PET-CT

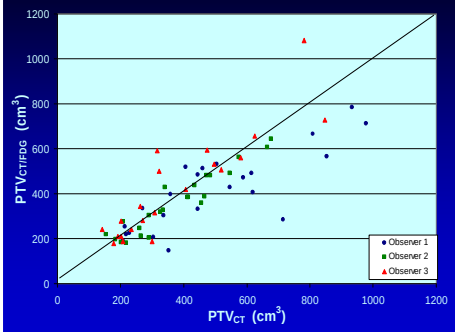
Table 4. American Joint Committee on Cancer stage before and after PET-CT.

		No. patients by post–PET-CT stage							
Pre–PET-CT stage	No. patients	I	II	III	IVA	IVB	IVC	Upstage ratio	Downstage ratio
I	1	1	—	—	—	—	—	0/1	0/1
II	2	—	1	—	—	—	1	1/2	0/2
III	10	—	1	8	1	—	—	1/10	1/10
IVA	21	—	—	—	20	—	1	1/21	0/21
IVB	2	—	—	—	—	1	1	1/2	0/2
IVC	0	—	—	—	—	—	—	0/0	0/0
Total	36	1	2	8	21	1	3	4/36	1/36

Abbreviation: PET, positron emission tomography.

From Koshy, Paulino, Howell et al., Head & Neck, 27:6 494-502, 2005.

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

Courtesy of K Mah, Univ Toronto, Sunnybrook

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

FDG PET and Radiation Treatment

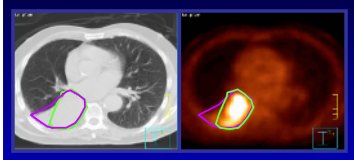
Change in PTV and prescribed dose

Table 5. Summary of changes in management with PET-CT.

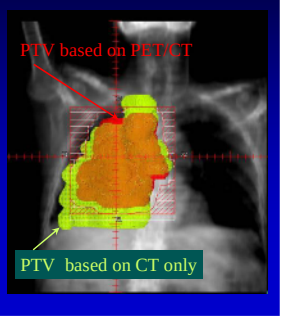
Patient no. and disease site	Pre–PET-CT TNM (AJCC stage)	Post–PET-CT TNM (AJCC stage)	Management changes
1 Maxillary sinus	T3N0M0 (III)	T4aN0M0 (IVA)	Increase in PTV to encompass tumor identified on PET
2 Unknown primary (base of tongue)	T0N2bM0 (IVA)	T1N2bM0 (IVA)	Decrease in initial PTV as primary site was found (nasopharynx not included); primary tumor in oropharynx received higher RT dose
3 Unknown primary (vallecula)	T0N1M0 (III)	T1N1M0 (III)	Decrease in initial PTV as primary site was found (nasopharynx not included); primary tumor in oropharynx received higher RT dose
4 Tonsil	T2N2bM0 (IVA)	T2N2cM0 (IVA)	Increase in PTV to include PET identified tumor extension to deep muscles of tongue and contralateral (right) neck disease; increase in RT dose to right neck
5 Larynx	T2N0M0 (II)	T2N2cM1 (IVC)	Diffuse metastatic disease and bilateral neck metastasis seen only on PET; RT intent changed from curative to palliative; RT volume decreased to include only esophageal mass causing dysphagia; and RT dose decreased to palliative 30 Gy.
6 Tonsil	T2N1M0 (III)	T2N0M0 (II)	No change in RT dose or volume; based on the finding of N0 status with PET, a decision to not give chemotherapy and treat with RT alone

From Koshy, Paulino, Howell et al., Head & Neck, 27:6 494-502, 2005.

PET may decrease target volumes vs CT



CT: Purple PET/CT: Green



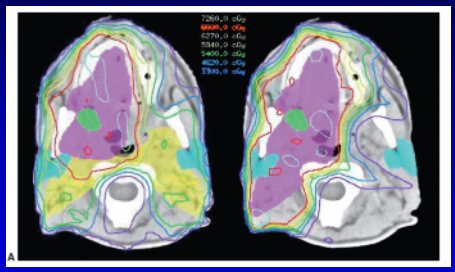
Changes in target outline translate to reduced treatment field size

Courtesy of K Mah, Univ Toronto, Sunnybrook

GTV: CT v PET-CT

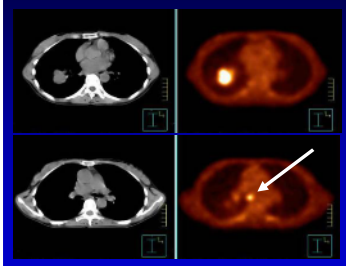
Use of PET-CT may **reduce** GTV/CTV

GTV-CT GTV-PET-CT



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

Ex: *FDG-PET* *<u>increased</u>* *the target volume*



Pre-PET : RLL lesion with right paratracheal node

Post-PET: RLL lesion with right paratracheal; subcarinal; and hilar lymphadenopathy (some < 1 cm on CT)

GTV increased to encompass these nodal regions.

Courtesy of K Mah, Univ Toronto, Sunnybrook

Impact of PET-CT on RT Volume Delineation Using Combined PET-CT Scanner: Wash U Group

- Prospective study : 26 NSCLC patients
  - 8/26 (31%) PET changed staging
  - Of 24 still planned radically
    - In 3, PET/CT reduced volume compared to CT alone due to atelectasis
    - In 10, PET/CT increased volume as unsuspected nodal disease was detected
    - In 1, new separate tumor focus was found in same lung
  - Overall PET/CT resulted in alterations in radiation planning in over 50% of patients by comparison to CT alone.

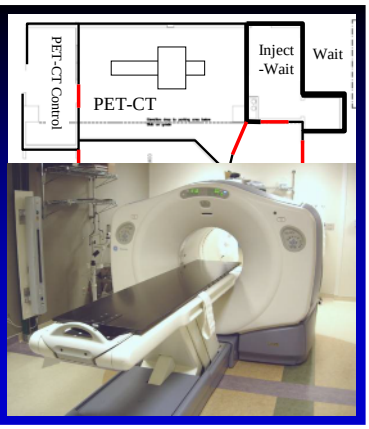
Bradley, J et al. IJROBP 59, 2004

Process: PET in Radiation Treatment

- Cancer diagnosis → biopsy, imaging
- Treatment position, immobilization
- PET imaging in treatment position
- Expert image review
- Image transfer – DICOM, other?
- Image registration (if needed)
- Target localization and definition
- Treatment planning

PET-CT Simulator

- Adjacent control, scanner, inject-wait, lab, and toilet
- 1/8 in Pb; control, scanner
  - adjacent waiting, scanner bkg
- 1/2 in Pb; inject-wait, toilet
- Isotope prep near on-site
- CT, PET-CT operation is quality – future additional QA testing
- Shared Virtual Simulation
- Laser marking system
- Automated PACS archive, selective push to TPS
- Normal access security



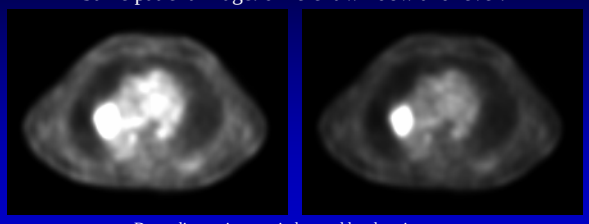
Target Definition

- Qualitative: Expert clinical review
  - Visual, inclusion of clinical history and data
  - Above background
- Quantitative: Voxel intensity values
  - 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

Radiation Treatment Planning with PET

Target Definition

Same patient image: different window and level!



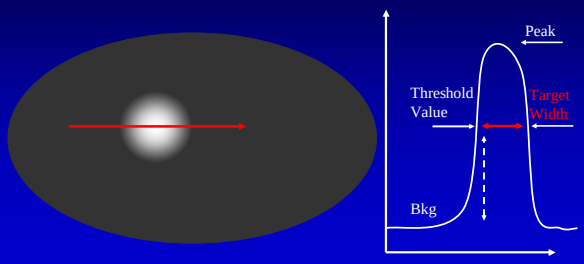
Washington University in St. Louis School of Medicine

Depending on image window and level setting, target volume can change by 50%. Also:

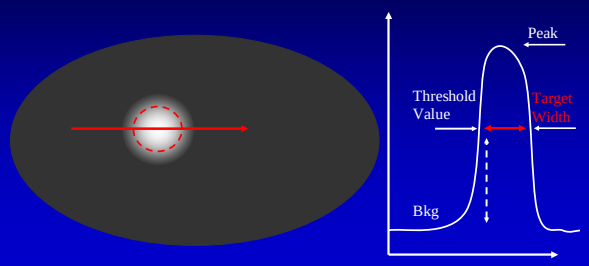
a) SUV not a part of DICOM data

b) SUV utility unclear

The Digital Contour
A Threshold Process



The Digital Contour
A Threshold Process



Standardized Uptake Value (SUV)

- Semi-quantitative measure of glucose metabolism
- Essentially: Average voxel value within an ROI
  - normalized by activity and body weight
- Relative to an individual patient
  - Malignancy v benign
  - Tumor grade
  - Treatment response
  - Prognosis (?) – biological models

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

SUV Limitations

- Semi-quantitative measure of glucose metabolism
- Definition of the ROI (CT? self-referencing), and its location over time (ie, scan to scan)
- Tumor heterogeneity: necrosis, variable grade
- Tumor volume changes with time
- Small tumors difficult to image (size → resolution)
- Glucose load?

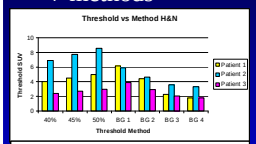
  Consensus? Quantification of FDG uptake?

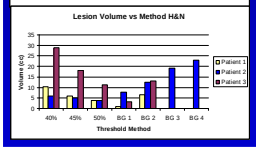
In part from Greven: Sem Rad Onc 14:2, 2004.

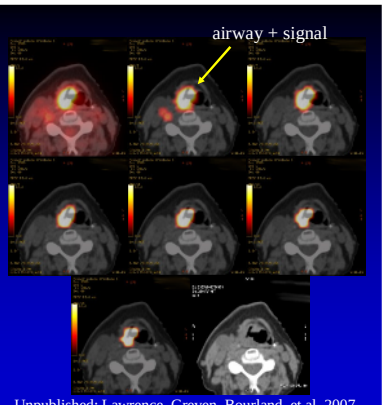
PET-Based Targeting – H/N

K Greven, PI

- 7 methods

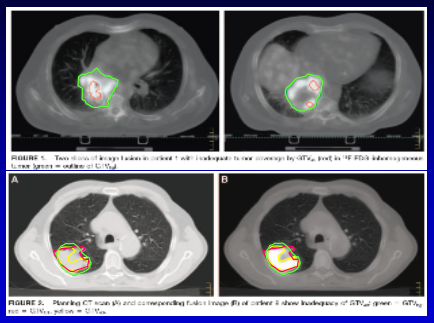






Unpublished: Lawrence, Greven, Bourland, et al. 2007

Target Definition: “a mess” (R Jeraj)



Nestle et al 2005, J Nucl Med 46 (8), 1342.

Target Definition: “a mess”

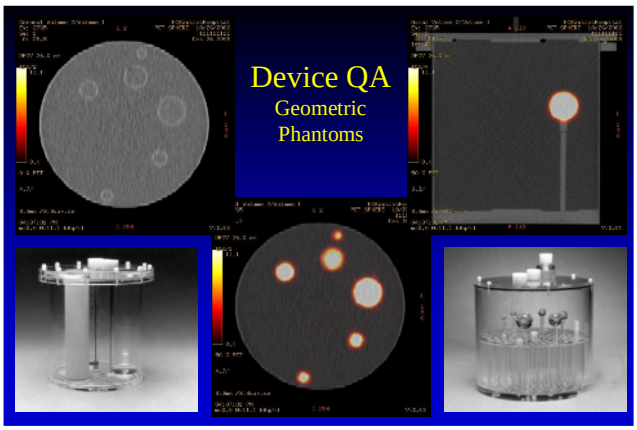
Results of GTV Delineation Following Different Philosophies for Contour Definition: Patients with Grossly Inhomogeneous ^{18}F-FDG Accumulation

Patient no.	SUV_{max}	GTV_{4h} Volume (mL)	GTV_{4h} Radius* (cm)	$GTV_{2.5}$ Volume (mL)	$GTV_{2.5}$ Radius* (cm)	GTV_{4c} Volume (mL)	GTV_{4c} Radius* (cm)	GTV_{bg} Volume (mL)	GTV_{bg} Radius* (cm)
1	20.1	497.7	4.82	494.0	4.80	96.8	2.86	264	3.98
6	23.8	699.2	5.42	655.7	5.39	136.5	3.19	318	4.23
9	20.4	223.9	3.77	188.9	3.56	97.0	2.86	137	3.20
10	11.9	159.9	3.37	167.0	2.94	52.5	2.32	73.0	2.60
13	19.5	375.0	4.47	428.9	4.68	68.2	2.55	260	4.06
14	15.9	182.7	3.52	271.4	4.02	111.8	2.99	112	2.99
22	22.4	176.2	3.48	179.5	3.50	59.1	2.53	67.8	2.86
23	25.7	371.3	4.46	377.5	4.48	168.3	3.43	286	3.85
Mean	19.7	327.9	4.18	337.9	4.18	88.2	2.81	190.2	3.47

Results of GTV Delineation Following Different Philosophies for Contour Definition: Patients with Clearly CT-Defined Tumors

Patient no.	SUV_{max}	GTV_{4h} Volume (mL)	GTV_{4h} Radius* (cm)	$GTV_{2.5}$ Volume (mL)	$GTV_{2.5}$ Radius* (cm)	GTV_{4c} Volume (mL)	GTV_{4c} Radius* (cm)	GTV_{bg} Volume (mL)	GTV_{bg} Radius* (cm)	GTV_{CT} Volume (mL)	GTV_{CT} Radius* (cm)	$GTV_{CT\text{-}bg}$ Volume (mL)	$GTV_{CT\text{-}bg}$ Radius* (cm)
4	30.1	164.2	3.40	151.1	3.30	56.2	2.38	82.0	2.70	88.4	2.51	109.0	2.76
5	6.1	38.2	2.11	30.0	1.93	41.4	2.15	12.4	1.44	12.1	1.42	25.9	1.67
7	1.7	9.3	1.3	—	—	5.7	1.11	3.7	0.96	5.5	1.1	17.0	1.6
9	17.2	62.3	2.32	35.5	2.04	14.1	1.50	21.4	1.72	12.7	1.46	19.5	1.70
18	16.3	67.8	2.33	42.7	2.17	13.2	1.47	23.1	1.77	32.3	1.97	55.3	2.22
Mean	14.7	68.5	2.33	64.0	2.36	28.1	1.72	28.5	1.72	25.7	1.68	45.8	1.94

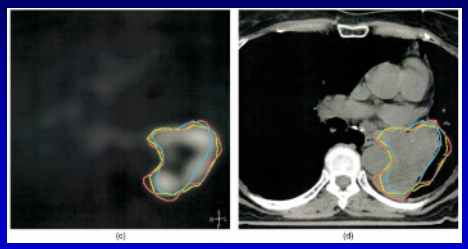
Nestle et al 2005, J Nucl Med 46 (8), 1342.



Device QA
Geometric
Phantoms

GTV-CT and GTV-PET
Other Issue: Inter-observer Variation

PET CT



From Caldwell, Mah, Ung, et al., IJROBP 51(4):923-931, 2001

Acknowledgements

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- Kathy Mah, University of Toronto, Sunnybrook
- Sasa Mutic, Washington University in St. Louis
- Assen Kirov, Memorial Sloan Kettering, NY, NY

Summary: Part 1

- Physics of PET and PET-CT
- PET in oncology: Staging → Treatment Path
- PET and Radiation Treatment Planning
  - Localization of regions to be treated
  - Targeting, contour delineation, with limits

Robert Jeraj, PhD

PET in Treatment Assessment