PET/CT for Tumor Response Evaluation

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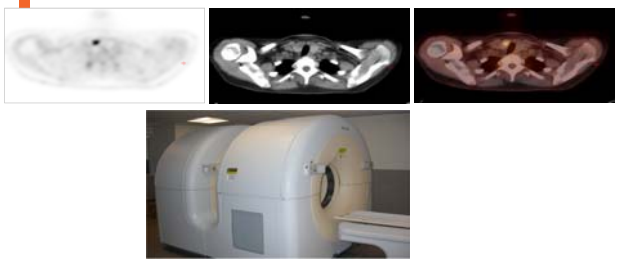
FDG PET/CT for Cancer Imaging

- Staging and restaging
- Early treatment response evaluation
- Guiding biopsy

- NOT for: cancer diagnosis or screening - very low (3%) positive predict value

PET/CT scanner



PET/CT scanner

Anatomic Tumor Response Assessment in CT or MRI

- Imaging as surrogate for
  - Survival, response, time to tumor progression
- RECIST criteria based on longest diameter
  - Complete response (CR): disappear
  - Partial response (PR): ≥ 50% decrease
  - Stable disease (SD): others
  - Progressive disease (PD): ≥ 25% increase or new tumor

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Metabolic Tumor Response Assessment in FDG-PET

- Strong correlation between FDG uptake and cancer cell number
- Metabolic (functional) change may occur earlier and more markedly than tumor size (anatomic) change

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Qualitative (Visual) PET Response Evaluation

- Distribution and intensity of FDG uptake in tumor are visually compared with uptake in normal tissues
- Requires clinical experience, knowledge of disease patterns

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Visual PET Response Evaluation in Lymphoma

- Deauville 5 point scale
  - Score 1, no uptake
  - Score 2, uptake ≤ mediastinum (blood)
  - Score 3, uptake > mediastinum (blood) but ≤ liver
  - Score 4, uptake moderately higher than liver
  - Score 5, uptake markedly higher than liver, and/or new lesions

Barrington, et al. 2014. J Clin Oncol 32: 3048-58.

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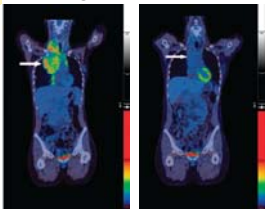
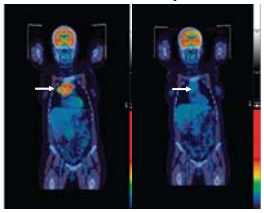
Example 5 Point Scale

Score 3: > blood & < liver



Score 4: moderately > liver



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Semi-Quantitative PET Response Assessment

- Clinic: SUVmax
- PERCIST criteria (SULpeak hottest tumor)
  - CMR: normalize to background level
  - PMR: ≥ 30% decrease and ≥ 0.8 unit in SUL
  - SMR: others
  - PMD: ≥ 30% increase and ≥ 0.8 unit in SUL or visible increase in extent of uptake, or new FDG-avid lesion

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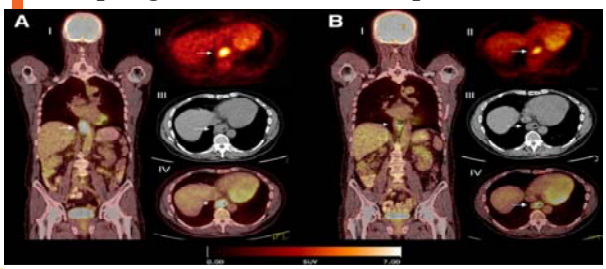
Esophageal Cancer – A Responder



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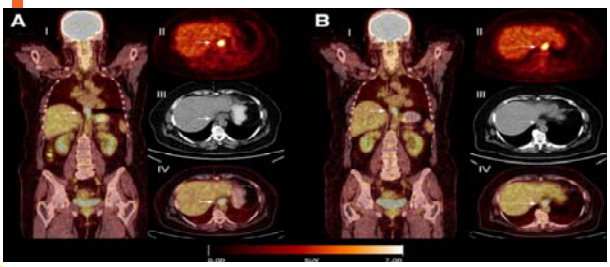
Esophageal Cancer – A Non-Responder



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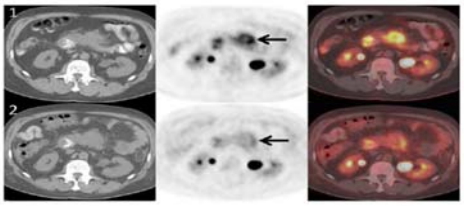
PET/CT for Tumor Response: An Example in Pancreatic Tumor



Large decline in SUL (-41%) despite stable pancreatic mass anatomically (arrows) → Partial metabolic response.

Wahl, J Nucl Med. 50(Suppl 1): 122S–150S.

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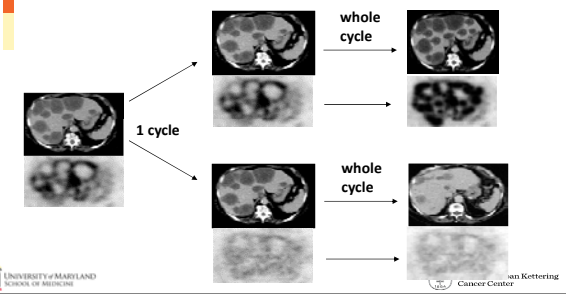
Early Therapy Response Evaluation



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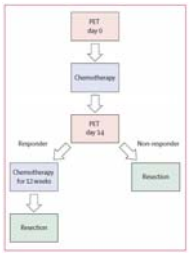
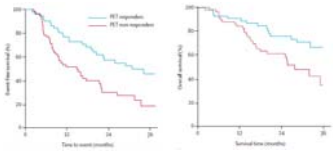
Early PET-Guided Chemotherapy: MUNICON Phase II Trial





- 110 PTs w/ esophagogastric junction tumor
- PET response defined as >35% reduction of SUV at 2 weeks of induction chemo
- 58% of PET responders achieved pathological response vs. none of PET non-responders

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Lordick, et al. 2007. Lancet Oncology 8: 797-805.

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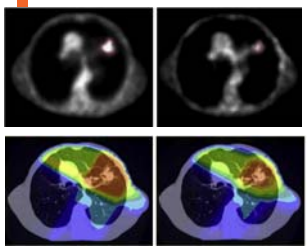
Mid-RT (40-50 Gy) PET-Guided ART



- PET tumor volume decreased in 6 of 14 PTs
- Allowed dose escalation of 58 Gy or reduction in NTCP of 2%

Feng, et al. 2009. Int J Radiat Oncol Biol Phys 73: 1228-34.

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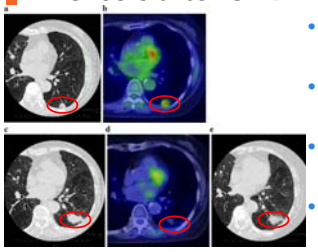
Differentiate Tumor Recurrence from Fibrosis after SABR for Lung Cancer



- Mass-like consolidation 19 m after SABR
- Hard to differentiate from tumor recurrence in CT
- Completely resolved in FDG PET → fibrosis
- Follow-up CT confirmed radiation-induced fibrosis

Nakajima, et al. 2013. Ann Nucl Med 27: 261-70.

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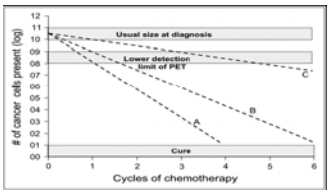
Limitation of Metabolic Tumor Response Assessment in PET

- Poor resolution: smallest tumors PET can detect: 4-10 mm diameter, 10^8 cells
- Depends on time to normalization (positive to negative) of the PET scan



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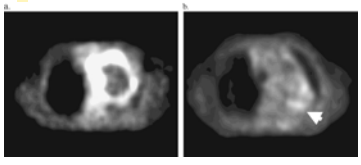
Normal Tissue Inflammation due to RT



- Lung inflammation in RT field hindered tumor delineation
- Hard to differentiate inflammation uptake from viable residual tumor uptake

Feng, et al. 2009. Int J Radiat Oncol Biol Phys 73: 1228-34.

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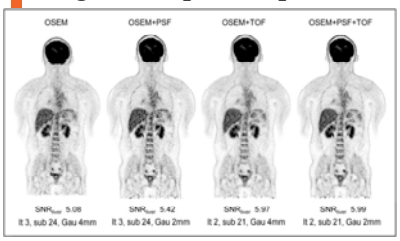
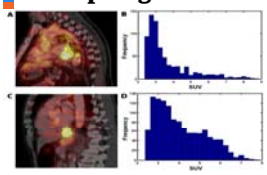
Image reconstruction with time-of-flight and point-spread function



- TOF more accurately locates annihilation point
- PSF compensate for the geometric distortion
- Improves image quality and SNR

Akamatsu, G., et al., J Nucl Med, 2012. **53**(11): p. 1716-22.

Esophageal Cancer

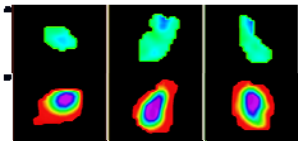


SUV skewness pre-CRT

- Top: responder, more skewed (fewer higher SUVs)
- Bottom: non-responder, less skewed (more higher SUVs)

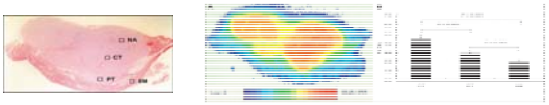
Three texture features post-CRT – Inertia, Correlation, and Cluster Prominence

- Top: responder, homogeneous FDG uptake post-CRT
- Bottom: non-responder, heterogeneous FDG uptake post-CRT

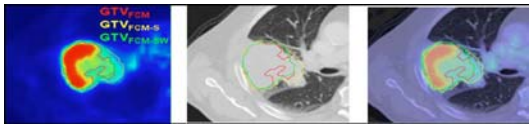


Tan, Lu et al. 2013. Int J Radiat Oncol Biol Phys 85: 1375-82.

Texture: Spatial Variation in FDG Uptake is Important Prognostic Factor



Zhao, et al. 2005. J Nucl Med



Belhassen and Zaidi 2010. Med Phys

Accuracy of Individual Spatial-Temporal FDG-PET Features

Table 3 AUC and *P* values of the most accurate SUV features for the prediction of pathologic response to neoadjuvant chemo-radiation therapy in patients with esophageal cancer

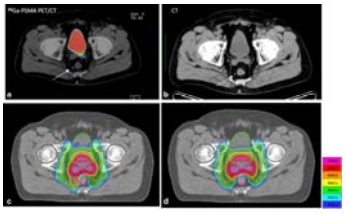
Feature	VOI	Image	AUC	*P* value
Traditional SUV intensity features				
SUV_{max} decline*	SUV_{max} point	Pre, Post	0.76	.05
SUV_{max} ratio†	SUV_{max} point	Pre, Post	0.76	.05
SUV_{max} Pre	SUV_{max} point	Pre	0.70	.14
SUV_{max} Post	SUV_{max} point	Post	0.61	.47
Intensity features				
SUV_{mean} decline*	$VOI\_SUV_{2.5}$	Diff	0.79	.03
Skewness	$VOI\_SUV_{2.5}$	Pre	0.76	.05
Texture features				
Inertia	$VOI\_SUV_{2.5}$	Post	0.85	.01
Correlation	$VOI\_SUV_{2.5}$	Post	0.80	.03
Cluster prominence	$VOI\_SUV_{2.5}$	Post	0.78	.04
Geometry features				
Roundness	$VOI\_SUV_{2.5}$	Pre	0.71	.12
Volume change*	$VOI\_SUV_{2.5}$	Pre, Post	0.71	.12
Diameter change*	$VOI\_SUV_{2.5}$	Pre, Post	0.64	.30
Geometry-intensity feature				
TGV change*	$VOI\_SUV_{2.5}$	Diff	0.74	.08

Abbreviations: Diff = Pre−Post; Post = Post-CRT SUV; Pre = Pre-CRT SUV; TGV = total glycolytic volume; VOI = volumes of interest.
* Decline or change = Pre−Post.
† Ratio = Post/Pre.

Tan, Lu et al. 2013. Int J Radiat Oncol Biol Phys 85: 1375-82.

Beyond FDG PET, and beyond traditional sites

- FMISO PET for imaging hypoxia
- FLT PET for imaging cell proliferation
- Prostate cancer (PSMA)
- Brain cancer (amino acid: ^{11}C-methionine, ^{18}F-FDOPA, PET/MR)



Sterzing, et al. 2015. Eur J Nucl Med Mol Imaging.

Summary

- FDG PET/CT shows advantages over CT for tumor response evaluation in many cancers
  - More accurate
  - Earlier evaluation
- Radiomics, particularly FDG uptake heterogeneity, is likely prognostic
- Non-FDG tracers, PET/MRI are useful in certain diseases/applications

Acknowledgements

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