

Mediterranean Thematic Workshops in Advanced Molecular Imaging, Corsica 2016

Nuclear Medicine & Molecular Imaging for Minimizing Medical & Surgical Interventions

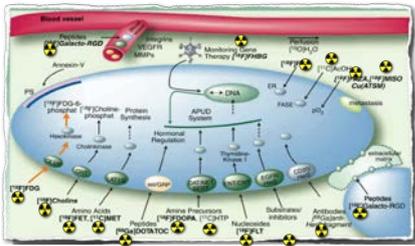
Prof. John Prior, PhD MD
Nuclear Medicine & Molecular Imaging, Lausanne University Hospital

Plan

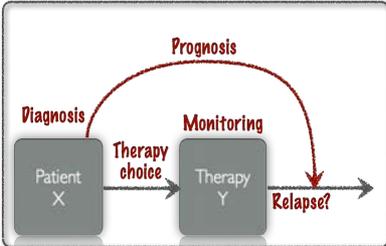
- Early detection of suspicious lesions
- Easier targeting of biopsies
- Better detection of micro-metastases & tumor margins during surgery
- Deciding minimal invasive, standard surgical, or watch-and-wait approaches
- Early detection of residual disease or recurrence

Introduction Molecular Imaging

Molecular processes targeted by radiopharmaceuticals



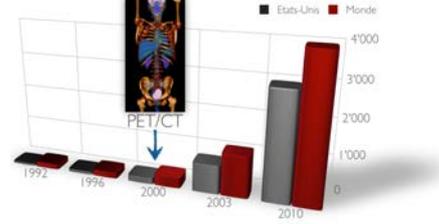
Molecular Imaging: Diagnosis? Not only...



Molecular Imaging:
→ More adapted management
→ Potential for healthcare care cost containment

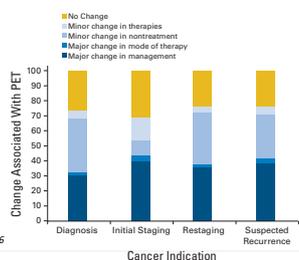
PET/CT

TIME Magazine's Medical Invention of the Year 2000



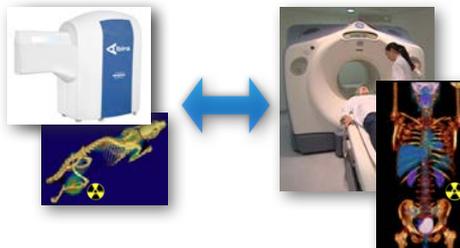
David Townsend

Personalized (Precision) Medicine: Change in treatment after a ¹⁸F-FDG PET/CT



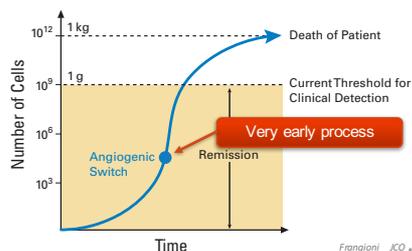
Hillner et al., JCO 2008

Translational hybrid imaging

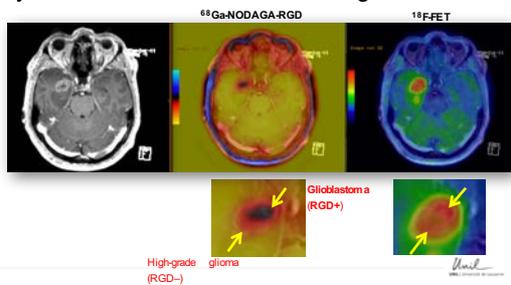


Minimizing Interventions

Tumor growth & angiogenic switch

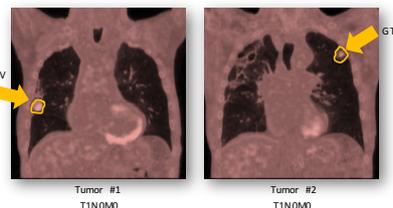


49-y Patient with Glioblastoma & High Grade-Glioma



Lung Function Preservation during SBRT

59-year-old man with a double primary tumor
No surgery possible due to comorbidities (COPD, cardiac & renal insufficiency)
Treatment by SBRT (5 x 11Gy / both lesions)



Lung Function Preservation during SBRT

Pre-SBRT Lung Scintigraphy

Radiation Therapy Plan with Lung Function information

PTV 45 Gy

50% Lung Perfusion

→ Optimal Radiation Planning

De Baat & Prior, 2015

Lung Function Preservation during SBRT

Pre-SBRT Lung Scintigraphy SPECT

Radiation Therapy Plan

50% Lung Perfusion

Post-SBRT Lung Scintigraphy SPECT

Outcome: → No significant reduction of lung function after SBRT

De Baat & Prior, 2015

Adaptive Radiation Therapy: Tumoral response assessment during RT

¹⁸F-FLT

Mac Manus (Sem Nucl Med 2012)

Deciding to avoid cardiovascular surgery

- Prosthetic valve endocarditis is a severe complication with high mortality
- AUC=0.9, +LR4.8, -LR0.3
- Helps decision to operate vs. watch-and-wait

Fagman et al. Int J Cardiovasc Imaging 2016

PET/CT-Guided Surveillance vs. Surgery

- N=282 patients with head and neck squamous-cell carcinoma (N2/N3 disease)
- Planned neck dissection vs. dissection only if residual disease on PET/CT @3months after chemoradiation therapy
- Same survival (non-inferiority) with considerably less operations (54 vs. 224) and more cost-effectiveness

Savings of \$2,190 per patient in PET/CT-guided approach

McConkey et al. NEJM 2016

Image-Guided Diagnosis of Chronic Osteomyelitis & Implant-Associated Infections

- N=212 patients with suspected osteomyelitis of implant-associated infections
- Final diagnosis positive in 101 patients
- PET/CT: Se 88% NPV 89% AUC 82%
- High sensitivity for detecting osteomyelitis and infection in patient with non specific symptoms

McConkey et al. NEJM 2016

Molecular Interventional Imaging

FET PET-guided radiation therapy

Molecular imaging-guided biopsy

Molecular Imaging-Guided Surgery

Molecular Imaging-Guided Intervention

Radiofrequency Ablation in PET/CT

Pitor, Kosinski, Bischof-Delaloye, Denys, *MIR* 2007

PET/CT-guided cryotherapy

Kidney, lung, breast, bone, pancreas and soft tissues

Local anesthesia, little or no pain during procedure, real-time monitoring of ablation with US, CT, MR

Still under-used than heat-based ablation techniques

Yilmaz et al, *Insight Imaging* 2016

Intraoperative Tumor Margin Imaging

Research Article
Intraoperative Molecular Imaging of Lung Adenocarcinoma Can Identify Residual Tumor Cells at the Surgical Margins
 Jose A. Madry, Chingping T. Chiu, Robert De Jager, Sean J. Lee

Figure 1 shows a 3x3 grid of images for each of three regions (a, b, c). The columns are labeled 'White Light', 'Fluorescence', and 'Overlay'. The rows show different views: top row is a wide view, middle row is a closer view, and bottom row is a histological section. The fluorescence images show bright spots indicating tumor cells.

Keatina et al. *MolImaging Biology* 2016

New imaging in hyperparathyroidism with ¹⁸F-choline for deciding mini-invasive vs. traditional surgery

pHTP → para-isthmic adenoma

sHTP → 4 hyperplastic glands

Figure 1: Primary hyperparathyroidism (patient #9). FCH-PET/CT: hyperfunctioning parathyroid gland below thyroid isthmus, which corresponded to adenoma on post-surgical histology. This parathyroid gland could not be exactly attributed to P3 or P4 origin, as bilateral neck exploration has not been performed.

Figure 2: Secondary hyperparathyroidism, after kidney grafting (patient #8). FCH-PET/CT: four hot spots corresponding to hyperplastic parathyroid glands on post-surgical histology (right P3 P4 and left P3 P4).

→ Mini-invasive Surgery

→ Traditional Surgery

Michaud et al. 2015

Endoscopic PET-US Probe (FP7 Project 2010-15)

ENDO TOFPET US
 Endoscopic TOFPET & Ultrasound

The diagram shows a probe with a PET crystal and an ultrasound transducer. It is shown being inserted into a patient's body for imaging.

ENDO TOFPET US
 Endoscopic TOFPET & Ultrasound

Molecular Imaging Radioguided Surgery

Role of Surgery in Cancer

Surgery still best option for most solid cancer

Metastectomy + cytoreductive surgery considered viable management in selected cases (e.g. melanoma)

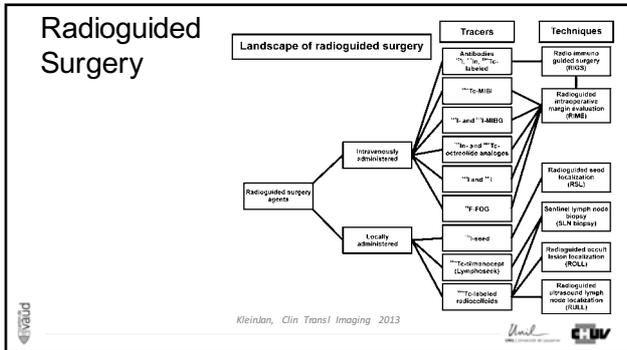
Need for detection of surgically occult disease (e.g. in scar tissue) or help in locating lymph node in axilla or abdomen

Radioguided Surgery

Developed 1950's; use of intraoperative probes for radionuclides detection

Established surgical discipline; management breast, melanoma, colorectal tumors & parathyroid disease

- real-time information on disease location/extent
- assessment of surgical margins
- minimizes invasiveness of diagnostic/therapeutic procedures, while maintaining max benefit to patient



Handheld Detection Probes

Shauer, Bader, Reiss, Poisinger: The Sentinel Lymph NodeConcept, Springer, 2005

Peroperative β^+ (positron) probes

FDG-Probe in clinical setting: minimum tumor-to-background 1.5 (Gulec S, Ann Surg Oncol 2006)
 Localization of FDG-avid tumor sites with positron probe (Piert M, EJNMMI 2007)
 β^+ probe: very sensitive, detectable tumor ~mg, >10 times better than PET/CT
 Applications: primary tumors detection, remaining tumoral tissue in resection beds, malignant lymph nodes, and tumor infiltrates in anastomotic rings, among others

Radioguided Detection of Lymph Node Metastasis in Non-Small Cell Lung Cancer

Better sensitivity Detection of micrometastases

Category	Number	Patients
Operating		
LNCC 2006 to LNCC 2008	1	
LNCC 2006 to LNCC 2008	1	
LNCC 2006 to LNCC 2008	1	

Swiss CTI "Science-to-Market" Grant to Lausanne University Hospital & SME

- Beta+ Probe collaboration started Forimtech 2005
- Phantoms, pilot cases led to writing the CTI grant in 2008
- CTI awarded 2009 started 01.04.2009 (MCHF 1.8)

Evolution of the prototype towards industrial probe

Swiss CTI "Science-to-Market" Grant to Lausanne University Hospital – SiPM Probe

IEEE ASSC 2011

Melanoma Metastasis

Pelvic metastasis from melanoma

F-18-FDG-Guided Surgery: Resection

F-18-FDG-Guided Surgery: Relapse

¹¹¹In-PSMA-Guided Prostate Cancer Surgery

¹¹¹In-PSMA-Guided Prostate Cancer Surgery

Maurice, Eur Urology 2015

Beta⁻ Probes for Radioguided Surgery

Collamat, JNM 2015

Intraoperative 3-D mapping of parathyroid adenoma

Rahbar et al. 2012

Navigated fSPECT/US imaging

Freesmeyer et al. 2014

Hybrid modality : combined radio-/(near infra-red) fluorescence-guided surgery

Klein, Clin Transl Imaging 2013

Summary

- Early detection of suspicious lesion
- Easier targeting of biopsies
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