Clinical Oncological imaging:

**PET-CT** and its role in RT

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www.nucpetmrc.com
Evolution of Technology

CT
PET
PET/CT

1973
2000
2001
Structure without function is a corpse...function without structure is a ghost.
PET-CT the Mol Imaging.

Positron emission tomography (PET) enables *in vivo* imaging of the distribution of (FDG) (and other positron-emitting ligands) with high (< 1 cm) resolution and high (nanomolar) sensitivity.

The addition of transmission (CT) to PET instruments results in images that provide both functional/molecular information and structural images,

PET/CT has consequently become the most rapidly developing medical imaging modality.

Time Magazine honored PET/CT as the "Medical Science Invention of the Year" in 2000, noting that the PET/CT scanner has "provided medicine with a powerful new diagnostic tool."
Existing Spectrum of Pre-Clinical Imaging

Morphology
- X-Ray
- CT
- Ultrasound
- MRI

Function
- Optical Imaging
- SPECT/PET

Molecule
- $10^{-2} \text{ M}$
- $10^{-6} \text{ M}$
- $10^{-12}$
Imaging Protocol

Patient
- Fast 4 hrs prior to exam
- Inject tracer
- Start scan 60 min later

CT
- Topogram (scout)
- CT scan (1 min)

PET
- Brain (10 min)
- Heart (10 min)
- Body (20 min)
Positron Emission Tomography
[18F]FDG
[18F]FESP
[15O]H2O
[13N]AMMONIA
in [11C]hydroxyefedrine
[11C]FLUMAZENIL
[11C]RACLOPRIDE
[11C]FE-β-CIT
[11C]SCH23390
[11C]CARAZOLOL
[11C]MCN5652
[11C]Methycoline
[11C]FLUVoxamine
[11C]CGP62349
[11C]Fluvalanerol-L-carnitine
[11C]PNUN167760
[11C]BISOPROLOL
[11C]ICI118551
[11C]OLANZAPINE
[11C]SB235753
[11C]E2020
[11C]A 84543
[11C]VC195
[11C]VC193M
[11C]VC198M
[11C]WAY100635
[11C]RN5
[11C]VA100
[11C]CARFENTANIL
[11C]ZOFENOPRIL
[18F]FLUORO CAPOTRIL
[11C]CNR1
[11C]PK1113195
[11C]F167
[11C]PD60
[11C]PD78

RADIOTRACERS PREPARED AT HSR
H.S., 077-64-28

PET

CT

PET/CT

130 kV
75 mA
5 mm

FDG Bed
15 mCi
1 min

KVs mAs Slice
What Are the Advantages of PET/CT?

Advantages of CT

- high spatial resolution

Advantages of PET

- better lesion characterization
- enhanced lesion detection
Applications of PET-CT

- epilepsy
- tumor
- dementia

- perfusion
- viability

1.5 million exams performed annually

- tumor
- infection
- bone
“Off hand, I'd say you're suffering from an arrow through your head, but just to play it safe, I'm ordering a bunch of tests.”
PET - CT in Tumor Imaging

• Detect radiographically occult lesions
• Characterize radiographic abnormalities
• Evaluate extent of disease
• Evaluate response to therapy
F-FDG WHOLE BODY PET

- DIAGNOSIS
- STAGING
- RE-STAGING AND FOLLOW-UP
- RADIOTHERAPY
Role of PET imaging in Onco.

- Diagnosis of Malignancy. Eg SPN and Brain scan vs post tt recc.
- Grading Malignancy:- The so called metabolic Bx Prov info reg grading tumor indirectly provides info about Prog.
- Staging and Restaging Disease:- PET is found sup to other diag.
- Residual disease evaluation:- Lack of ch feature of anat imaging PET helps in this eg Lymphoma and Testicular abd masses.
- Detection of Recurrence:- eg treated cases of CRC with rising CEA.
- Measuring therapy response:- It is imp to plan future therapy strategy based on response to initial treatment and PET helps in this. Eg HL
- To Identify site of active disease:- to guide biopsy when disease is heterogenous eg STS.
- CUPS:- when an enlarged Mets node is seen to find the primary.
- For Guided biopsy and RT planning.
Normal PET - CT Body Scan
Normal PET/CT scan

QuickTime™ and a decompressor are needed to see this picture.
Abnormal PET - CT Body Scan
## Approved Indications for PET-CT

**Diagnosis, Staging, and Restaging (unless otherwise indicated)**

<table>
<thead>
<tr>
<th>Indication</th>
<th>Criteria</th>
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<tbody>
<tr>
<td>Head &amp; Neck</td>
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<tr>
<td>Thyroid</td>
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<td>Breast</td>
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<td>Lung</td>
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<td>Esophagus</td>
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<td>Colon &amp; Rectum</td>
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<td>Cervix</td>
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<td>Lymphoma</td>
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<td>Melanoma</td>
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<td>Other Cancers</td>
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</tbody>
</table>

- **Head & Neck**
- **Thyroid**
- **Breast**
- **Lung**
- **Esophagus**
- **Colon & Rectum**
- **Cervix**
- **Lymphoma**
- **Melanoma**
- **Other Cancers**

- follicular: I-131 neg, Tg >10 ng/dL
- not breast masses or regional nodes
- only non-small cell
- CT/MRI neg for extra-pelvic mets
- not regional nodes
- when enrolled in NOPR
<table>
<thead>
<tr>
<th>Cancer Type</th>
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<tbody>
<tr>
<td>Acute Myeloid Leukemia</td>
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<tr>
<td>Bladder Cancer</td>
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<tr>
<td>Bone Cancer</td>
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<tr>
<td>Breast Cancer</td>
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<tr>
<td>Central Nervous System Tumors</td>
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<tr>
<td>Cervical Cancer</td>
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<tr>
<td>Chronic Myelogenous Leukemia</td>
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<tr>
<td>Colorectal Cancer</td>
</tr>
<tr>
<td>Esophageal Cancer</td>
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<tr>
<td>Gastric Cancer</td>
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<tr>
<td>Head and Neck Cancer</td>
</tr>
<tr>
<td>Hepatobiliary Cancer</td>
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<tr>
<td>Hodgkin’s Disease</td>
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<tr>
<td>Kidney Cancer</td>
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<tr>
<td>Melanoma</td>
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<tr>
<td>Myelodysplastic Syndromes</td>
</tr>
<tr>
<td>Multiple Myeloma</td>
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<tr>
<td>Neuroendocrine Tumors</td>
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<tr>
<td>Non Hodgkin’s Lymphoma</td>
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<tr>
<td>Non-Small Cell Lung Cancer</td>
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<tr>
<td>Occult Primary Cancer</td>
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<tr>
<td>Ovarian Cancer</td>
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<tr>
<td>Pancreatic Cancer</td>
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<tr>
<td>Prostate Cancer</td>
</tr>
<tr>
<td>Soft Tissue Sarcoma</td>
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<tr>
<td>Skin Cancer (except Melanoma)</td>
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<tr>
<td>Small Cell Lung Cancer</td>
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<tr>
<td>Testicular Cancer</td>
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<tr>
<td>Thyroid Cancer</td>
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<td>Uterine Cancer</td>
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<td>Melanoma</td>
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PET-CT and Lung Cancer

- The first FDA approved application of PET was in characterization of SPN.
- The accuracy of detection of malignant pulmonary lesions using FDG PET is very high, typically > 90%.
- The ability to image the whole body enables evaluation of nodal status and distant metastases.
47 year old man with multiple trauma from a MVA who was incidentally discovered to have a pulmonary nodule
84 year old man with chronic cough found to have a 13 mm nodule on CXR
Figure 1d. Images in a 62-year-old man with history of lung cancer who now has hemoptysis and was referred for evaluation for recurrent disease.
Correlation of 18F-fluorodeoxyglucose uptake on positron emission tomography with Ki-67 index and pathological invasive area in lung adenocarcinomas 30mm or less in size

European Journal of Radiology, 08/13/2010

Murakami S et al. – 18F–fluorodeoxyglucose positron emission tomography (FDG–PET) is commonly used to distinguish benign from malignant lesion. Recently, maximum standardized uptake value (SUVmax) on FDG–PET has found to have prognostic value. SUVmax correlated significantly with Ki–67 index and diameter of the pathological invasive area. The present results suggest the potential role of FDG–PET in predicting adenocarcinomas with invasive characteristics.
73 year old woman s/p resection for colon cancer, rising CEA level and negative CT
Enhanced Detection
PRE THERAPY WB IODINE SCAN
Enhanced Detection

47 year old man with biopsy proven recurrent thyroid cancer 3 months after thyroidectomy
PET-CT and Rec Thy Ca

Positron emission tomography and positron emission tomography-CT evaluation for recurrent papillary thyroid carcinoma: Meta-analysis and literature review

Head & Neck, 08/16/2010 Evidence Based Medicine

Miller ME et al. – Sensitivity and specificity data regarding positron emission tomography (PET) and PET/CT for surveillance of well–differentiated thyroid cancer does not evaluate subtypes separately. **PET and PET/CT are useful modalities in surveillance of papillary thyroid carcinoma.** This is the first study to examine papillary thyroid carcinoma independently of other subtypes of well–differentiated thyroid carcinoma.
Unknown Primary

68 year old man who presented with right neck mass
Metastatic Cx LN with unknown primary, MR negative, PET +ve detection
49 year old man with new lung cancer
52 Yr F c/o Ca Breast with mets.
35/F with Ca Cx and post CT and RT for restaging.
43 Male with post op case of RCC for Restaging.
Recurrent Disease

64 year old man s/p laryngectomy, now has dysphagia
Tongue Ca ? Recurrent post Ch and RT

Figure 2B. Transaxial images in a 64-year-old man with tongue cancer; status after chemotherapy and radiation therapy.
Figure  Transaxial images in a 64-year-old man with tongue cancer; status after chemotherapy and radiation therapy. Now Rec Tongue ca not seen by CT.
Role of PET in Head and Neck Ca

- Assessment of Distant Mets
- Ass. Synchronous 2\textsuperscript{nd} primary.
- Detection of CUPS
- Ass. Residual and Recurrent disease.
- Precise delineation of tumor vol for RTP monitoring and providing prog information,
Clinical Application in H & N Ca

- Review Article
- Clinical Applications of FDG PET and PET/CT in Head and Neck Cancer
- Akram Al-Ibraheem, Andreas Buck, Bernd Joachim Krause, Klemens Scheidhauer, and Markus Schwaiger
- Department of Nuclear Medicine, Technische Universität München, Ismaninger Strasse 22, 81675 Munich, Germany
- Received 28 February 2009; Accepted 17 June 2009

Abstract

18F-FDG PET plays an increasing role in diagnosis and management planning of head and neck cancer. Hybrid PET/CT has promoted the field of molecular imaging in head and neck cancer. This modality is particular relevant in the head and neck region, given the complex anatomy and variable physiologic FDG uptake patterns. The vast majority of 18F-FDG PET and PET/CT applications in head and neck cancer related to head and neck squamous cell carcinoma. Clinical applications of 18F-FDG PET and PET/CT in head and neck cancer include diagnosis of distant metastases, identification of synchronous 2nd primaries, detection of carcinoma of unknown primary and detection of residual or recurrent disease. Emerging applications are precise delineation of the tumor volume for radiation treatment planning, monitoring treatment, and providing prognostic information. The clinical role of 18F-FDG PET/CT in N0 disease is limited which is in line with findings of other imaging modalities. MRI is usually used for T staging with an intense discussion concerning the preferable imaging modality for regional lymph node staging as PET/CT, MRI, and multi-slice spiral CT are all improving rapidly. In this review, we summarize recent literature on 18F-FDG PET and PET/CT imaging of head and neck cancer.
FDG PET – brain tumor post th
two foci on CT, only one viable tumor
Anaplastic Oligodendroblastoma
Post Sx
Post Sx Rec
Grading Tumor: Astrocytoma
Clinical application of PET in BT

1. **Initial Evaluation of Tum**
   - Determine grade/degree of malign
   - Determine optimal site for sterettac Bx.
   - Assessment of prognosis.

2. **Post Therapy evaluation**
   - Detection of recurrent tumor
   - Detection of residual/recurrent Tr post Sx
   - Monitoring treatment response
   - Diff rec/necrosis post RT
   - Grading Malignancy
PET and MR in Glioma

Advanced MRI and PET imaging for assessment of treatment response in patients with gliomas

The Lancet Neurology, 08/17/2010  Clinical Article

Dhermain FG et al. – T1–weighted MRI, with or without gadolinium, is the gold standard method. However, this technique only reflects biological activity of the tumour indirectly by detecting the breakdown of the blood—brain barrier. Therefore, especially for low–grade glioma or after treatment, T1–weighted MRI enhanced with gadolinium has substantial limitations. Development of more advanced imaging methods to improve outcomes for individual patients is needed. New imaging methods based on MRI and PET can be employed in various stages of disease to target the biological activity of the tumour cells (eg, increased uptake of amino acids or nucleoside analogues), the changes in diffusivity through the interstitial space (diffusion–weighted MRI), the tumour–induced neovascularisation (perfusion–weighted MRI or contrast–enhanced MRI, or increased uptake of amino acids in endothelial wall), and the changes in concentrations of metabolites (magnetic resonance spectroscopy). These techniques have advantages and disadvantages, and should be used in conjunction to best help individual patients.
Monitoring Response

63 year old man stage 3A lung cancer, has received 4 cycles of chemotherapy
Breast cancer: disease progression

28 min (8/05)
10.6 mCi, 115 min pi
4 min/bed, 7 beds
3i / 8s; 6f

15 min (5/06)
10.5 mCi, 104 min pi
3 min/bed, 5 beds
3i / 8s; 6f

Scan duration: 15

A 53-year-old female (200 lbs) with history of breast cancer. PET/CT on 8/05 showed increase in bilateral supraclavicular, mediastinal and right parasternal node disease. PET/CT on 5/06 showed significant disease progression including sternum and pelvis.

12/11/2007
B/L early and late PET scan histopathological responder (A) and a non-responder (B). Changes in tumor 

SUVpeak and tumor sizes are indicated.
Response assessment with PET vs CT
Ca Colon with rising CEA
CT + PET/CT vs PET/CT

MOST CASES

• Standard CT followed by PET/CT if needed

SOME CASES

• PET/CT

CT component can be low resolution or optimized
Problems and Pitfalls

• False negative findings

Tumor histology
Lesions smaller than 5 mm
Diabetes/Non-fasting patients

• False positive findings

Normal physiology
Granulomas and other infections
Adenomas
56 year man with HCV, end stage liver disease, and presumed hepatoma
Physiologic Uptake: Brown Fat
Figure 5. Infected bypass graft.

Infected vascular graft
Granulomatous Disease

62 year old man with hilar and mediastinal adenopathy. Biopsy: sarcoidosis
HCC

82 year old man with wt loss and liver masses
Cerci JJ et al. – The objective was to assess the prognostic value of 18F–FDG PET after 2 cycles of chemotherapy using doxorubicin, bleomycin, vinblastine, and dacarbazine (ABVD) in Hodgkin lymphoma (HL) patients overall and in subgroups of patients with early and advanced stages and with low and high risks according to the International Prognostic Score (IPS). PET2 is an accurate and independent predictor of EFS in HL. A negative interim 18F–FDG PET result is highly predictive of treatment success in overall HL patients, as well as in subgroups with early or advanced–stage disease and with low or high IPS risk.
Colonic Mass?

82 year old man with wt loss and liver masses
Metastatic LN with Unknown primary
Known case of Cervical LN Mets
Clinical Impact of PET/CT

- More accurate diagnosis
- Avoidance of unnecessary tests, and (potentially) harmful procedures
- Better treatment or management

* PET also Serves as Prognostic Indicator and predicts EFS
Newer approaches

- FET or MISO PET scan
- F18 Bone scan done with high diag acc
- New tracers make it possible to study the tumor hypoxia/Angiogenesis/Gene therapy.
- PET will have excellent role in drug trials
Pancreatic Mass
Mass in Pancreas with FDG PET
Pancreatic Mass
Ca Pancres FLT PET study
54/F Metastatic Endometrial Ca
48 Male with Metastatic Ca Bl.
68 Yrs F with Mets NET
PET/CT or PET/MR: Clinical Benefits

Improved oncological diagnosis
- improved localization of disease
- assistance with biopsy guidance
- monitoring chemo- & radiation therapy
- radiation therapy planning
- faster PET scanning time

*JNM 2000 (8)*:
Conclusions

1. CT is may be first imaging test of choice.
2. PET - CT is more accurate than CT or MR alone
   • Characterizes lesions
   *difficult to biopsy
   • Detecting occult cancer.
   • Determining extent of cancer and response to therapy.
3. PET - CT changes management 36%
Why PET-CT?

- Metabolic information (molecular imaging)
- Safe, non-invasive procedure
- Single test for the entire body
- Earlier detection, Precise staging
- Monitoring response to chemo/radiotherapy
- Avoidance of surgery or less extensive surgery
- Lowering the overall cost of care
Does it change the management of my patient?
Why PET-CT?

CLOSE TO HOME

"Good news! The exploratory surgery turned up negative!"
PET-CT and RTP

CT has remained the cornerstone for assessing tumor volume (GTV) for RT.

However, positron emission tomography (PET) overlay on CT has shown to impact the gross target volume (GTV), decrease intraobserver variability, and change the treatment planning in a significant number of patients.

The utility of FDG PET to delineate metabolically viable tumor has found increasing application in the identification of appropriate tumor volumes for external beam radiotherapy.

Frequently, structural imaging is inadequate for this purpose as metabolic events precede changes to that of structural imaging.

*Molecular imaging is invaluable in such instances for accurate identification of tumor; it can also aid in the delineation of tumor volumes for therapy.
PET-CT and RT

- Several published data of PET/CT have shown alteration of the (primary tumor) GTV using PET data in RT plan.

- There has been decrease in 36% of patients by differentiating atelectasis and postobstructive pneumonia from tumor GTV in a significant number of Lung cancer.

- There has been increase in GTV in 27% of cases in detecting additional tumor burden using PET data in RT.
Benefits of incorporating PET data

- PET for target volume delineation. 18F-FDG PET may reduce the interobserver variability in gross tumor volume (GTV) deliniateion.
- Addition of PET data may reduce the size of the GTV, identify tumor areas or lymph nodes missed by CT or MRI, and identify parts of the GTV potentially requiring an additional radiation dose.
- As PET-CT upstages or downstages in many cancer by 24 to 30% PET data may be useful for better targeting of biological active tumor site.
Advantages of Using PET in RTP

- PET can reveal target not det by CT/MR these may be remote mets or additional tumor region seen by PET alone.
- PET may enable to better delineate and characterise sites that donot contain active tumor eg Reactive nodes or tumor volume nearby eg Lung atelect.
- Imaging of biological inhomogenity (sub volume of tumor) may offer possibility to adapt doses to local diff in Radio sensitivity (dose paint).
- PET may be helpful to evaluate residual mass post chemo eg Lymphoma segregating active vs fibrotic area besides identifying microscopic tumor vs macroscopic disease site.
The treatment of cancer with ionising radiation is called Radiotherapy (RT) or Radiation Oncology.

External RT ± Intensity Modulated Radiotherapy (IMRT)

Brachytherapy

Radiosurgery - Stereotactic RT

Particle therapy with Protons or light ions
The Evolution of Radiation Therapy

1960’s
The First Clinac

1970’s
Cerrobend Blocking
Electron Blocking

1980’s
Multileaf Collimator
MLC leads to 3D conformal therapy which allows the first dose escalation trials.

1990’s
Computerized 3D CT Treatment Planning
Dynamic MLC and IMRT

2000’s
High resolution IMRT

Standard Collimator
The linac reduced complications compared to Co60

Blocks were used to reduce the dose to normal tissues
Objectives of IGRT & Dynamic Targeting

CTV – volume containing disease
PTV – volume that needs to be irradiated to ensure CTV is always treated
Advances in Radiation Therapy - The Pyramid

- Current Period
- Early Period
- Precise localization
- Geographic miss
- GTV
- Normal Tissue
Advances in Radiation Therapy - The New Pyramid

Current Period

Early Period

Precise localization
Geographic miss

BTV

GTV

Normal Tissue
18 FLT PET for Oropharyngeal T3 M0N0 tumor
Figure 5a. Transaxial images in a 44-year-old man with history of nasopharyngeal carcinoma which was treated with radiation therapy.
Figure 5c. Transaxial images in a 44-year-old man with history of nasopharyngeal carcinoma which was treated with radiation therapy.
2000, which was treated with radiation therapy.

Figure S5. Transaxial images in a 44-year-old man with history of nasopharyngeal carcinoma in
Pt with Gr Iia HL PET showing additional paratracheal LN & CT negative.
18FLT PET for image guided high precision RTP in Oropharyngeal Ca
METABOLICALLY AIMED RADIOTHERAPY (MART)

CT BASED

PET/CT BASED

TREATMENT PLAN
METABOLICALLY AIMED RADIOTHERAPY MART
METABOLICALLY AIMED RADIOTHERAPY (MART)

PET GUIDED IMRT/TOMOTHERAPY

IMPROVED TUMOR/NON TUMOR RADIATION DOSE

HYPO-FRACTIONATION
30-40 → 5-10 fractions
Metachronous vs. Synchronous Acquisition

Image-Based Radiation Therapy Planning for Brain Tumors with F-18-Fluorethyltyrosine (FET) PET and MRI:

Potential Impact on Target Volume Delineation


1Nuclear Medicine, 2Radio-oncology, 3Radiodiagnostic, 4Oncology
Centre Hospitalier Universitaire Vaudois (CHUV), Lausanne, Switzerland.
**FDG PET** improved oncological management:

- Improved detection of disease localization
- Monitoring chemo- and radiation therapy
- D.D. recurrence/residual tumor or necrosis
- Assistance with biopsy guidance* and RTP.
Facilities available @ AMRI NM

- 64 slice PET-CT 690 scanner
- 4slice SPECT-CT
- Dedicated Therapy ward for
  - High dose therapy for Ca Thyroid
  - High dose therapy for Neuroblastomas and NET.
  - Microsphere therapy for HCC
  - Treatment of Metastatic bone disease.
  - Therapy of Arthritis using RS.
Thanks for your kind attention

- My Personal thanks for all participants and organizers of this wonderful conference.

- Please call me (09874477385) or mail me pratapdoc@gmail.com for sugg/feed

- Please visit www.nucpetmrc.com for additional information