Role of Functional Imaging in Sarcomas

Dr Winnie Lam
Senior Consultant, Department of Nuclear Medicine & PET
Adj Assistant Professor, Radiological Sciences Academic Clinical Programme
5 November 2016
What is Nuclear Medicine / Functional Imaging?

- Nuclear medicine is the medical specialty that uses the **tracer principle**, most often with **radiopharmaceuticals**, to evaluate molecular, metabolic, physiologic and pathologic conditions of the body for the purposes of **diagnosis**, **therapy** and **research**.
■ PET for Sarcoma Detection & Grading
■ PET in Staging and Restaging Sarcomas
■ Sentinel Lymph Node Biopsy / Lymphoscintigraphy in Sarcomas
■ PET in Correlation to Prognosis & Monitoring Response
■ PET-guided Biopsy within a Suspected Sarcoma
Imaging Techniques

- **Anatomical Imaging Modalities:**
  1. Radiographs (X-ray)
  2. Computed Tomography (CT)
  3. Magnetic Resonance (MR)

- Primary diagnostic modalities
- Exact location, size, local extent, bony destruction (biologic activity), intratumoral calcifications (phleboliths, amorphous calcification), proximity to neurovascular structures
- CT chest for lung metastases
Imaging Techniques

- **Functional Imaging Modalities:**
  1. Bone scan (gamma camera)
     - Incidence of bone metastasis is low
  2. Lymphoscintigraphy / Sentinel Lymph Node Imaging (gamma camera / SPECT-CT)
  3. Positron Emission Tomography (PET)
     - $^{18}$F-fluorodeoxyglucose (FDG) – glucose analog
     - Complementary information in diagnosis & treatment planning
PET for Sarcoma Detection & Grading

- Very sensitive (91%) & specific (85%) for detection of high-grade sarcoma*
- Low positive predictive value (PPV) for nodal metastases
- Standardized uptake value (SUV) – semi-quantitative measure of radioactivity (FDG metabolic activity)
- Higher SUV correlated with histologic findings of increased mitosis rate & cellularity (grade estimation)

PET in Staging and Restaging Sarcomas

- Soft tissue / bone sarcoma metastasis predominantly (75%) to the lung
- Mixoid / round cell liposarcomas - retroperitoneum
- Synovial sarcoma / rhabdomyosarcoma / clear cell sarcoma / epithelioid sarcoma - LN
- Many studies on FDG PET/CT in sarcomas compared with conventional imaging (MR, CT, bone scan, U/S, CXR)
PET in Staging and Restaging Sarcomas

- Multicentre, 46 paediatric patients
- Ewing, osteo/rhabdomyosarcoma staging
- PET was superior in assessing LN involvement & bone localizations
- CT more accurate for pulmonary metastasis

PET in Staging and Restaging Sarcomas

- 19 paediatric patients
- Suspected sarcoma recurrence
- PET was useful for correct interpretation of conventional imaging findings
- PET detected otherwise unknown metastasis in 2 patients

PET in Staging and Restaging Sarcomas

- Retrospective study, 89 patients
- High-grade bone & soft tissue sarcomas
- LN involvement
  - PPV 27%
- Distant metastasis
  - Sensitivity 95%
  - Specificity 95%
  - PPV 87%
  - NPV 98%

PET in Staging and Restaging Sarcomas
PET/CT in Staging Gastrointestinal Stromal Tumours (GIST)

- Combined FDG-PET/CT is superior to either modality alone
- PET/CT located 282 lesions in 20 patients
- CT alone identified 242 lesions
- PET alone identified 147 lesions

Sentinel Lymph Node Biopsy / Lymphoscintigraphy in Sarcomas

- Commonly used in breast ca & malignant melanoma
- Radiopharmaceutical : Tc-99m Sulfur Colloid
- Dose 0.2mCi and volume 0.1ml
- Sentinel LN : LNs that first receive lymphatic drainage from tumour
- Can have more than one sentinel lymph node
- Efficient tool to reduce postoperative long-term morbidity (lymphoedema) without compromising local control of disease
Sentinel Lymph Node Biopsy / Lymphoscintigraphy in Sarcomas
Sentinel Lymph Node Biopsy / Lymphoscintigraphy in Sarcomas
Lymphoscintigraphy plus SPECT-CT

ANTERIOR
Tc–99m SENTINEL LYMPH NODE
SLNB plus SPECT-CT vs FDG PET in Paediatric & Adolescent/Young Adult Sarcoma

- Prospective study, 28 patients
- Rhabdomyosarcoma, epithelioid sarcoma, synovial sarcoma, soft tissue Ewing’s sarcoma, fibrosarcoma, other soft tissue sarcomas
- Median of 2.4 sentinel nodes / patient
- SLNB identified tumour in 7/28 (25%), including 3 with normal PET/CT
- PET/CT demonstrated hypermetabolic LN in 14
  - Sensitivity 57%
  - Specificity 52%
  - PPV 29%
  - NPV 79%
- SLNB can safely guide rational selection of LN for biopsy
- **SLNB can identify therapy-changing nodal disease not appreciated with PET/CT**

PET and Prediction of Prognosis

• Significant association between FDG uptake & several pathologic markers:
  – Histopathological grade
  – Tumour cellularity
  – Proliferative activity (mitotic figure counts)
  – Overexpression of p53
  – Ki67 values in GIST

PET and Prediction of Prognosis

- 238 patients with FDG-PET before chemotherapy / surgical resection
- PET result compared with OS & DFS
- **SUVmax & FDG heterogeneous distribution** can distinguish between higher-risk patients & lower-risk patients

PET in Monitoring Response to Therapy

- Assessment of tumour response based on changes in tumour size is not particularly helpful in sarcomas.

PET in Monitoring Response to Therapy

- PET allows detection of tumour regression/progression before morphologic alterations on CT & MR
- Metabolic response precedes volumetric decrease of tumours
- PET findings can aid in decision making about maintaining/modifying therapy
- Reduction in FDG uptake of >35% from pretherapy value predictive of histologically assessed treatment response

PET in Monitoring Response to Therapy

- Study of early response in GISTs
- FDG-PET able to differentiate metabolic responders (11) from metabolic nonresponders (4) after 1 week of imatinib treatment compared with clinical & radiologic response according to RECIST
- Mean SUVmax decreased in responders (65%), increased in nonresponders
- FDG-PET also correlated with clinical disease course (PFS)
- No significant difference in FDG uptake between scans 1 & 8 weeks after treatment initiation
- FDG response to imatinib is genuinely an early response

PET in Monitoring Response to Therapy

- Case story of significant reduction in SUVmax (from 13 to 4) **24 hours** after a single dose of imatinib (400 mg)

- Comparison with morphologic therapy assessment
- SUVmean decrease of 60% on day 8 of imatinib
- Partial response according to RECIST after 23 weeks


PET in Monitoring Response to Therapy

PET in Monitoring Response to Therapy

- Progression / secondary resistance to imatinib as re-emergence of FDG uptake
- Suggest more complex interrelation with heterogeneous intratumoral & intertumoral clonal dedifferentiation:
  - After cessation of imatinib, flares of FDG uptake observed in lesions that were metabolically inactive during therapy
  - Some lesions may still be responsive to initial treatment, whereas some clones progress to resistance
- This may provide basis for combination therapy for different TKIs, like imatinib & sunitinib, instead of traditional complete switch in therapy
- Literature favours use of FDG-PET as primary method for treatment assessment in GISTs

PET in Monitoring Response to Therapy

- Clinical trial of novel IGF1R antibody in Ewing sarcoma
- PET was superior to anatomic imaging in identification of response
- Early signal with FDG-PET on day 9 was the best predictor of benefit (OS)

PET in Monitoring Response to Therapy

- Source of misinterpretation:
  - Infectious/inflammatory diseases
  - Postsurgical change
  - Postradiotherapy inflammation
PET/CT in Biopsy

- PET/CT-guided biopsy combines anatomic information from CT with PET metabolic characterization
- Large malignant lesions can be heterogeneous
- FDG PET/CT to guide biopsy of highest metabolic activity, reducing probability of tumour grade underestimation & consequential inappropriate approach
- PET-guided biopsy enables evaluation of lesions with exclusively FDG uptake without corresponding anatomic findings on CT
- When biopsy results are inconclusive / inconsistent with clinical & radiologic pictures, patient may benefit from PET-guided second biopsy
PET/CT in Biopsy

- Histology of biopsy site of 8 malignant lesions (as suggested by FDG-PET) showed the most pleiomorphism & highest mitotic index within the sarcoma

Pitfalls

- Benign skeletal lesions with intense FDG uptake:
  - Osteochondromas
  - Giant cell tumours
  - Chondroblastomas
  - Langerhans cell histiocytosis
  - Desmoid tumours
  - Fibrous dysplasia
What the Referring Clinician Needs to Know

1. **FDG PET** provides **metabolic** information about primary tumour (T) but its main advantage is evaluation of LN involvement (N), distant metastasis (M), and local relapse.

2. PET/CT does not provide anatomic details, so cannot be used to evaluate local infiltration.

3. **Sentinel Lymph Node Biopsy** can guide rational selection of LNs for biopsy in sarcoma patients & identify therapy-changing nodal disease not appreciated with PET/CT.

4. SUVmax before therapy is **prognostic** & useful for **therapy assessment** as compared with posttherapy SUVmax.

5. After radiotherapy, some false positives may occur because of RT-related inflammation (reduces with time after RT).

6. PET has lower sensitivity than CT in detecting lung metastases (CT can be acquired on PET/CT tomographs).

7. Some benign diseases especially in the bone can be hypermetabolic (false positive).