

IMPACT OF FDG PET/CT STUDIES ON NON CNS PEADIATRIC MALIGNANCIES

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Topics covered

Lymphomas including Burkitts

Pediatric solid tumors (non CNS)

- Musculoskeletal – Ewings & osteosarcoma.
- Neuroblastomas
- Nasopharyngeal carcinomas
- Liver tumors
- Wilms tumor

Lymphoma

STAGING

- ◎ Sensitivity > 80% and specificity ~ 90%
- ◎ 15 – 20% patients show additional sites of disease
- ◎ Extranodal disease – better sensitivity.

NCCN guidelines recommend use of PET for staging when available.

International Harmonization Project guidelines for baseline:

- Baseline scan not mandatory for HL and DLBCL and other FDG avid NHL. But can be used for staging when CT equivocal
- If FDG uptake of the type of lymphoma is doubtful, baseline scan would be useful if plan to utilize for treatment response assessment.

Literature –staging lymphoma

¹⁸F]FDG in childhood lymphoma: clinical utility and impact on management
European Journal of Nuclear Medicine and molecular Imaging
Vol 29 (2002), No 9

42 studies.

Staging, restaging and treatment response.

FDG PET altered the management of 23% of patients.

Impact of PET-CT on involved field radiotherapy design for pediatric Hodgkin lymphoma

Pediatric blood cancer

August 2011

53 patients underwent staging with conventional imaging and PET/CT .

19/53 patients had discordant findings, with 23 sites of discordance.

Change in stage 5 /53 PET-CT findings(9.4%) : 3 upstaged and 2 downstaged.

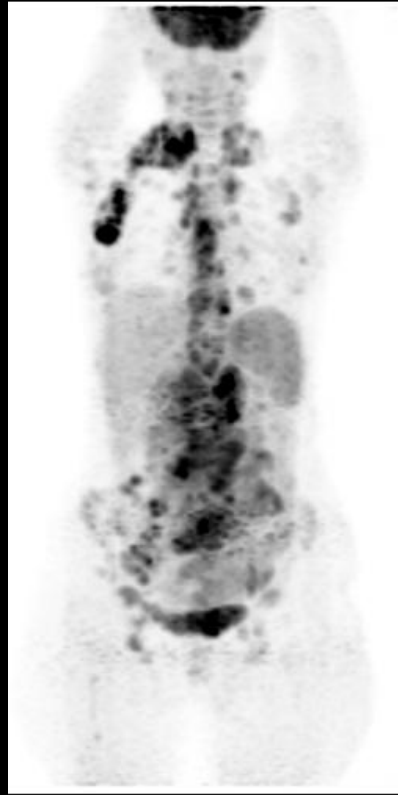
Change in the radiotherapy field in 9/53 patients(17.0%)

(eight patients the radiotherapy fields were more extensive while in 1 it was less extensive.)

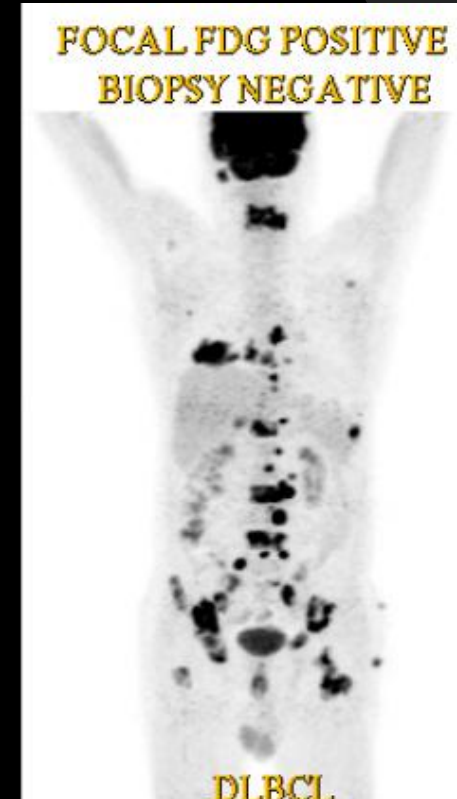
STAGING



Left neck node –
clinically negative



Splenic involvement



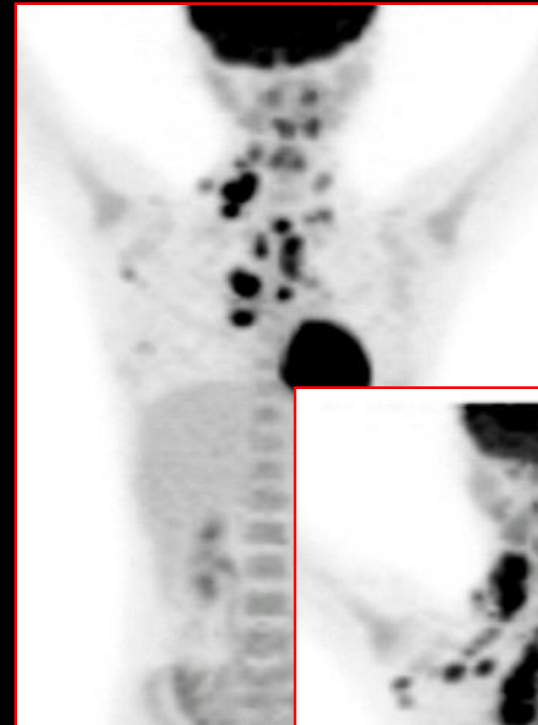
Focal marrow lesion
Marrow biopsy negative

Treatment response

- ◎ Identify non responders at end of treatment
- ◎ Interim PET – no significant fall in uptake suggest poor DFS. Bad prognosis

COULD BE INCLUDED AS A PROGNOSTIC MARKER

Treatment response



COMPLETE RESPONSE

PROGRESSION

Literature – treatment response

Early and Late Therapy Response Assessment With [^{18}F]Fluorodeoxyglucose Positron Emission Tomography in Pediatric Hodgkin's Lymphoma: Analysis of a Prospective Multicenter Trial

JCO September 10, 2009 vol. 27 no. 26 4385-4391

- ⊙ Multi centric trial - 40 patients.
- ⊙ Baseline (PET 1), early (PET2) and late (PET3) response assessment.
 - PET was superior to CIMs with regard to specificity in early and late therapy response assessment (68% v 3%, and 78% v 11%, respectively)
 - Cut off 58% reduction – higher specificity

Early FDG PET/CT in predicting final therapy outcome in pediatric lymphoma
J Nucl Med.

2009; 50 (Supplement 2):51

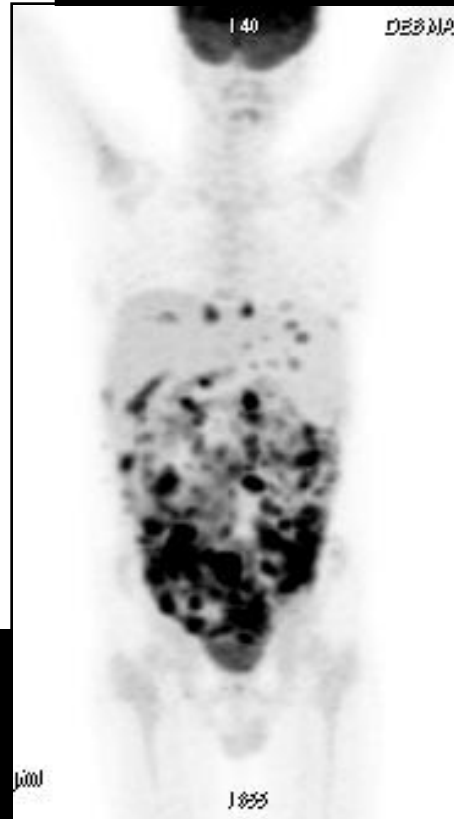
Early FDG PET/CT after 2 cycles

Accurately predict the final treatment response in pediatric lymphoma and may be crucial to for planning risk adapted treatment strategy

Burkitt's lymphoma

- ◎ Highest evidence -Treatment response assessment
- ◎ Treatment response – residual disease
- ◎ Advocate : Management changes – interim study!

Treatment response



PARTIAL RESPONSE

COMPLETE RESPONSE

Lymphoma - follow up

- ◎ **Not** a indication for **routine surveillance**.
- ◎ Symptomatic or clinical suspicion.

Definitions of the appropriateness criteria for the utility of PET

<i>Relevance of Test</i>	<i>Description</i>
Appropriate	◦ evidence of improved diagnostic performance (higher sensitivity and specificity) compared with other current techniques ◦ the information derived from the PET scan influences clinical practice ◦ the information from PET has a plausible impact on the patient's outcome, either through adoption of effective practice or non adoption of ineffective or harmful practice
Probably Appropriate	evidence of improved diagnostic performance (higher sensitivity and specificity) compared with other current techniques, but lacking evidence for an impact on treatment and outcome
Potentially Appropriate	Insufficient evidence available for assessment, although there is a strong rationale for a benefit of PET.
Inappropriate	Clinical situations for which improved accuracy of stage will not alter management, or for which the performance of PET is inferior to other current techniques.

Summarize - lymphoma

Appropriateness criteria for PET

- ◎ Staging – appropriate
- ◎ Treatment response – appropriate
- ◎ Interim treatment response – probably appropriate.
- ◎ Follow up - inappropriate

Solid non CNS tumors

Few systematic studies with subtype evaluation available.
Majority are retrospective analysis

18F-FDG PET/CT in Evaluating Non-CNS Pediatric Malignancies

J Nucl Med

Volume 48: 1923–1931/2007

Retrospective review

n – 55, 151 scans.

Diagnostic accuracy of PET/CT was 90% as compared to CI.

Additional information was available in 1/3rd (approx 34%) patient population.

True negative in post treatment scenario as compared to false positive with CI.

Literaturecontd

Early experience with PET/CT scan in the evaluation of pediatric abdominal neoplasms

Journal of Pediatric surgery

Volume 43, 2186–2192/ December (2008)

Retrospective analysis

n – 36

FDG positive in all tumors pre treatment scans,

Describes utility in staging, site for biopsy, locating distant metastases, treatment response and follow up for recurrence.

Diagnostic value of PET/CT for the staging and restaging of pediatric tumors

European Journal of Nuclear Medicine and Molecular Imaging

Volume 36, Number 1 / January, 2009

Retrospective analysis

n – 43

High sensitivity of PET/CT for distant metastases, specificity greater if pulmonary met > 0.5 cms and lymphnode size < 1 cms as compared to CT.

Musculoskeletal malignancies

STAGING

- ⊙ Useful in N and M staging.
- ⊙ Specificity of identifying skeletal metastases is the highest with FDG PET/CT Vs CI
- ⊙ Sensitivity for pulmonary lesions $> 5\text{mm}$ is similar to CT, however reduced for smaller nodules.
- ⊙ Sensitivity and specificity for nodal disease or soft tissue metastases and rare sites with skeletal disease but common in soft tissue sarcomas is HIGH.

TREATMENT RESPONSE

- ⊙ Early data suggests responders to NACT/induction therapy have a better prognosis.
- ⊙ Non responders could be deferred from morbid surgeries, especially with disease in the axial region.

FOLLOW UP AND RESTAGING

- ⊙ No role in surveillance
- ⊙ Good sensitivity for identifying recurrence in skeletal disease;
Not enough evidence for utility in this setting in soft tissue sarcomas.

Ewings group of tumors

Useful in nodal and metastatic staging – N & M

Impact of FDG PET for staging of Ewing sarcomas and primitive neuroectodermal tumours.

Nucl Med Commun.

2006 Jan;27(1):17-24.

PET is superior to bone scintigraphy in the detection of bone metastases .
Lower sensitivity for small pulmonary lesions as compared to helical CT.

Positron emission tomography for staging of pediatric sarcoma patients: results of a prospective multicenter trial

J Clin Oncol

2007;25(34):5435–5441

The superiority of FDG PET to bone scintigraphy in detecting osseous metastases was significant (sensitivity, 88% vs 37%).

Nodal metastases were also identified better, local imaging may not include the nodal regions.

TMH study – staging of Ewings with FDG PET/CT Vs

Bone scan (analyzed, unpublished)

n - 45

	Concordance	Discordance
Primary	100%	-
Osseous metastases	3/45 (6%)	7 (additional sites identified on FDG PET/CT)*

- FDG identified 10 metastatic skeletal lesions (22%).
- 85% (6/7) of the additional metastatic lesions detected on PET/CT were marrow lesions.

TMH study: Comparison CI Vs PET/CT

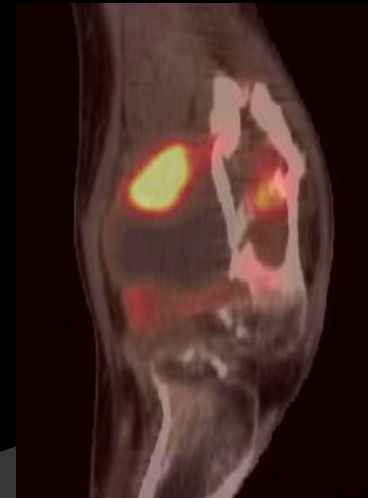
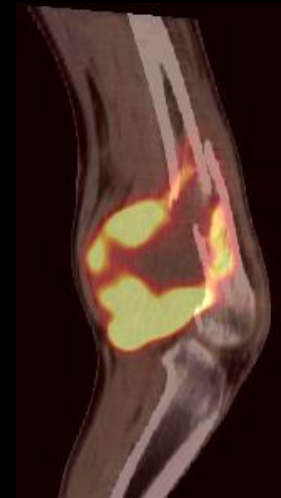
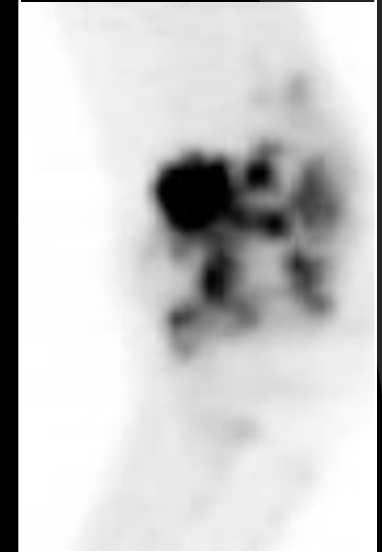
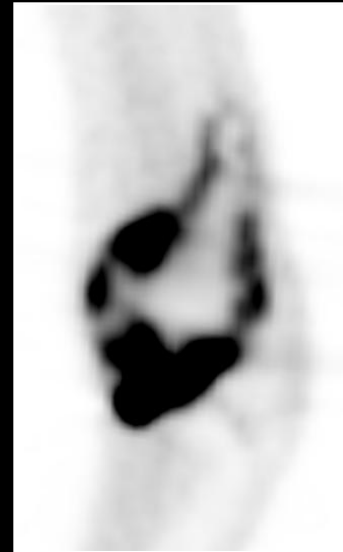
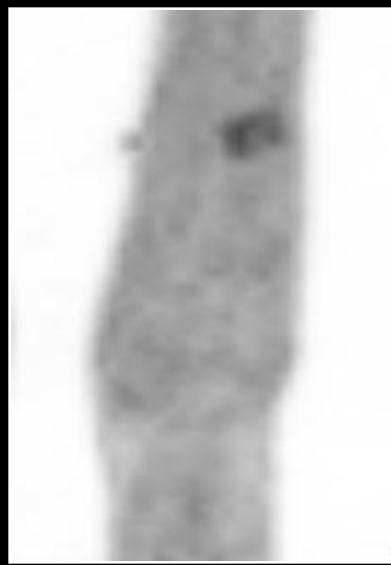
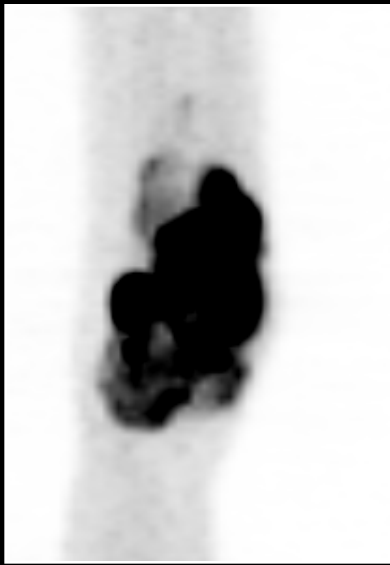
	CWP	FDG PET/CT
Primary	45	45
Osseous mets	3/45(6%)	10/45(22%)
Pulmonary mets	12 lesions	12 lesions
Nodal mets	0	4

Extra-skeletal metastases were identified in 35% (16/45) patients
8/45 – Only skeletal metastases (17%)
07/16 - Both skeletal and non skeletal metastases. (46%)

Osteosarcoma

- ◎ Useful in staging – N and M.
- ◎ Skip lesions identified.
- ◎ Certain studies have shown utility in grading the tumor.
- ◎ Utility in treatment response assessment. Studies have shown response to NACT correlate with histological response.
- ◎ Good responders – better DFS and survival.
- ◎ Trials ongoing – management changes based on PET/CT

Treatment response



Responder

Non responder

Summarize - MSK

- ◎ Staging – appropriate
- ◎ Treatment response (post induction)-
probably appropriate
- ◎ Recurrence – appropriate
- ◎ Follow up - inappropriate

Neuroblastoma

- ◎ Useful in staging.
- ◎ Studies show concordant results with MIBG
- ◎ Subtle marrow lesions – upper edge.
- ◎ Recurrent setting – good sensitivity
- ◎ Treatment response – evidence lacking.

Evidence for NB

Neuroblastoma: positron emission tomography with 2-[fluorine-18]-fluoro-2-deoxy-D-glucose compared with metaiodobenzylguanidine scintigraphy.

Radiology :

Volume 199/3: 743/ 1996

n - 17

FDG positivity in 16,

Increased uptake prior to therapy and reduced after Rx.

Useful in non MIBG concentrating tumors.

Extending Positron Emission Tomography Scan Utility to High-Risk Neuroblastoma: Fluorine-18 Fluorodeoxyglucose Positron Emission Tomography as Sole Imaging Modality in Follow-Up of Patients

J Clin Oncol

Volume 19 (14):3397-3405/ 2001

Retrospective analysis

n – 51

FDG PET was compared with conventional imaging, minimal test required identified.

A FDG PET and BM would be accurate in staging 97.5% of the patient population.

Better modality for soft tissue and extra cranial skeletal structure delineation.

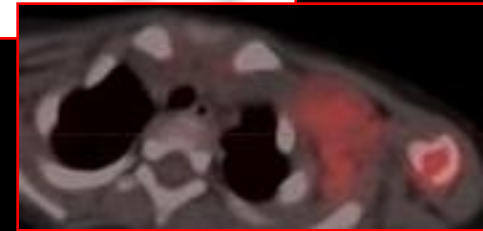
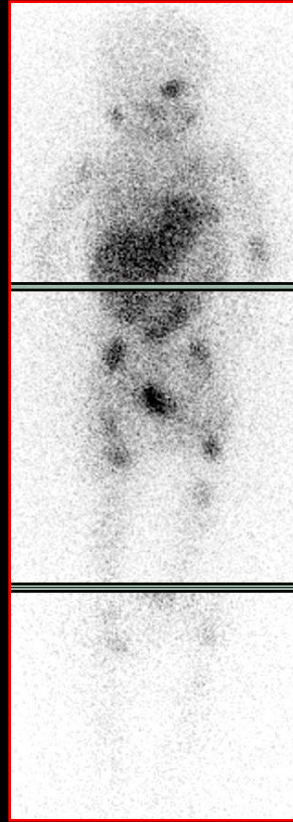
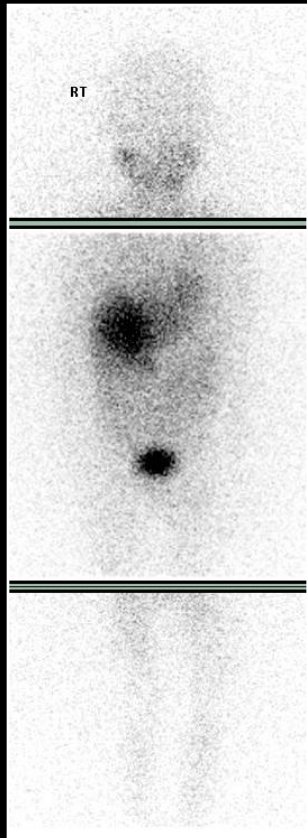
TMH data (analyzed, unpublished)

◎ n – 85

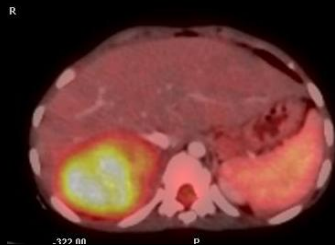
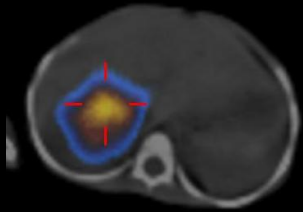
Indication	Concordance	Discordance	superiority
Staging	50% (12/24)	50%(12/24)	FDG
Restaging	11% (1/9)	91%(8/9)	FDG
Rx response	65% (26/40)	35%(14/40)	12.5%FDG
			22.5% MIBG
Follow up	100% 12/12		EQUAL

MIBG superior for assessing viability of mass lesion.

STAGING



Left axillary & pleural

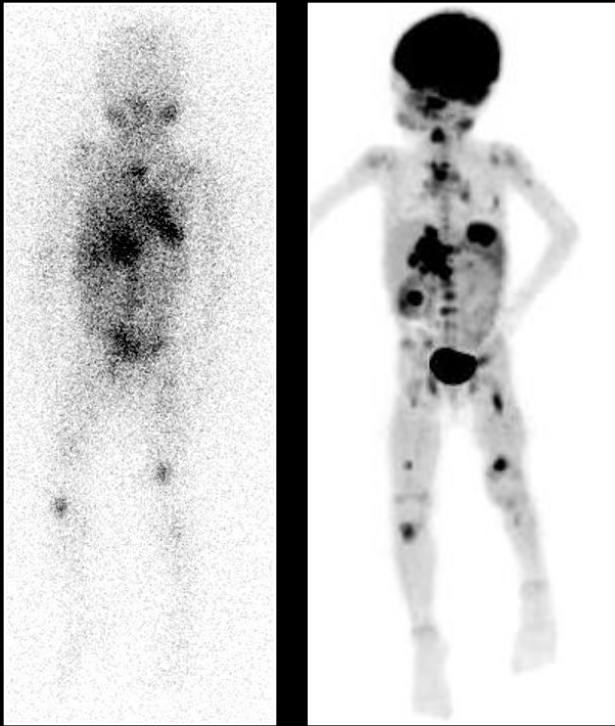


CONCORDANCE

DISCORDANCE

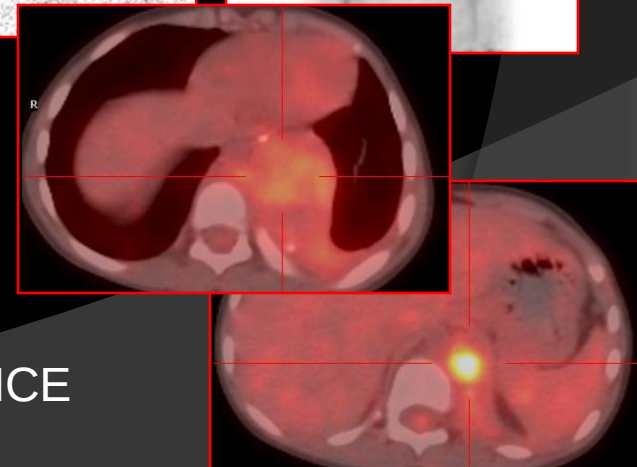
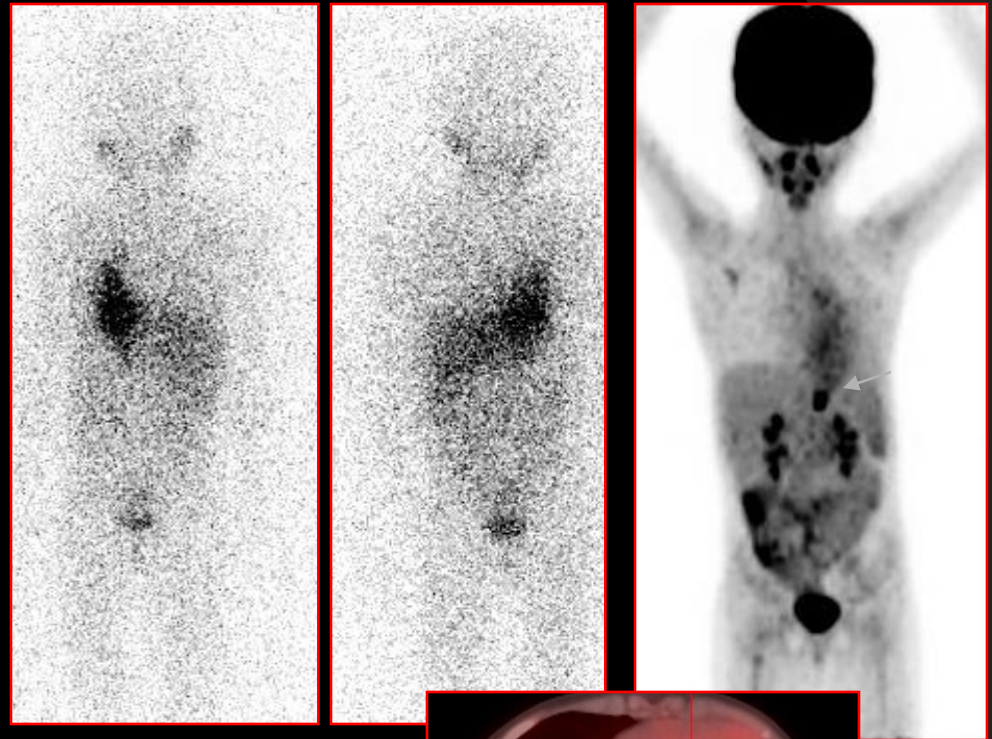


RESTAGING



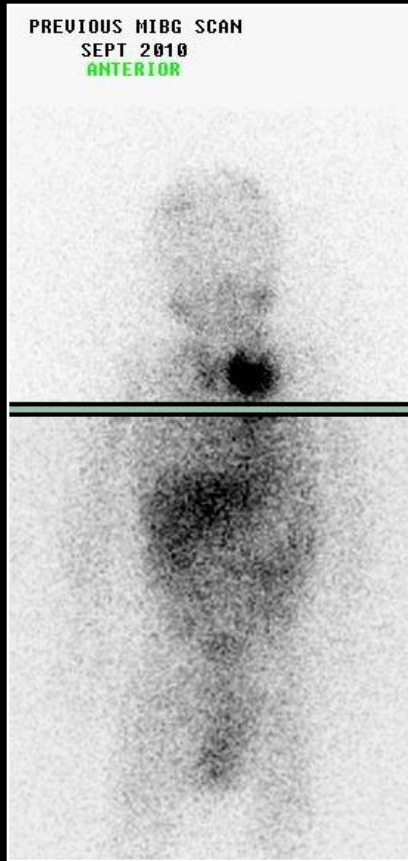
Rt suprarrenal recurrence
Marrow lesions
Left pulmonary lesion.

CONCORDANCE

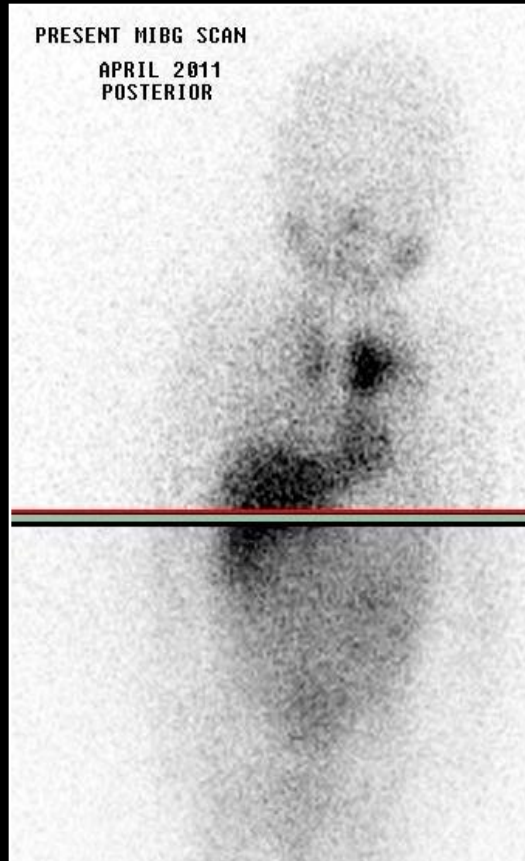


DISCORDANCE

Treatment response

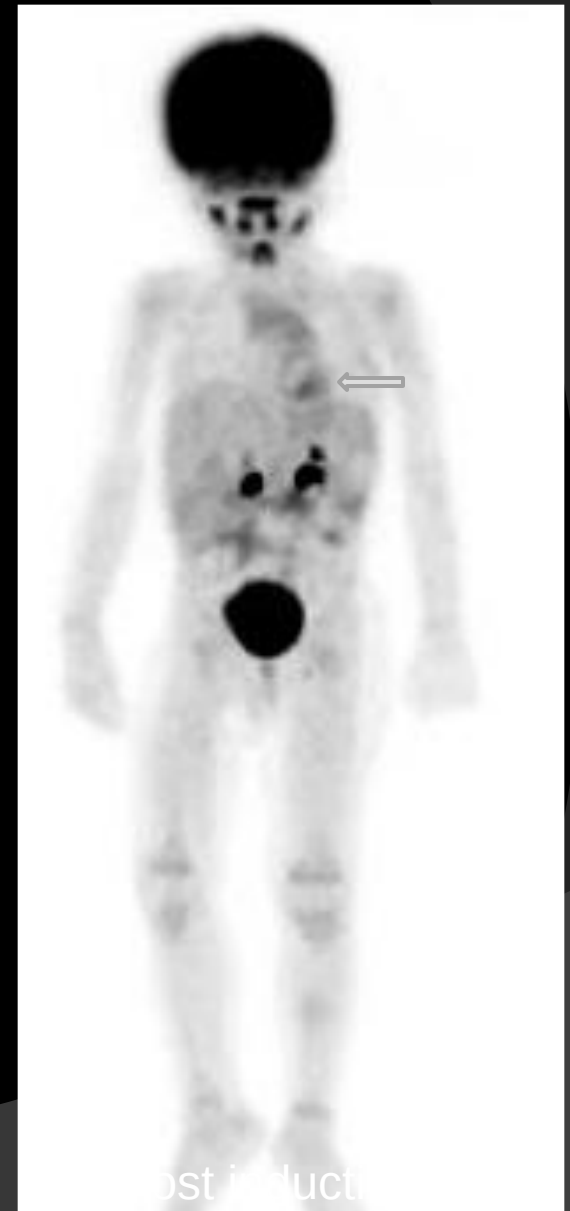


Pretreatment



Post induction - MIBG

Low FDG uptake suggestive of reducing metabolism
MIBG concentration suggests viable tumor
NEEDS VALIDATION



Summarize - Neuroblastoma

- ◎ Staging – probably appropriate
- ◎ Treatment response – potentially appropriate
- ◎ Recurrence – probably appropriate
- ◎ Follow up – not enough data

Nasopharyngeal carcinoma

- ◎ Malignancy occurring predominantly in adolescence
- ◎ Aggressive tumor, high propensity for spread.
- ◎ Useful in N and M staging.

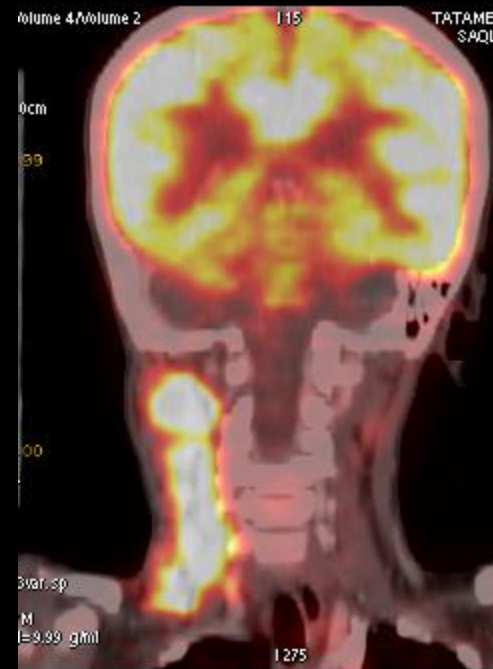
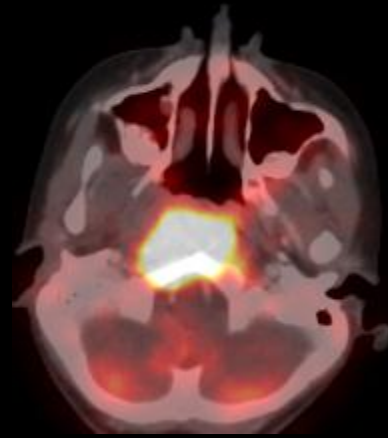
The utility of PET/CT in staging and assessment of treatment response of nasopharyngeal cancer.

J Med Imaging Radiation Oncol
2011 Apr;55(2):199-205

Valuable staging tool for the detection of occult metastatic disease and defining the extent of neck nodal disease.

Role of 18F-FDG PET/CT in diagnosis and staging of nasopharyngeal carcinoma
Ai Zheng 2008 Sep;27(9):974-8

68 patients
evaluated with MRI and PET/CT
superiority of PET/CECT for nodal staging and occult disease.



Primary tumor
Neck nodal disease - extent

Treatment response and restaging

- ◎ Sensitivity high in assessing local disease and nodal metastases.

The utility of PET/CT in staging and assessment of treatment response of nasopharyngeal cancer

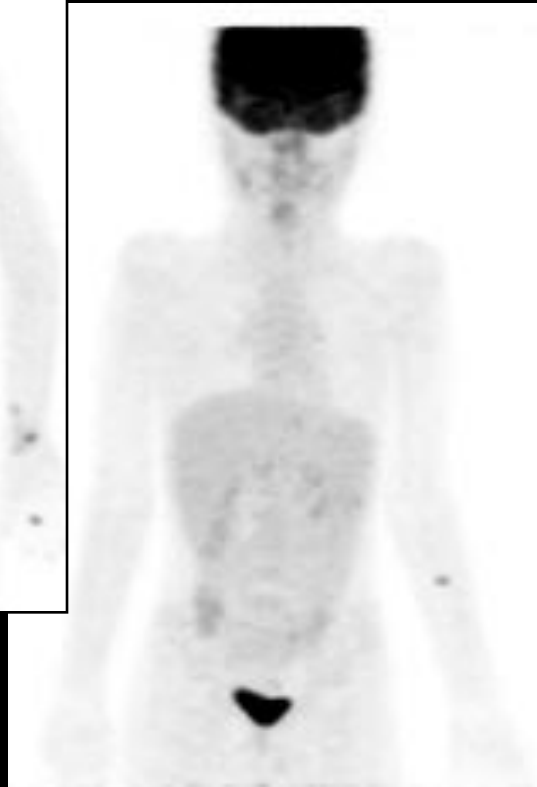
J Med Imaging Radiation Oncol

2011 Apr;55(2):199-205

Post-treatment, a complete metabolic response on PET/CT has a very high negative predictive value with fewer equivocal results than MRI.

Early assessment – false positives high

Infective changes and radiation osteonecrosis – difficult to differentiate.



Treatment response – CR

Summarize – Nasopharyngeal carcinoma

- ◎ Staging – probably appropriate
- ◎ Treatment response - probably appropriate
- ◎ Follow up – potential appropriate
- ◎ Recurrence - probably appropriate

Evidence in Wilms Tumors

Use of positron emission tomography for staging, preoperative response assessment and post therapeutic evaluation in children with Wilms tumour.

Eur J Nucl Med Mol Imaging.

Volume 35/9:1642-50/ Sept 2008

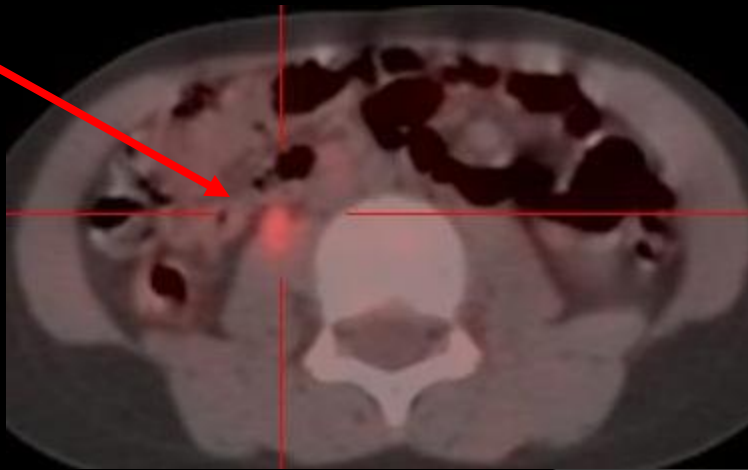
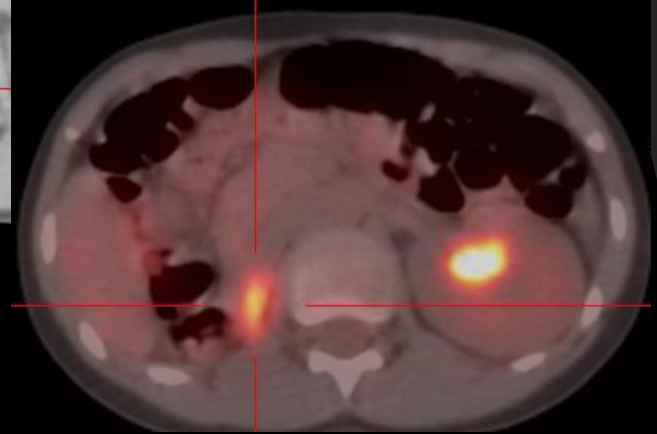
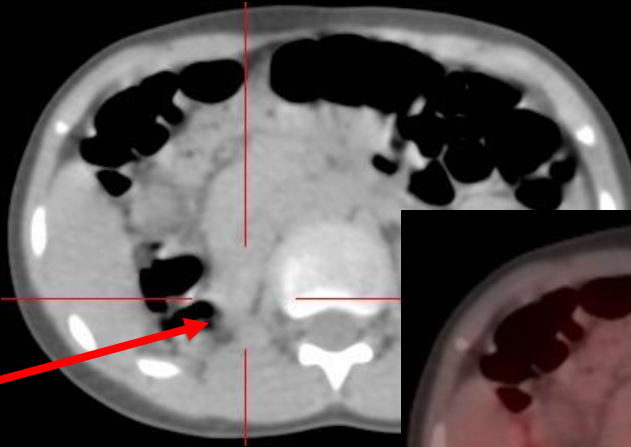
n – 12

FDG PET was concurrent for primary tumor staging.

PET was superior for tumor recurrence or residual disease evaluation.

An initial study evaluated 3 patients who showed concentration of FDG in all patients and showed an impact in management by detecting recurrence

And a case report mentions uptake in metastatic sites.



Recurrence of Wilms tumor

FDG PET in Hepatic malignancies

FDG PET for the Study of Primary Hepatic Malignancies in Children

Pediatr Blood Cancer

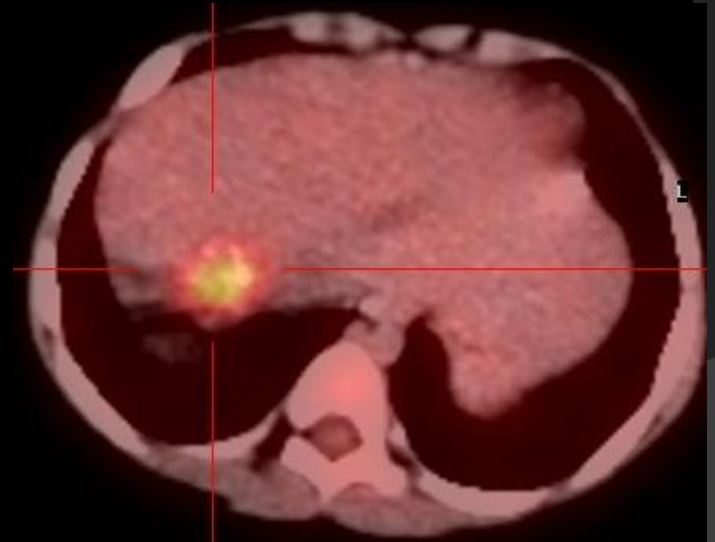
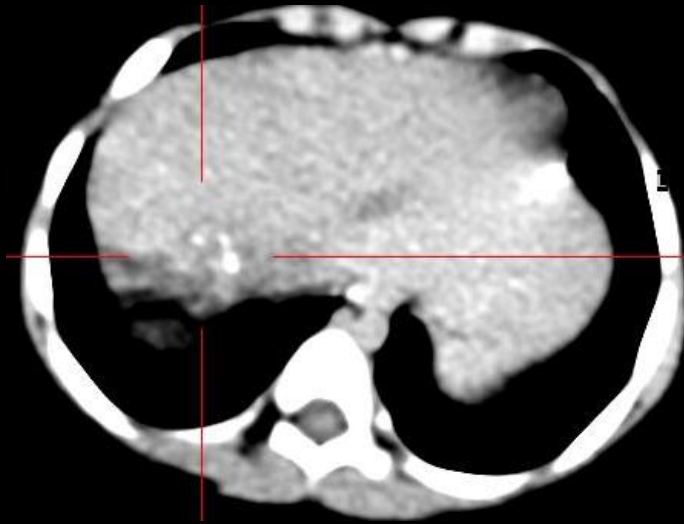
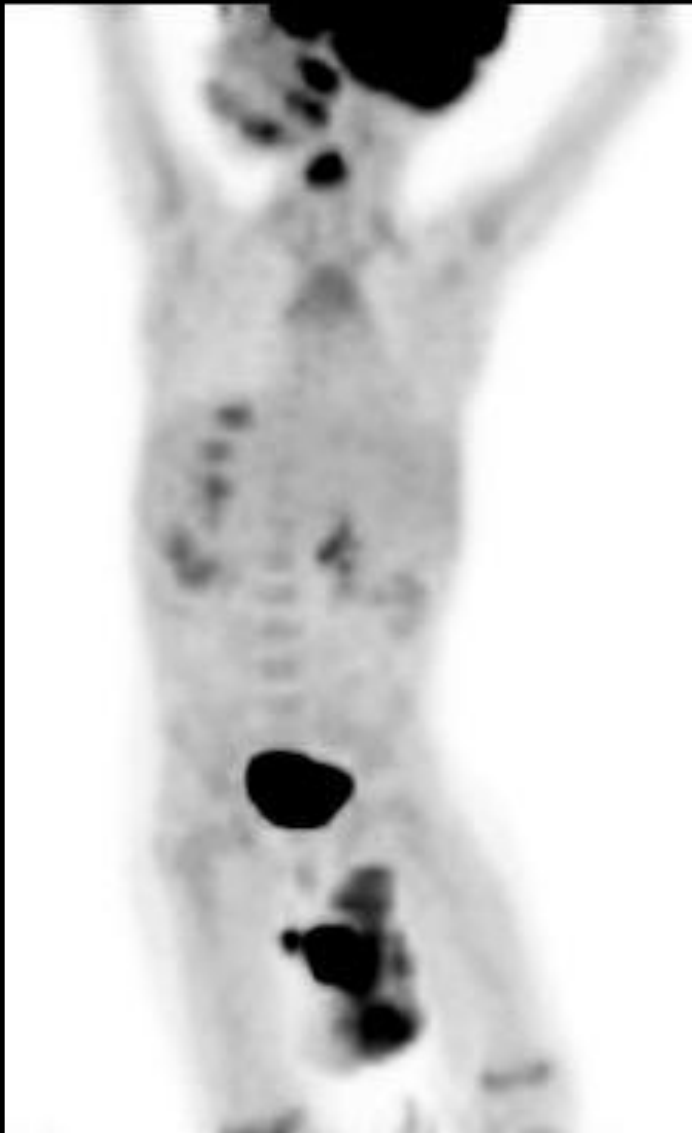
Volume 47:51–55/ 2006;

Retrospective study,

n – 7

Positive in all recurrent disease and in infection.

In a study of 3 patients, PET localized recurrent disease while the CI were negative
Another case report also reveals a similar finding.



Post operative site infection – false positive.

Summarize – Wilms & Hepatic

- ◎ Not enough data for assessing the impact.

Definitions of the appropriateness criteria for the utility of PET

<i>Relevance of Test</i>	<i>Description</i>
Appropriate	◦ evidence of improved diagnostic performance (higher sensitivity and specificity) compared with other current techniques ◦ the information derived from the PET scan influences clinical practice ◦ the information from PET has a plausible impact on the patient's outcome, either through adoption of effective practice or non adoption of ineffective or harmful practice
Probably Appropriate	evidence of improved diagnostic performance (higher sensitivity and specificity) compared with other current techniques, but lacking evidence for an impact on treatment and outcome
Potentially Appropriate	Insufficient evidence available for assessment, although there is a strong rationale for a benefit of PET.
Inappropriate	Clinical situations for which improved accuracy of stage will not alter management, or for which the performance of PET is inferior to other current techniques.

Summarize

Appropriateness criteria	Disease	Indication
Appropriate	lymphoma	staging, treatment response, recurrence
	MSK	N& M staging
	Neuroblastoma	N & M Staging
Probably appropriate	Lymphoma	Interim response
	MSK	Post induction treatment response Recurrence
	Neuroblastoma	recurrence
Potentially appropriate	Neuroblastoma	Treatment response
Inappropriate	Lymphoma, MSK	Follow up/surveillance