F-18 FDG PET/CT and C-11 Methionine Studies in Pediatric and Young Adult Patients

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Memphis, TN
Conflicts of Interest

• Completeness
• Full disclosure
• Transparency
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Caveat lector

a Latin phrase meaning "Let the reader beware"
(in this case, let the listener beware)
Objectives

• 1. Discuss the use of FDG PET/ CT in the pediatric oncologic population.
• 2. Describe the use of C-11 Methionine in brain tumors.
• 3. Evaluate how the experience with C-11 Methionine can be translated to the adult population
Conclusions

• FDG PET CT is used widely in pediatric oncology
• C-11 methionine is the single best imaging agent for brain tumors in children and young adults
• We should try to make C-11 methionine more widely available for both children and adults
Audience Options
Audience Options

• Walter Durham Lecture: Interventions and Clinical Skills: Assessment, Stress, and ACLS.
• Janice Preslar, CNMT
Audience Options

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- Janice Preslar, CNMT
- NCAA men’s basketball tournament
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10 Florida Gators at 2 Michigan Wolverines
NCAA Tournament - Second Round
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NCAA men's basketball · Today, 4:15 PM

10 Florida Gators at 2 Michigan Wolverines

NCAA Tournament - Second Round
SJCRH- The Concept- A Chance Encounter

• 1938 – Morocco Club in Detroit
• 2nd or 3rd day of 7th week of 8 week run
  • Business bad
  • Expected club to close
  • Sat at bar after performance
SJCRH- The Concept

• A drunk customer “kept drooling out the words “St. Jude Thaddeus””
• Customer’s wife was in hospital with terminal cancer of uterus
• Prayed to St. Jude Thaddeus, the patron of hopeless cases
• Entire tumor passes from her body
• Customer’s bargain with St. Jude was that “if he answered my prayers, I would tell everyone I could about the forgotten saint.”
SJCRH- The Concept

• The next day DT went to the Church of Saints Peter and Paul and prayed to St. Jude.

• “Help me to find my way in life, and I’ll build you a shrine”

• Club closed, back to Toledo for a short vacation, but something kept saying to him “Chicago...Chicago...Chicago”
SJCRH- The Concept

- 1942 – DT doing well as a nightclub performer, and had opportunity to buy into the business
- Went to church – noticed a pamphlet about St. Jude, and that there was already a shrine in Chicago
- Prayed again to St. Jude to show him the way: declined the nightclub offer
SJCRH- The Concept

• About 10 years later, Abe Lastfogel, DT’s coach, agent, promoter prompted him to do something about the vow to St. Jude
• Went to see Cardinal Stritch in Chicago who he knew from Toledo
• DT said “How about a hospital”
• Somewhere in the south, near a medical center
SJCRH- The Concept

• Cardinal Stritch said to take a look at Memphis, home of his first parish.
• Referred him to Ed Barry, prominent Memphis businessman, owner of baseball team and park
• Barry supported but others skeptical until Dr. Diggs of UT said “What we really need here is a research hospital for catastrophic children’s diseases – especially leukemia, and in black children, sickle cell anemia.”
SJCRH- The Concept

• Completed and dedicated Feb 4, 1962
• 9000 attendees
• “It took a rabble-rousing, hook nosed comedian to get your attention, but it took your hearts, loving minds, and generous souls to make it come true. If I were to die this moment, I’d know why I was born.”
Danny Thomas Pavilion

• "He who denies his heritage has no heritage."

• "No child should die in the dawn of life."

• "Those who work for the good are as those who do the good."
Practice Question – not for CME

• The Founder of St. Jude Children’s Research Hospital was
  A. Danny Thomas
  B. Danny Williams
  C. Amos Jacobs
  D. Elvis Presley
  E. Elvis Costello
  F. Abbott and Costello
Practice Question – not for CME

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   A. Danny Thomas  
   B. Danny Williams  
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   E. Elvis Costello  
   F. Abbott and Costello
Practice Question – not for CME

• St. Jude Children’s Research Hospital is located close to which one of the following river systems (single best answer)
  A. Trinity
  B. Brazos
  C. Canadian
  D. Guadalupe
  E. Mississippi
Practice Question – not for CME

- St. Jude Children’s Research Hospital is located close to which one of the following river systems (single best answer)
  A. Trinity
  B. Brazos
  C. Canadian
  D. Guadalupe
  
  **E. Mississippi**
FDG Imaging

- Excellent for most tumor types
  - Lung
  - Breast
  - Colon
  - Melanoma
FDG Imaging

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  - Lung
  - Breast
  - Colon
  - Melanoma

F-18 FDG
- The radiotracer: F-18
- The radiopharmaceutical: 2-deoxy-2[18F]fluoro-D-glucose
- The process: principally glucose transport
- ~ 2 hour half life
- Commercially available
Caveats from doing this for 30 years

• Pawn Stars

I'm Rick Harrison, and this is my pawn shop. I work here with my old man and my son, "Big Hoss." Everything in here has a story and a price. One thing I've learned after 21 years - you never know what is gonna come through that door.
Childhood Cancer is Uncommon

- In patients <20 y/o, ~ 16,400 new patients yearly
  - 12,000 0-14 y/o
  - 4,400 15-19 y/o
Distribution of specific cancer diagnoses for children (0 to 14 years) and adolescents (15 to 19 years), 1973 to 2010. Percent distribution by International Classification of Childhood Cancer diagnostic groups and subgroups for younger than 15 years and 15 to 19 years of age (all races and both sexes). ALL, acute lymphoblastic leukemia; CNS, central nervous system; RMS, rhabdomyosarcoma; STS, soft tissue sarcoma. (Incidence data are from the Surveillance, Epidemiology, and End Results [SEER] program, National Cancer Institute.)
Principal Tumor Types for FDG PET/CT in Pediatric and Young Adult Oncology

• Most, although uptake of FDG variable and often heterogeneous
  • **Lymphoma** - leukemia: HL and NHL
    • Chloromas (AML)
  • **Sarcomas**: OS, EWS, RMS, etc
  • NBL
  • Wilms and other renal tumors
  • HBL
  • DSRCT
  • CNS
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• NBL
• Wilms and other renal tumors
• HBL
• DSRCT
• CNS

HINT: Underlined words may represent Answers to questions that follow
How Many Pediatric Lymphomas and Sarcomas Are There?
Lymphomas

• Hodgkin lymphoma
  • ~8000 per year USA total
  • ~1200 peds

• NHL
  • ~74000 per year
  • ~1100 peds
    • Indolent rare

Sarcomas

• Osteosarcoma
  • ~800 to 900 per year USA total
  • ~500 peds

• ESFT
  • ~200 per year almost all peds and young adults

• Rhabdomyosarcoma
  • 400 to 500 per year
  • Great majority in peds

• NRSTS non rhabdo soft tissue sarcomas
  • 12,750
  • ~700 peds
CME QUESTION 1

In which one of the following pediatric tumors is 18F-FDG PET/CT most commonly performed?

1. Neuroblastoma
2. Hodgkin lymphoma
3. Craniopharyngioma
4. Hematogenous myolipofibrous carcinoma
5. Papillary thyroid carcinoma
CME QUESTION 1

- For which one of the following pediatric tumors is 18F-FDG PET/CT most commonly used for staging and restaging.
  1. Neuroblastoma
  2. Hodgkin lymphoma
  3. Craniopharyngioma
  4. Hematogenous myolipofibrous carcinoma
  5. Papillary thyroid carcinoma

Where/when FDG PET may be useful in Pediatric Oncology

- Malignant vs Benign?
  - Where is the best site to biopsy?
- Staging
- Restaging – details may vary per tumor type
  - Early response to therapy/ risk stratification
  - Residual disease vs scar following therapy: restaging
  - Monitoring for recurrent disease
When Do Patients Undergo FDG PET CT

• Depends on the disease, risk classification, and the protocol
• For example Hodgkin lymphoma
  • Pretreatment
  • Early response (8 weeks, 2 courses of chemotherapy)
  • Off therapy if positive at 8 weeks
  • Further off therapy scans only if there is clinical suspicion for relapse
A Few Tips on How to Perform FDG PET/CT
A Few Tips on How **WE** Perform FDG PET/CT
Patient Preparation and Scan Performance – Guidelines under development through SNM

- No strenuous exercise for 24 hours
- No caloric intake for at least 4 hours
  - Includes NG tube, IV glucose
  - Non caloric liquids
  - Anesthesia guidelines may supersede
- FBS rarely an issue: prefer < 120 mg/dl but
  - Diabetes
  - Glucocorticoids may complicate the situation

Clinical context – urgency, resources, availability

- Brown Adipose Tissue – Degrades scan quality
  - Prevention
    - Warm quiet room for an hour prior to injection
    - Propranolol, 1 mg/kg up to 40 mg max, 1 hour prior to injection orally for patients 8 and older
      Rarely add oral diazepam if needed
      - Very low dose fentanyl
      - Diazepam

Exercise

13 y/o with ALL off therapy
Exercise

13 y/o with ALL off therapy
Played paintball the night prior
To study
18 month old with embryonal rhabdomyosarcoma of the liver
Patient’s father admitted giving child one half of a can of apple juice after injection and before imaging to help her settle down.
8 year old boy with 2-month history of right neck swelling and night sweats.

Right neck bx shows classical HL
Baseline

3 days later
Diazepam (before we instituted propranolol)
CME Question #2

• Which of the following methods are useful to prevent brown adipose tissue uptake (more than one answer may apply)
  1. Warm uptake room
  2. Propranolol prior to injection
  3. Fentanyl
  4. Diazepam
  5. Large bore needles for tracer administration
CME Question #2

• Which of the following methods are useful to prevent brown adipose tissue uptake (more than one answer may apply)
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  4. Diazepam
  5. Large bore needles for tracer administration

Patient Preparation and Scan Performance – Guidelines under development through SNM

- How much to scan
- Where to place the patient arms
- Dosimetry Considerations

How much to Scan

• Whole Body (top of head through toes)
  – Most neoplasms in children and young adults are systemic diseases
8 y/o boy with abdominal and testicular masses removed and shown consistent with Burkitt lymphoma
Outside study of April 28
20 year old man recurrent EWS for relapse protocol
20 year old man recurrent EWS for relapse protocol
20 year old man recurrent EWS for relapse protocol
20 year old man recurrent EWS for relapse protocol
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20 year old man recurrent EWS for relapse protocol
Patient Preparation and Scan Performance – Guidelines under development through SNM

– How much to scan
  • Almost always head to toes
  • Occasional exception for HL and NHL where disease at diagnosis did not involve distal extremities

– Where to place the patient arms

• Dosimetry Considerations

Where To Place Patient’s Arms

- By patient side
  - More comfortable
  - Entire arms included
  - Monitor injection site
    - SUVs
  - Degrades CT quality of chest and abdomen
  - Problems in comparing PET/CT and CT of chest and abdomen regarding position

- Above patient head
  - CT artifacts skull
  - May miss part of arms
  - May miss injection site
  - Hard to maintain for long periods
  - Good for comparison with dedicated CT as position is equivalent
What We Do Regarding Arms and Legs

• Arms
  • Usually by patient’s side
  • Except if we have particular interest in the chest – abdomen
    • Arms up mostly for lymphomas where primary disease is chest or abdomen

• Legs
  • Completely imaged except
    • Lymphomas without involvement of the lower extremities
Dosimetry Considerations

• FDG
  • As little as you need for quality studies (ALARA)
  • 0.10 – 0.14 mCi/kg
• Fluids – sometimes
  • Oral – not for anesthesia
  • Dilute urine - good
  • Full bladder - bad
    • May need catheterization

• CT – Numerous Options
  • AC only – as with rotating rod sources prior to PET/CT
  • CTAC localization
    • w/wo oral and/or IV contrast
  • “Diagnostic” CT
    • Breath hold
CT options
FDG PET/CT – How We Do it

• Preparation
  • NPO per anesthesia regulations if needed
  • Arrive one hour prior to injection
  • For 8 years and older, 1 mg/kg propranolol orally upon arrival
  • Warm uptake room
  • After one hour, 0.14 mCi/kg 18F-FDG intravenously
  • One hour uptake
  • Void

• Scan
  • CT – low dose, non breath hold
    • ASIR software
  • PET imaging
    • Head to toes
    • 3 min body
    • 2 min legs
    • Bladder catheterization if needed
“Diagnostic CT” PET/CT Considerations – At Our Institution

• Desire to keep radiation levels low by avoiding a 2\textsuperscript{nd} CT (i.e. CTAC)
• Optimizing one component compromises the other
  • Breath hold CT – banana artifact PET
  • Non breath hold CT – atelectasis and nodules
• The standalone CT device was substantially more advanced than the CT on the PET/CT
  • 4 slice PET/CT, 64 slice standalone
  • 64 slice PET/CT, 128 slice standalone with dual energy and MAR (metal artifact reduction)
• Now –FDG and CT doses have been reduced such that dosimetry is no longer much of an issue
  • Technology allows optimization of both aspects of the scan
    • Deviceless respiratory gating
    • Fast PET and CT
Yogi Berra

• “When You Come to a Fork in the Road, Take It”
Yogi Berra

• “When You Come to a Fork in the Road, Take It”

• While traveling to Berra’s house one may choose the left fork or the right fork and both are acceptable decisions because both efficiently lead to his house:
How to Perform a High Quality PET Scan in Children and Young Adults

• Guidelines under development by Pediatric Council of SNMMI in conjunction with EANM pediatric nuclear medicine participants.

• There are numerous approaches
  • All are mostly right
  • None are entirely wrong
A Few More Examples of Pediatric Young Adult FDG/PET Scans
A Few More Examples of Pediatric Young Adult FDG/PET Scans

One month old
Staging for LCH
Langerhans cell histiocytosis
A Few More Examples of Pediatric Young Adult FDG/PET Scans
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One month old
Staging for LCH
Langerhans cell histiocytosis

Why all the diaphragmatic uptake?
A Few More Examples of Pediatric Young Adult FDG/PET Scans

One month old
Staging for LCH
Langerhans cell histiocytosis

Why all the diaphragmatic uptake?
Baby crying during uptake time
6 month old boy with recently excised Ewing sarcoma of the upper lip
6 month old boy with recently excised Ewing sarcoma of the upper lip

Why all the tongue uptake?
6 month old boy with recently excised Ewing sarcoma of the upper lip

Why all the tongue uptake? Pacifier during uptake period
A Few More Examples of Pediatric Young Adult FDG/PET Scans
Granulocyte colony stimulating factors

- **gCSF – filgrastim**
  - Neupogen
  - Peg filgrastim
    - Neulasta

- **gmCSF – a few brands**
  - Sargramostim

- Bone marrow uptake
- Wait 3 weeks if you can

CME Question # 3

- What is the currently recommended interval between gCSF administration and FDG PET/CT scans to reduce confounding bone marrow stimulation?

1. 3 days
2. 3 weeks
3. 3 fortnights
4. 3 months
CME Question # 3

• What is the currently recommended interval between gCSF administration and FDG PET/CT scans to reduce confounding bone marrow stimulation?

1. 3 days
2. **3 weeks**
3. 3 fortnights
4. 3 months

Infectious/Inflammatory Lesions in Pediatric Oncology

• Not usually what we’re looking for
Infectious/Inflammatory Lesions in Pediatric Oncology

• Not usually what we’re looking for
Infectious/Inflammatory Lesions in Pediatric Oncology

• Not usually what we’re looking for
• Stumble upon them
• Not everything metabolically active is neoplastic
Infectious/Inflammatory Lesions in Pediatric Oncology

• Not usually what we’re looking for
• Stumble upon them
• Not everything metabolically active is neoplastic
• FP vrs NTFP
  • False positive
  • Not truly false positive
Infectious/Inflammatory Disorders

- Bacterial
  - Osteomyelitis
  - Pneumonia
  - Other
- Fungal
  - Pneumonia
  - Extrapulmonary
- Viral
  - Pneumonia
  - Extrapulmonary
- Sarcoidosis
Febrile Neutropenia


Adults

• 20 patients studied prospectively
  • Persisting fever >38C (100.4F)
  • Neutropenia (ANC <500/ul)
  • 5 days after onset of febrile neutropenia
  • Whether on not a cause had been identified
  • Compared with conventional imaging

• PET evaluation scale
  • Negative – physiologic activity only
  • Equivocal – uptake greater than physiologic but uncertain etiology
  • Positive – uptake greater than physiologic and suggestive of infection

• High
  • Prompted additional investigations of procedures included consultation
  • Detected infection not identified on conventional evaluation
  • Resulted in change in antimicrobial management (prolongation, alteration or withholding)

• Low
  • Confirmed results of conventional evaluation
  • No other management alterations
  • Did not show infection identified by conventional evaluation
Results - Adults

- FDG PET/CT positive in 16
- Equivocal in 1
- Negative in 3
- 22 likely sites of infection
- Located 9 additional foci not identified by conventional imaging
  - Pneumonitis
  - Enterocolitis
  - Prevertebral abscess
  - Muscle abscess
  - Perianal infection
  - Pancreatitis
  - Tonsillitis with regional lymphadentitis

- High impact in 75%
- Identified additional likely infections in 9 pts – 8 subsequently confirmed
- 5 pts – antifungal therapy discontinued
Pediatric

- 14 patients identified retrospectively (pts who underwent FDG PET/CT for tumor were excluded)
  - Fever ≥ 38C
  - 72 hours
- Same criteria for impact
  - High
  - Low
- Mean age 11 (range 1-17)

- FDG PET/CT showed additional sites of infection/inflammation in 7 patients
  - 3 patients invasive fungal infections in lungs

- Impact high in 11 of 14 patients (79%)
  - Referral of 5 pts to specialists
  - 9 alteration of antibiotic therapy
  - 5 cessation
Febrile Neutropenia

• FDG PET CT useful both when negative and positive
Conditions that can mimic neoplasm

- CRMO
- Bacterial osteomyelitis
- Histoplasmosis
- Abscesses
- Trauma
- EBV
- Cat Scratch
CNS tumors in children and young adults

- 2nd most common pediatric cancer
- Approximately 25% of childhood cancers
- 4,350 (for ages <20 years) expected in 2013
- 2nd leading cause of cancer death for children lesser than 20 years of age
- Overall survival 75%
- Morbidity
  - Physical deficits
  - Neuropsychological
  - Neuroendocrine sequelae
“Benign” Brain Tumors

- Craniopharyngioma and others
- Major morbidity
  - Location
  - Treatment
CNS tumors in adults

- New cases US 2019: about 24000
- Deaths: about 1800
- Anaplastic astrocytomas and glioblastomas (38% of primary brain tumors)
- Meningiomas and other mesenchymal tumors (27% of primary brain tumors)

- John McCain
- Ted Kennedy
- Beau Biden
- At least one of my medical school classmates
Are there any major tumor types for which FDG PET (or PET/CT) is generally not helpful?

- CNS
Clinical Impact of Amino Acid PET in Gliomas

- Imaging of brain tumors with 18F-FDG was the first oncologic application of PET.
- Glucose consumption is increased in brain tumors, especially in malignant gliomas

GBM cpa inf cerebellum - FDG
Recurrent GBM- FDG
21 year old, History of GBM, recurrent disease
Bx x2 Ganglioganglioma WHO 1
Challenges of Brain Tumor Imaging with 18F-FDG

• Differentiating tumors from normal tissue or nontumorous lesions is often difficult because of the high metabolism in normal cortex
• uptake in low-grade tumors is usually similar to that in normal white matter
• uptake in high-grade tumors can be less than or similar to that in normal gray matter
• sensitivity of detection of lesions is further decreased by the high variance of 18F-FDG uptake and its heterogeneity within a single tumor

Imaging Pathophysiology Now – Tracers and Technology

- Glucose transport

- Amino Acid transport
Amino Acids

• Building blocks for protein
• Methionine
  • An essential amino acid
  • When labeled with C-11, a true tracer
• IND 104, 987
• Approved 4/17/09
Labeled Amino Acids for Brain Tumor Imaging

• particularly attractive for imaging brain tumors because of the high uptake in tumor tissue and low uptake in normal brain.

• increased amino acid uptake, especially in gliomas, is related to increased transport mediated by type L amino acid carriers

• not
  • a direct measure of protein synthesis nor
  • dependent on blood–brain barrier breakdown

Interrogating the function of LAT1

• LAT1 is Na\(^+\)-independent and functions as an amino acid exchanger

• 507 amino acids with a molecular weight of ~55 kDa and 12 transmembrane-spanning non-glycoproteins

• the transporter for amino acid–related molecules such as L-dopa, thyroxine, and tri-iodothyronine, as well as the chemotherapeutic agent melphalan

• LAT1 is found in brain, placenta, and liver, and it is overexpressed in many types of tumors including gliomas
Labeled Amino Acids for Brain Tumor Imaging

• The most frequently used radiolabeled amino acid is $^{11}$C L-methionine

• Especially in low-grade gliomas, amino acid uptake is related to prognosis and survival

• $^{11}$C labeled tracers can be used only in centers with an onsite cyclotron

Labeled Amino Acids for Brain Tumor Imaging

• The most frequently used radiolabeled amino acid is 11C L-methionine

• Especially in low-grade gliomas, amino acid uptake is related to prognosis and survival

• 11C labeled tracers can be used only in centers with an onsite cyclotron – not completely accurate

Labeled Amino Acids for Brain Tumor Imaging

- Clinically relevant findings have been obtained mainly with two F-18 varieties O-(2-18F-fluoroethyl)-L-tyrosine (FET) and 6-18F-fluoro-L-dopa (FDOPA).
- 18F-FET and 18F-FDOPA are transported into the brain and tumor but are not further metabolized.
- Responses after chemotherapy can be detected by amino acid PET early in the course of disease suggesting that deactivation of amino acid transport is an early sign of response to chemotherapy.
Imaging LAT1

- Large amino acid transporter
  - 507 amino acids
  - 12 transmembrane domains

- Neutral amino acids that have large, branched or aromatic side chains
  - Methionine, leucine, isoleucine, phenylalanine, tyrosine, histidine, tryptophan, and valine

- Amino acid–related molecules
  - L-dopa, thyroxine, and triiodothyronine, melphalan

- Overexpressed in many types of tumors
# COMMON PET RADIONUCLIDES

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<thead>
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<th>ISOTOPE</th>
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<tr>
<td>N-13</td>
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<td>C-11</td>
<td>20</td>
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<tr>
<td>F-18</td>
<td>110</td>
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Requirements to Produce $^{11}$C-Methionine

Cyclotron

Chemists

Chemistry
PET Protocols

- **FDG**
  - Inject
  - 60 min uptake
  - Imaging
    - Brain: 8 min
    - Body: 3 min per bed position torso, 2 min legs

- **MET**
  - Inject
  - 5 min uptake
  - Imaging
    - Brain: 15 min
    - Body: 3 min per bed position
Normal Distribution of C-11 methionine
Normal Distribution of C-11 methionine

- Pancreas
- Liver
- Bowel
- Bladder
- Very little in normal brain

7 year old girl with DIPG; images of 2 intensities
CME Question #4

Concentration of C-11 methionine is most intense in the (single best choice)

1. Lungs
2. Spleen
3. Pancreas
4. Muscle
CME Question #4

Concentration of C-11 methionine is most intense in the (single best choice)

1. Lungs
2. Spleen
3. Pancreas
4. Muscle

19 y/o with 5 year history of GBM; off therapy 3 years

- MRI: new enhancing nodule at the periphery of the right posterior frontal pericavitary T2 prolongation
Why the uptake in the anterior frontal lobe?

False positive?
There is a punctate focus of enhancement in the right frontal cortex which is new since prior, and appears to correspond to a second focus of increased uptake on MET-PET study performed today.
Biopsy

- Of the new anterior lesion performed to avoid motor strip
- Recurrent glioblastoma multiforme
- Impact – changed surgical management and reduced risk of adverse consequences
13 y/o with ependymoma treated with >100 GY XRT: MRI Probable Radiation Necrosis
13 y/o with ependymoma treated with >100 GY XRT: MRI Probable Radiation Necrosis
13 y/o with ependymoma treated with >100 GY XRT: MRI Probable Radiation Necrosis
11 y/o boy recent resection of glioblastoma multiforme
11 y/o boy recent resection of glioblastoma multiforme

Comments NO: very useful
Comments RO: Confirm we have this in our target, but also will be good to have baseline when we have to deal with progression vs RT effect
7 year old boy with recurrent ependymoma, most recent resection about 2 weeks before imaging
7 y/o boy with recurrent ependymoma. 2 resections, most recently about 2 weeks prior to PET scans. Part of a research protocol and not intended for clinical use. FDG negative. MET identified small area of uptake not identified as tumor on MRI. MRI report subsequently amended. Neurosurgeon confirmed small area of residual tumor between anterior cerebral arteries that could not be resected.
Clinical Impact

• Not intended for direct clinical impact
  • Biodistribution
  • Difficult to ignore the additional information provided
  • Negatives are useful too

• As a result, with IRB encouragement, we have added an “open access” expanded cohort in which physicians can request a scan for a patient
CME Question #5

Which of the following tracers are useful for brain tumor imaging? (more than one choice may apply)

1. C-11 methionine
2. F-18 fluorodopa
3. F-18 fluoroethyltyrosine
4. F-18 NaF
5. I-124 mIBG
CME Question #5

Which of the following tracers are useful for brain tumor imaging? (more than one choice may apply)

1. C-11 methionine
2. F-18 fluorodopa
3. F-18 fluoroethyltyrosine
4. F-18 NaF
5. I-124 mIBG

Heiss WD. Clinical Impact of Amino Acid PET in Gliomas. J Nucl Med August 1, 2014 vol. 55 no. 8 1219-1220
What about C-11 methionine in other tumors

- Focus on sarcomas in conjunction with RO therapeutic trial
8 y/o boy with orbital rhabdomyosarcoma
6 y/o girl with history of embryonal rhabdomyosarcoma, persistent abnormality on MRI in the right adductor brevis muscle
Current Status of C-11 methionine

• IND
• NDA?
  • Why bother?
  • Does the short half life prohibit distribution?
    • Select areas/institutions: give example
  • Make it available elsewhere for patients who need it particularly adults with CNS tumors
    • Reimbursement
  • Very preliminary discussions with other interested investigators to discuss indication and requirements
    • How many patients?
      • Retrospective
      • Prospective
    • Safety documentation
    • Measure of truth
      • Histologic verification
      • Clinical course
      • Outcome
Conclusions

• FDG PET CT is used widely in pediatric oncology
• C-11 methionine is the single best imaging agent for brain tumors in children and young adults
• We should try to make C-11 methionine more widely available for both children and adults
Questions

• Answers to follow
I was gratified to be able to answer promptly. I said I don’t know.
I was gratified to be able to answer promptly. I said I don’t know.

Mark Twain (1835-1910)
I wish I had an answer to that because I'm tired of answering that question
I wish I had an answer to that because I'm tired of answering that question

Yogi Berra
A problem has been detected and Windows has been shut down to prevent damage to your computer.

Attempt to reset the display driver and recover from timeout failed.

If this is the first time you've seen this stop error screen, restart your computer. If this screen appears again, follow these steps:

Check to make sure any new hardware or software is properly installed.

If this is a new installation, ask your hardware or software manufacturer for any windows updates you might need.

If problems continue, disable or remove any newly installed hardware or software. Disable BIOS memory options such as caching or shadowing.

If you need to use Safe Mode to remove or disable components, restart your computer, press F8 to select Advanced Startup Options, and then select Safe Mode.

Technical information:

*** STOP: 0x00000116 (0xFFFFFA80,0xFFFF880042EA3BC,0x0000000000000000,0x0000000000000002)

*** atikmpag.sys - Address FFFFFFF880042EA3BC base at FFFFFFF880042E3000, DateStamp 4d409c8d

Collecting data for crash dump ...
Initializing disk for crash dump ...
Physical memory dump complete.
Contact your system admin or technical support group for further assistance.
Osteomyelitis

• Acute
  • Radiographs
  • Three phase bone scan
  • MRI
  • CT

• Chronic
  • FDG PET/CT is the study of choice for adults with chronic osteomyelitis: sensitivity 100%, specificity 88%, accuracy 93%
7 y/o girl with suspected Ewing sarcoma
CRMO – chronic recurrent multifocal osteomyelitis

• Inflammatory disorder of children and young adults
• Multifocal involvement in areas typical for osteomyelitis
• Non infectious – no response to antibiotics
• Recurrent – images may show multiple sites of involvement
• Can be confused with bone malignancy which is how patients come to have FDG PET/CT scans
• Mostly evaluated with skeletal scintigraphy, MRI, CT
CRMO

- Some are hot, some are not.
- Example of a patient with some hot and other
AAV 35622

12 y/o with pain in right arm
12 y/o with pain in right arm: flow phase of triple phase bone scan
12 y/o with pain in right arm: soft tissue phase
12 y/o with pain in right arm: 2 hour delay bone scan
12 y/o with pain in right arm
Biopsies x 2 one week apart

• Changes consistent with chronic osteomyelitis
• Propionibacterium acnes
12 year old boy

- Right neck and shoulder pain
- Developed after jumping on trampoline a month ago
- Enlarging mass
Biopsy

• Abundant mixed inflammation consisting of numerous plasma cells, lymphocytes, and neutrophils in a vascular fibroblastic background surrounding skeletal muscle.
  – compatible with an infectious process
  – if malignancy is suspected, then it may represent an inflammatory tissue surrounding an underlying bone disease that is represented in the sample
Biopsy #2 One week later

- Subacute and chronic suppurrative osteomyelitis
- Rare Gram-positive cocci identified
Biopsy #2 One week later

- Subacute and chronic suppurative osteomyelitis
- Rare Gram-positive cocci identified
- Biopsy tissue culture
  - MRSA; methicillin resistant Staphlococcus Aureus
It’s Never (Rarely) Easy

- Rapid extension of erythema
- Admitted for intravenous vancomycin
  - Red man syndrome
    - hypersensitivity reaction caused by the medication vancomycin
    - commonly to develop symptoms in about five to 10 minutes after first vancomycin infusion starts. However, symptoms can also develop shortly after the infusion is complete.
    - In majority of the cases, it is thought that red man syndrome develops because of the rapid infusion of the first dose of vancomycin, which is defined as less than an hour.
    - severity can vary each time the patient is exposed to vancomycin or other medicines. There are some patients who will not have this reaction until after the patient has received multiple doses or has had a slow infusion.
• Went to OR for extensive debridement of bone and soft tissue
• Prolonged oral antibiotics
Thus far, what have we seen

Osteomyelitis and CRMO can masquerade as neoplasms
14 y/o male syncope, palpitations, weight loss, mediastinal mass, suspected lymphoma
Biopsy

- Mediastinal mass, needle biopsies of:
- Necrotizing granulomas with no organisms identified with … stains
- Histoplasma yeast antigen 32 (normal < 8)
Histoplasmosis

• First discovered in Panama Canal zone 1905
• Grows as a mold in the soil and is
• Found primarily in microfoci containing large amounts of rotted guano where starlings have roosted or bats have inhabited
• Source: Infectious Diseases (3rd Edition)
  Editors: Gorbach, Sherwood L., Bartlett, John G., Blacklow, Neil R.
  Publisher: Lippincott Williams & Wilkins, 2004 Histoplasma Chapter 270 au Joe Wheat
Histoplasmosis

- Most cases within Ohio and Mississippi River valleys
- Spores can be blown for miles, exposing individuals without contact with the contaminated site
- After low exposure, about 1% of patients become symptomatic
- After heavy exposure, nearly 100% become symptomatic
Areas Endemic for Histoplasmosis

https://www.cdc.gov/fungal/diseases/histoplasmosis/maps.html
Now thought likely due to Coccidiomycosis

https://www.cdc.gov/fungal/diseases/histoplasmosis/maps.html  Based on skin test data from late 1940s and 1905s
Histoplasmosis

• Acute self limited illness:
  – fever
  – chills
  – headache
  – myalgia
  – anorexia
  – nonproductive cough
  – retrosternal or pleuritic chest pain
Histoplasmosis

- Disseminated
  - 1 in 2000 acute infections
  - Immunosuppression
  - Age extremes
How We Usually Encounter Histoplasmosis

• 17 y/o s/p thyroidectomy for Hurthle cell carcinoma
How We Usually Encounter Histoplasmosis

- 17 y/o s/p thyroidectomy for Hurthle cell carcinoma
How We Usually Encounter Histoplasmosis

• 17 y/o s/p thyroidectomy for Hurthle cell carcinoma
Histoplasmosis ICTY

• It can trick you
13 y/o boy OS left tibia
13 y/o boy OS left tibia

- Two week history of left knee pain and swelling
- No fever, chills, weight loss
Numerous and diffuse noncalcified pulmonary nodules are seen scattered throughout the lung fields.

In the setting of probable osteosarcoma, these most likely represent metastatic disease.
FDG PET/CT
FDG PET/CT Report

- Adenopathy and lung nodules consistent with osteosarcoma
Biopsy
Biopsy

Lingula, wedge biopsy:

1. Three caseating granulomas with central dystrophic calcification.
2. All positive for numerous small oval budding yeasts consistent with Histoplasma species.
3. Negative for a neoplastic process.
Biopsy of Tibia
Biopsy of Tibia

• Osteosarcoma
FDG PET/CT at 6 weeks and 12 months
FDG PET/CT about 2 years
The Future

• The dark side clouds everything. Impossible to see the future is.
The Future

• The dark side clouds everything. Impossible to see the future is.
Beware

• You can prove anything with an anecdote
Masses

Anything goes
21 y/o large B cell mediastinal lymphoma
What’s the residual uptake?
Oct 3 2011

Biopsy showed inflammation, no tumor
Why the uptake
Fell on knees skating 2 weeks prior
11 year old girl, flank and abdominal pain, weight loss. CT shows retroperitoneal masses. ? Soft tissue sarcoma
11 year old girl, flank and abdominal pain, weight loss. CT shows retroperitoneal masses. ? Soft tissue sarcoma
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11 year old girl, flank and abdominal pain, weight loss. CT shows retroperitoneal masses. ? Soft tissue sarcoma
Multiple biopsies
Multiple biopsies

- Non caseating granulomatous inflammation
Multiple biopsies

• Non caseating granulomatous inflammation
• Sarcoidosis
Sarcoidosis

- [https://www.nhlbi.nih.gov/health-topics/sarcoidosis](https://www.nhlbi.nih.gov/health-topics/sarcoidosis)
- Sarcoidosis can affect any organ. Most often it affects the lungs and lymph nodes in the chest.
Sarcoidosis

Sarcoidosis is a rare condition in which groups of immune cells form lumps, called granulomas, in various organs in the body. Inflammation, which may be triggered by infection or exposure to certain substances, is thought to play a role in the formation of granulomas.

Sarcoidosis can affect any organ. Most often it affects the lungs and lymph nodes in the chest. You may experience fatigue, which is extreme tiredness or fever, but you may also experience other signs and symptoms depending on the organ that is affected. Your doctor will diagnose sarcoidosis in part by ruling out other diseases that have similar symptoms.

Determining whether treatment is needed and what type depends on your signs and symptoms, which organs are affected, and how well those organs are working. Medicines used to treat sarcoidosis help reduce inflammation or suppress the immune system. Many people recover with few or no long-term problems. Sometimes the disease causes permanent scarring in the affected organs. When scarring happens in the lungs, this is called pulmonary fibrosis.

Explore this Health Topic to learn more about sarcoidosis, our role in research and clinical trials to improve health, and where to find more information.

Causes
Risk Factors
Screening and Prevention
Signs, Symptoms, and Complications
Diagnosis
Signs, Symptoms, and Complications

Diagnosis

Your doctor will diagnose sarcoidosis based on your symptoms, a physical exam, imaging tests, or a biopsy of an affected organ. The doctor will also perform tests to rule out other diseases that have similar signs and symptoms.

Diagnostic tests and procedures

To diagnose sarcoidosis and determine which organs are affected, your doctor may have you undergo some of the following tests and procedures:

- **Biopsy** of the lungs, liver, skin, or other affected organs to check for granulomas
- **Blood tests**, including complete blood counts, to check hormone levels and to test for other conditions that may cause sarcoidosis
- **Bronchoscopy**, which may include rinsing an area of the lung to get cells or using a needle to take cells from the lymph nodes in the chest
- **Chest X-ray** to look for granulomas in the lungs and heart and determine the stage of the disease. Often, sarcoidosis is found because a chest X-ray is performed for another reason.
- **Neurological tests**, such as electromyography, evoked potentials, spinal taps, or nerve conduction tests, to detect problems with the nervous system caused by sarcoidosis
- **Eye exam** to look for eye damage, which can occur without symptoms in a person with sarcoidosis
- **Gallium scan**, which uses a radioactive material called gallium to look for inflammation, usually in the eyes or lymph nodes.
- **High-resolution computed tomography (CT) scan** to look for granulomas
- **Magnetic resonance imaging (MRI)** to help find granulomas. Learn more in our Chest MRI Health Topic.
- **Positron emission tomography (PET) scan**, a type of imaging that can help find granulomas
- **Pulmonary function tests** to check whether you have breathing problems
- **Ultrasound** to look for granulomas

Tests for other medical conditions

Stages of sarcoidosis

Reminders

Treatment

Living With
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62 y/o with bilateral hilar adenopathy on CXR

• Strong family hx breast cancer
• Mother died in her mid 40s, grandmother in her early 50s
• ~25 years off therapy for unilateral disease
• Periodic bone scans and CXR
• Asymptomatic
• Underwent FDG PET/CT
What’s the Lesson Here?
What’s the Lesson Here?

Avoid being an interesting case in your cousin’s reaching collection
20 year old man presented with syncope, CXR shows mediastinal mass, suspected lymphoma
Cervical lymph node biopsy

• Non-caseating granulomas with multinucleated giant cells
• Sarcoidosis
Questions