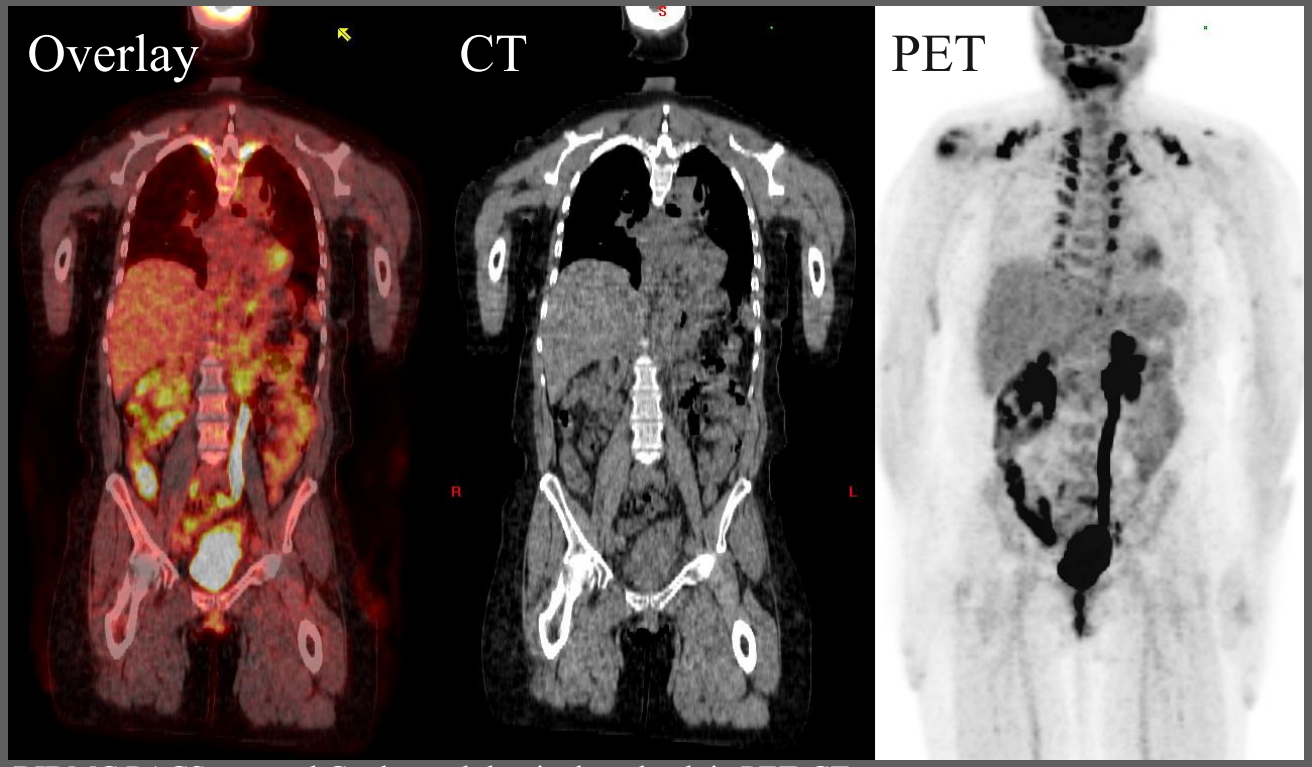
Beth Israel Deaconess Medical Center
Michael Lin, HMS III
Gillian Lieberman, MD

July 2011

Imaging Brown Adipose Tissue



BIDMC PACS, coronal C- chest, abdominal, and pelvic PET-CT

Michael Lin, Harvard Medical School Year III

Gillian Lieberman, MD

Agenda

- Meet index patient
- Introduction to brown adipose tissue (BAT)
- Introduction to PET-CT imaging of BAT
- Typical examples of patients with BAT
- An atypical presentation of BAT
- Methods for minimizing interference from BAT in oncological PET-CT imaging

- Abbreviations:
  - BAT: brown adipose tissue
  - C-: without intravenous contrast
  - FDG: ^{18}F-fluorodeoxyglucose
  - PET-CT: positron-emission tomographic and computed tomographic scan
  - UCP1: uncoupling protein 1

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Index Patient: Clinical Presentation

- 60 year old female with HIV and HCV
- Now has locally invasive squamous cell carcinoma of bladder
- PET-CT ordered to evaluate for lymph node involvement and metastases, surgical planning

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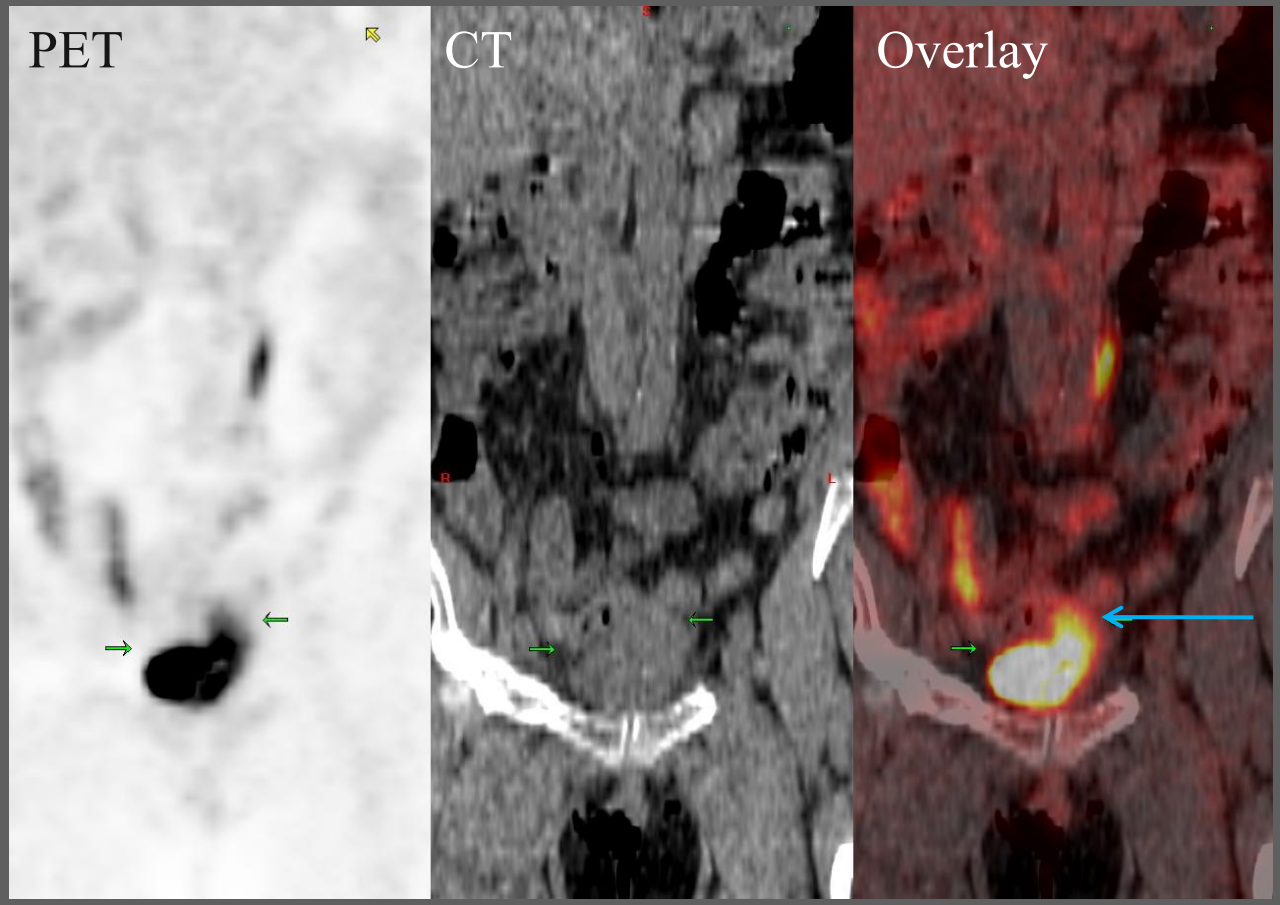
Index Patient: Bladder on Coronal PET-CT

- FDG avidity in region of known bladder carcinoma mass



Coronal C- abdominal and pelvic PET-CT

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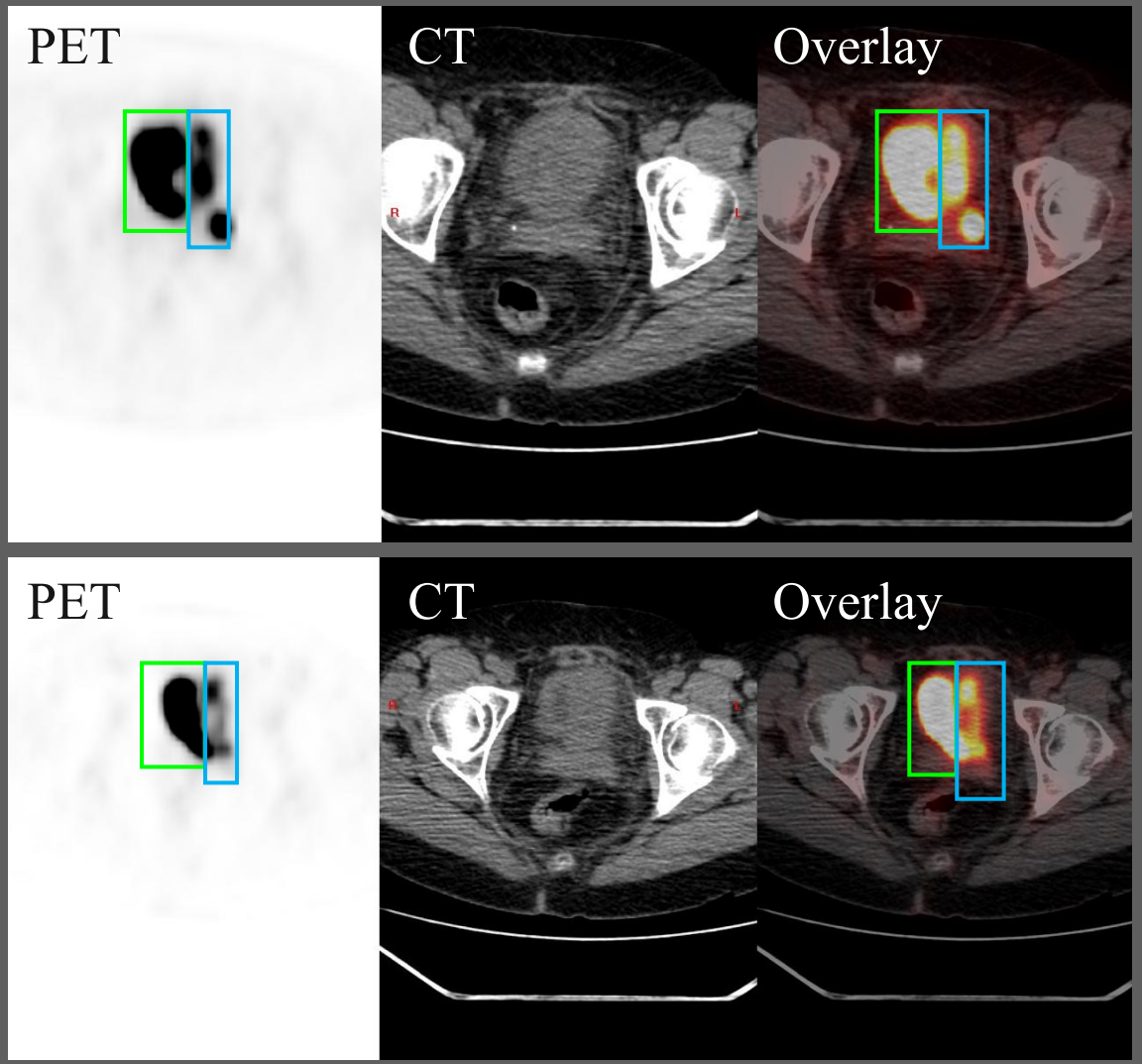
Index Patient: Bladder on Axial PET-CT

- FDG avidity in region of known bladder carcinoma mass (less avid) and bladder lumen (more avid)



Axial C- pelvic PET-CT

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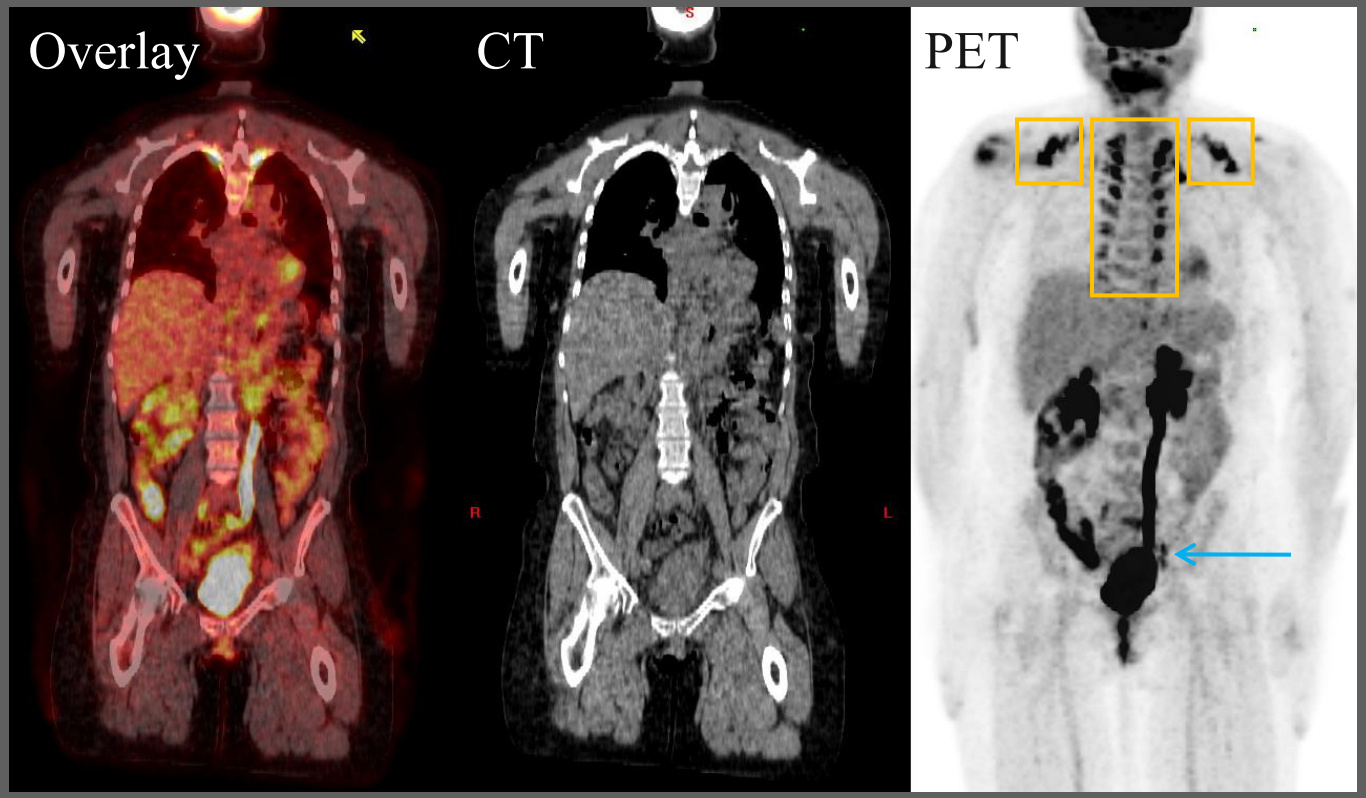
Index Patient: Coronal PET-CT

- FDG in bladder carcinoma and left renal collecting system
- What about the bilateral supraclavicular and paravertebral areas of FDG avidity?



Coronal C- chest, abdominal, and pelvic PET-CT

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What is Brown Adipose Tissue (BAT)?

- Significant depots in anterior neck to thorax (cervical, supraclavicular, superior mediastinal depots)
- High number of mitochondria relative to white adipose tissue
- Expresses uncoupling protein 1 (UCP1) that mediates non-shivering thermogenesis by dissipating mitochondrial proton gradient
- Found in rodents and young humans, previously thought not to be physiologically relevant in adult humans

Cannon and Nedergaard, 2004; Cypess et al., 2009

Who Has BAT?

- 7.5% of women and 3.1% of men
  - Other PET-CT studies reported 25% (Döbert et al., 2004) to > 80% of patients (Rousseau et al., 2006)
  - Autopsy series found BAT in necks of 26/31 patients over age 20 (Heaton, 1972)
- Women have greater mass of brown adipose tissue (median 12.3 g vs. 11.6 g) and higher FDG uptake activity
- Probability of detection inversely correlated with age, outdoor temperature at scan time, beta-blocker use, body-mass index

Cypess et al., NEJM, 2009

Importance of BAT

- To radiologists and oncologists:
  - High FDG avidity can cause confusion when evaluating tumors using PET-CT scans
  - Mistaking BAT for cancer metastasis may alter clinical decision making (e.g., whether to treat cancer surgically)
- To endocrinologists:
  - Mediator of metabolism and energy balance
  - Potential to be harnessed to control weight

- Historically, PET was done without concurrent CT
  - Cervical and supraclavicular areas of FDG avidity were thought to be muscle

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PET-CT Basics

- Most common radiotracer, FDG, has radioactive fluorine attached to glucose, half-life of 110 minutes, emits positrons
  - Other radiotracers have carbon-11, nitrogen-13, oxygen-15
- One hour after intravenous FDG, non-contrast CT images obtained, then series of PET images obtained
- Metabolically active tissue (e.g., tumor) absorbs more glucose than do other tissues
- Positron encounters electron, annihilation produces two photons moving in opposite directions that are detected by PET machine scintillator
- CT images co-registered and overlaid with PET images to assist with anatomic localization of tracer uptake

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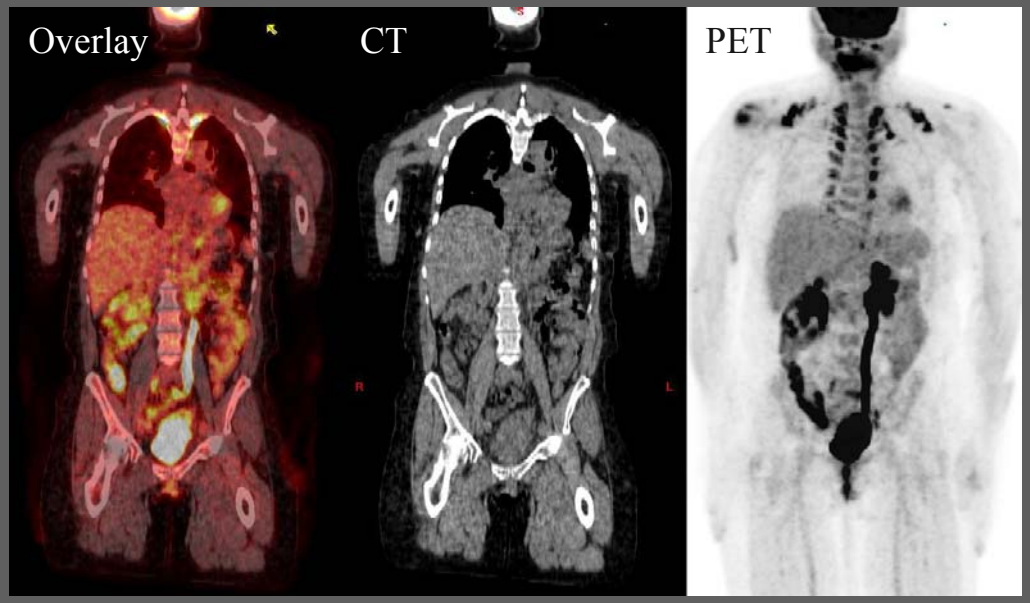
Physiology of Identifying BAT by PET-CT

- Body can not metabolize FDG the way it would metabolize normal glucose because ^{18}F substituted for 2'OH
- Phosphorylation normally prevents glucose from leaving cell, FDG is similarly phosphorylated, trapped, accumulated in cells
- Most intense areas of normal uptake: brain, myocardium, liver, kidneys, urinary bladder (FDG is renally excreted)



Coronal C- chest, abdominal, and pelvic PET-CT

Criteria for Identifying BAT

- Putative BAT:
  - Collections of tissue > 4 mm in diameter
  - Density of adipose tissue on CT (-250 to -50 Hounsfield units)
  - Maximal standardized uptake values* of ^{18}F-FDG ≥ 2.0 g/mL (high metabolic activity)
  - Symmetric body distribution (vs. asymmetric distribution of metastases)
- Confirm by detecting UCP1 by immunostaining and RT-PCR on biopsy specimens from cervical and supraclavicular regions

- *Standard uptake value: decay-corrected activity per mL within region of interest divided by injected dose in megabecquerels per gram of body weight

Cypess et al., NEJM, 2009; Virtanen et al., NEJM, 2009

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Other BAT Imaging Modalities

- ^{18}F-FDG PET-CT is modality of choice, others rarely used

- MIBG (metaiodobenzylguanidine, a noradrenaline analog)
- Technetium (^{99m}Tc) sestamibi (indicator of vascular perfusion)
- PET-MRI

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Back to the index patient…

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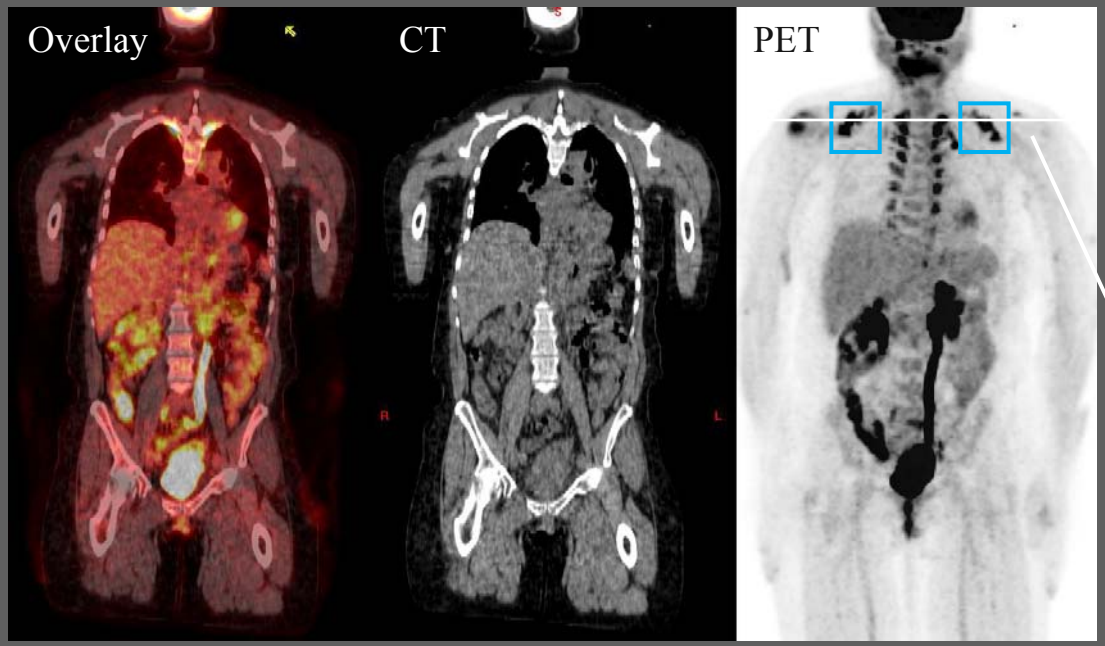
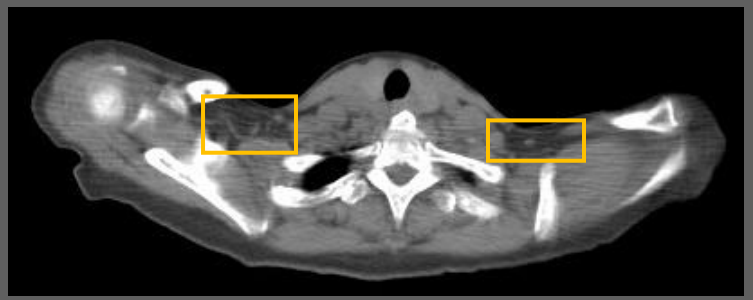
Index Patient: Supraclavicular BAT on Axial and Coronal PET-CT

Symmetric supraclavicular distribution of high FDG avidity



Coronal C- chest, abdominal, and pelvic PET-CT

Supraclavicular adipose tissue density



Axial C- chest CT

Companion Patient #1: Clinical Presentation

- 67 year old female with carcinosarcoma of uterus status post hysterectomy and bilateral salpingo-oophorectomy
- Now presenting with large retroperitoneal mass, has had 4 cycles of paclitaxel and carboplatin chemotherapy
- PET-CT ordered to evaluate treatment response, FDG avidity seen in pelvic area and neck

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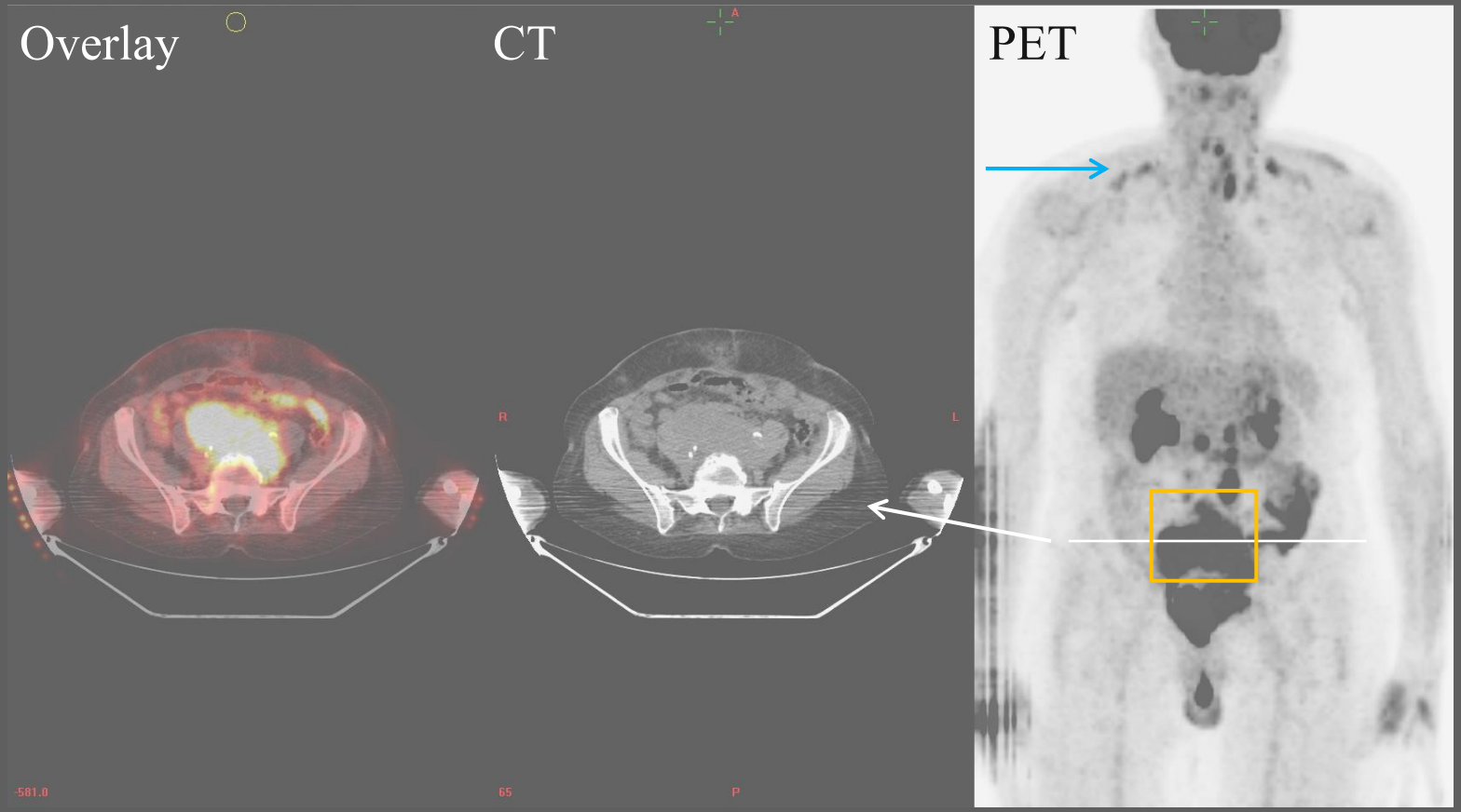
Companion Patient #1: Axial PET-CT

- FDG avid pelvic mass consistent with known recurrence of uterine carcinosarcoma, supraclavicular BAT



Axial C- pelvic PET-CT

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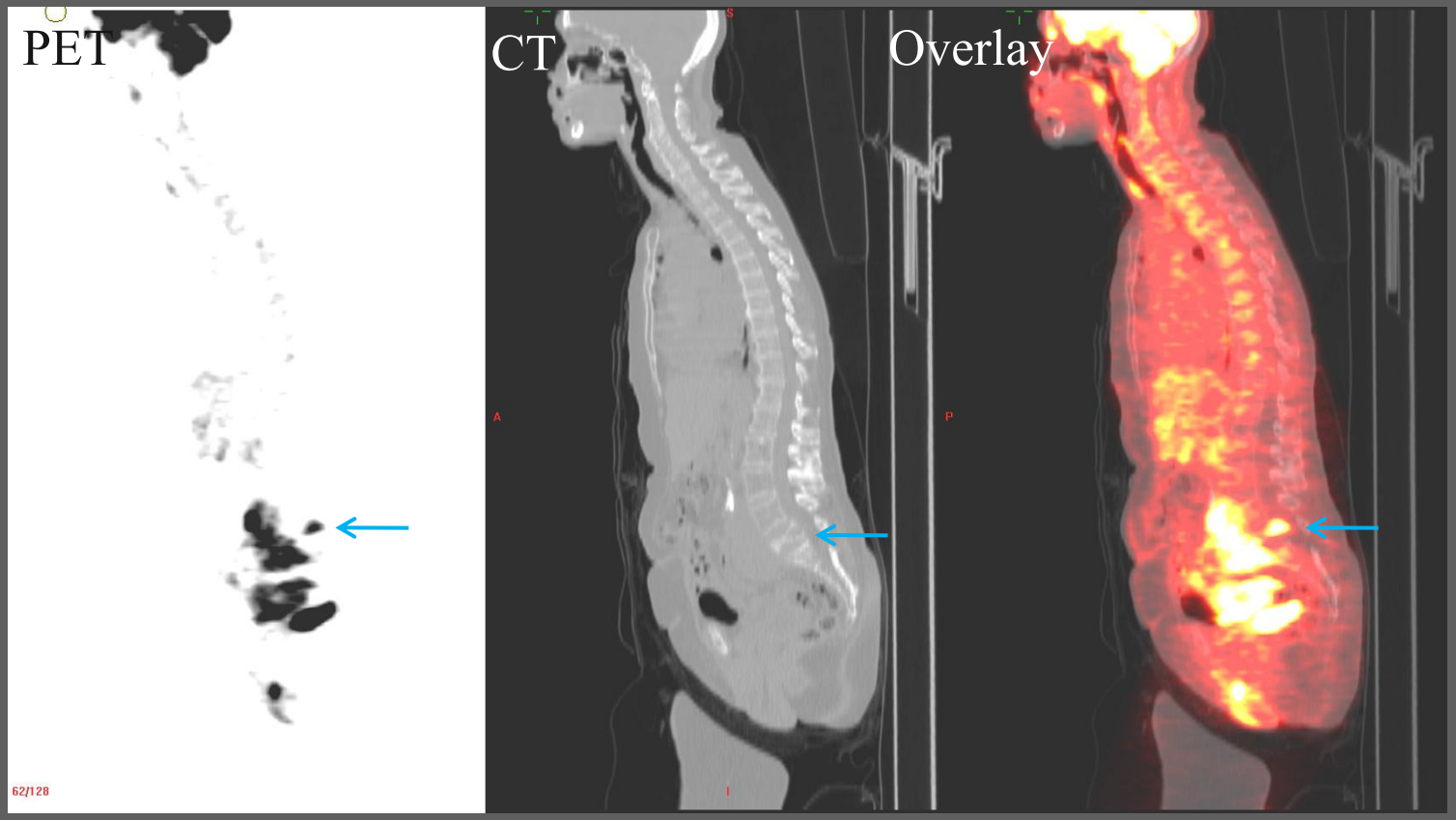
Companion Patient #1: Lateral PET-CT

- FDG avidity helped identify secondary neoplastic involvement of L5 vertebra in an area not classically associated with BAT



Sagittal C- chest, abdominal, and pelvic PET-CT

BIDMC PACS

Companion Patient #2: Clinical Presentation

- 54 year old female with 2 months of mid-back pain radiating to right side
- Chest X-ray followed by CT chest revealing left lower lobe 1.7cm lung nodule with mediastinal and hilar adenopathy and T9 fracture

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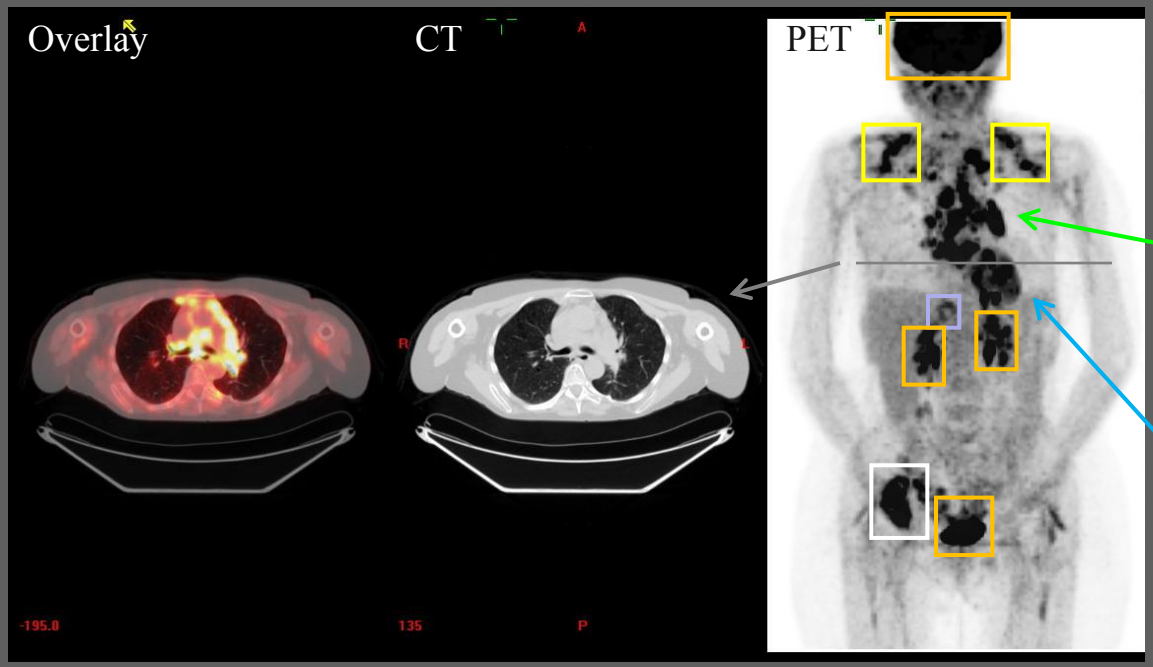
Companion Patient #2: Lung Cancer with Metastases and BAT on Axial PET-CT



Axial C- abdominal PET-CT

Normal physiologic FDG uptake in brain, kidneys, and bladder

BAT

Extensive mediastinal, hilar, and supraclavicular FDG avid lymphadenopathy

FDG avid left lower lobe lung nodular opacities

FDG avid adrenal gland uptake, likely metastasis

FDG avid right iliac bone sclerotic metastasis

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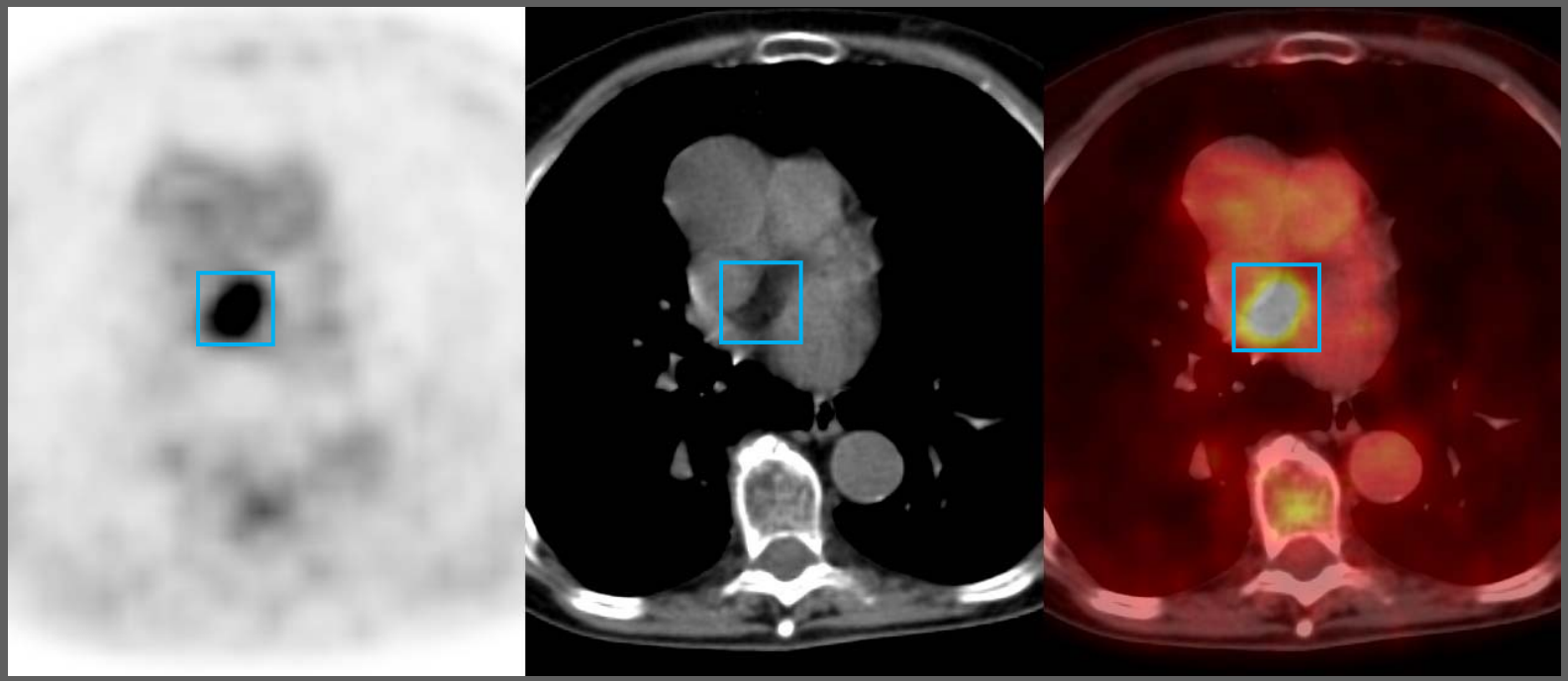
Companion Patient #3: An Unusual Location for BAT on Axial PET-CT

- 75 year old female with esophageal cancer, initial staging
- Lipomatous hypertrophy of interatrial septum (Fan et al., 2005)
- Notice corresponding adipose tissue density on CT



Axial C- chest PET-CT

Courtesy J. Anthony Parker, MD PhD

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Methods to Decrease BAT FDG-avidity

- Important because BAT FDG avidity decreases availability of FDG to possible tumors, decreases sensitivity of PET

- Increase temperature of imaging room
- High-fat, low-carbohydrate diet the night before imaging
- Benzodiazepines (diazepam, lorazepam)
- Propranolol
- Fentanyl
- Avoid nicotine

Williams and Kolodny, 2008

Summary

- BAT is present in adults, not just newborns and rodents
- High metabolic activity allows BAT to be visualized by PET
- Must take BAT's high FDG avidity into account on PET-CT used for oncological evaluation – not all "hot spots" are metastases
- Concurrent CT with PET aids in anatomic localization, distinction between BAT and cancer metastasis
- Many methods of decreasing BAT FDG avidity

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