THE PET INCIDENTALOMA
COMMON UNEXPECTED ONCOLOGIC IMAGING DILEMMAS, THEIR SIGNIFICANCE, AND HOW TO HANDLE THEM
I HAVE NO DISCLOSURES
WHO, WHAT, WHEN, WHERE

WHO:
4 – 21% of FDG PET/PET-CT oncologic exams \(^1,2\)

WHAT & WHEN:
- Unexpected foci of FDG avidity
- Unlikely physiologic
- Unlikely related to primary malignancy of interest

WHERE:
Most common:
Colon, thyroid, proximal aerodigestive tract,
Ovaries
Less common:
Breast, prostate, uterus, lung

52 year-old woman with prior endometrial cancer.

---

1. Ishimori T, Patel PV, Wahl RL. Detection of unexpected additional primary malignancies with PET/CT. *JNM* 2005;46(5):752-757
WHY

1.2 - 4.8% risk of underlying 2nd primary 1,3,4

Significant variation in risk of malignancy based upon location

Knowledge of risk of malignancy essential in order to guide further evaluation/management of FDG PET incidentalomas

LOCATION, LOCATION, LOCATION

– Occult secondary primary of greatest concern in...
  • Breast
  • Colon
  • Thyroid
  • Prostate
– In certain sites, most frequently inflammatory, physiologic, or iatrogenic
  • Uterus
  • Proximal aerodigestive tract
  • Lung
– Occasionally, risk affiliated with menopausal status
  • Ovaries
  • Endometrium

HIGH RISK

LOW RISK

FOCAL FDG UPTAKE IN COLON
FOCAL FDG UPTAKE IN COLON

Frequency: 2.6 - 3% \(^5,6\)

Appearance:
- Focal or multifocal nodular increased uptake
- May have associated anatomic abnormality
  - Fecal stasis
  - Wall thickening
  - Intraluminal mass
  - Pericolonic infiltration

FOCAL FDG UPTAKE IN COLON

Risk of Malignancy: HIGH
- Approximate 60% risk of being cancerous or precancerous \(^5,6,7\)
- 1716 patients with non-colorectal malignancies \(^5\)
  - 45 with focal nodular colonic uptake
  - 20 patients (21 foci) underwent colonoscopy, 13 advanced neoplasms (carcinoma, villous adenoma, etc)

FOCAL FDG UPTAKE IN COLON

Risk of Malignancy: **HIGH**
- Approximate 60% risk of being cancerous or precancerous \(^5,6,7\)
- 818 patients with lung cancer \(^6\)
  - 84 with focal nodular colonic uptake
  - 49 patients underwent colonoscopy
  - 27 (55%) advanced neoplasms (carcinoma or tubovillous adenoma)

---

56 YO FEMALE
H/O LYMPHOMA
CLINICALLY NED
SURVEILLANCE EXAM
56 YO FEMALE. H/O LYMPHOMA. CLINICALLY NED. SURVEILLANCE EXAM
INCREASED RISK OF CANCER WHEN ANY INCIDENTALOMA HAS AN ASSOCIATED ANATOMIC CORRELATE

FOCAL FDG UPTAKE ‡ ADENOCARCINOMA
36 YO FEMALE. H/O CERVICAL CANCER. FOLLOW-UP TREATMENT.
FOCAL FDG UPTAKE ♦ VILLOUS ADENOMA

PHYSIOLOGIC URETERAL ACTIVITY
74 YEAR-OLD MAN WITH HX OF LUNG CANCER. FU EXAM.
FOCAL FDG UPTAKE ‡ TUBULAR ADENOMA
FOCAL FDG UPTAKE IN COLON

Potential false positives include:

- Physiologic
  - usually diffuse or segmental, mold-to-moderate intensity
  - large bowel usually more intense than small, particularly cecum and rectosigmoid (reversed in children)  
- Metformin usage
  - usually diffuse or long segment, moderate-to-severity intensity
- Infectious/inflammatory
  - Colitis
  - Diverticulitis
- Anal sphincter, ileocecal valve

71 YEAR-OLD MAN WITH PLEURAL THICKENING & CHRONIC LUNG DISEASE.
FOCAL FDG UPTAKE ≠ DIVERTICULITIS

UPTAKE LIKELY DIVERTICULITIS IF CT SHOWS:
- DIVERTICULA
- MURAL THICKENING
- PERICOLONIC FAT STRANDING
80 YEAR-OLD WOMAN WITH NEWLY DIAGNOSED BREAST CANCER.
UPAKE AT A SPHINCTER MAY BE CONSIDERED BENIGN/PHYSIOLOGIC IF:
- CIRCUMFERENTIAL
- UNIFORM
- WITHOUT CT ANATOMIC ABNORMALITY
FOCAL FDG UPTAKE IN COLON

Discussion:

• $SUV_{\text{max}}$ may be higher with malignant lesions (mean 11.2 vs. 7.1)\(^5\), but difference not proven to be statistically significant

Focal nodular colonic activity needs to be reported and should be referred for colonoscopy

FOCAL FDG UPTAKE IN THYROID
FOCAL FDG UPTAKE IN THYROID

Frequency: 2.5% ⁹

Appearance:
- Focal increased FDG avidity
- May see associated nodule on CT

Risk of Malignancy: **HIGH**
- Pooled data from 27 studies encompassing 147,505 patients revealed a 35% malignancy rate for thyroid incidentalomas ⁹
  - Papillary most common histology

10. Smith C, Schoder H, Yeung H. Thymic extension in the superior mediastinum in patients with thymic hyperplasia: potential cause of false-positive findings on ¹⁸F-FDG PET/CT

NOTE:
SEGMENTAL FDG AVIDITY IN COLON IS TYPICALLY PHYSIOLOGIC
53 YEAR-OLD MAN UNDERGOING COLON CANCER SURVEILLANCE.
FOCAL FDG UPTAKE ⚫ PAPILLARY CA
63 YEAR-OLD MAN WITH INDETERMINATE PULMONARY NODULE.
FOCAL FDG UPTAKE ‡ MEDULLARY CA
FOCAL FDG UPTAKE IN THYROID

Mimics:
- Thyroiditis
  - Focal or diffuse
- Benign adenoma
- Parathyroid adenoma
- Thymic extension $^{10}$
FOCAL FDG UPTAKE IN THYROID

Mimics:
- Thyroiditis
  - Focal or diffuse
  - More often Hashimoto’s than Graves disease
75 YEAR-OLD WOMAN WITH INDETERMINATE PULMONARY NODULE.
FOCAL FDG UPTAKE + PARATHYROID ADENOMA

Tc99m MIBI – 2 HR DELAY
17 YEAR-OLD WOMAN WITH HISTORY OF LYMPHOMA AND CLINICALLY IN REMISSION
FOCAL FDG UPTAKE † THYMIC EXTENSION
FOCAL FDG UPTAKE IN THYROID

Hypermetabolic nodule in superior mediastinum represents accessory thymic tissue if:
- Anterior to left brachiocephalic vein
- Associated with anatomic findings of thymic hyperplasia
- Thymus is FDG avid
- Soft tissue nodule avidity similar to thymus
FOCAL FDG UPTAKE IN THYROID

Discussion:
- No safe $SUV_{\text{max}}$ cutoff to discriminate benign from malignant pathology
- Differentiated thyroid carcinoma is most common malignancy
- Level of uptake may correlate with histology with anaplastic > poorly differentiated > differentiated
  - Inverse pattern of iodine avidity
- $^{18}$F-FDG PET may have problem solving role in setting of indeterminate/insufficient fine needle aspiration
  - Several studies show a high negative predictive value (75-100%)

Hypermetabolic thyroid nodules on PET/CT have high risk of malignancy, particularly papillary thyroid carcinoma, and warrant further evaluation with US
FOCAL FDG UPTAKE IN BREAST
FOCAL FDG UPTAKE IN BREAST

Frequency: <1%

Appearance:
- Focal increased FDG avidity in breast
- Many will have an anatomic correlate

Risk of Malignancy: **HIGH**
- 45-57% malignant \(^{11,12}\)
  - Invasive ductal carcinoma most frequent
  - Less commonly invasive lobular carcinoma, ductal carcinoma in situ, lymphoma, metastasis

---

47 YEAR-OLD WOMAN WITH HISTORY OF COLON CANCER & RISING CEA
47 YEAR-OLD WOMAN WITH HISTORY OF COLON CANCER & RISING CEA
47 YEAR-OLD WOMAN STATUS POST LEFT MASTECTOMY. STAGING EXAM

FOCAL FDG UPTAKE ✧ INVASIVE LOBULAR CARCINOMA

FOCAL FDG UPTAKE IN BREAST

- Potential false positives include
  - focal
    • fibroadenoma, papilloma, ductal hyperplasia, granuloma, gynecomastia, physiologic areolar activity
  - more diffuse
    • proliferating glandular tissue (pediatric), post-partum/lactation

67 YEAR-OLD MAN WITH POORLY DIFFERENTIATED PROSTATE CANCER

NODAL DZ

BONE METS
FOCAL FDG UPTAKE ‡ GYNECOMASTIA
30 YEAR-OLD WOMAN WITH MEDIASTINAL MASS. 2 WEEKS POST-PARTUM.
74 year-old man with lung cancer

DIFFUSE FDG UPTAKE ♦ LACTATING BREAST
Discussion:
• second most common cancer in women
• infrequent incidental PET finding but frequently malignant
• malignant lesions with higher $SUV_{\text{max}}$ than benign
  • proposed cutoff of 2.0-2.3$^{12}$
• histology may affect FDG avidity
  • lobular carcinoma may be false negative

FOCAL FDG UPTAKE IN BREAST

Discussion:
• second most common cancer in women
• infrequent incidental PET finding but frequently malignant
• malignant lesions with higher $SUV_{max}$ than benign
  • proposed cutoff of $2.0-2.3^{12}$
• histology may affect FDG avidity
  • lobular carcinoma may be false negative

Focal hypermetabolic abnormal breast uptake has a high risk of malignancy, particularly invasive ductal carcinoma, and should receive additional evaluation with diagnostic mammogram and/or ultrasound

FOCAL FDG UPTAKE IN PROSTATE
FOCAL FDG UPTAKE IN PROSTATE

63 yo male with history of melanoma.
63 yo male with history of melanoma. Focal FDG avidity seen in right base of prostate without anatomic correlate (red arrow).
FOCAL FDG UPTAKE IN PROSTATE

Frequency: 0.05-1.2% ¹³,¹⁴,¹⁵

Appearance:
- focal FDG uptake in periphery of prostate
- often without anatomic correlate

¹³. Han EJ, Choi WH, Yoo IR, Chung SK. Significance of incidental focal uptake in prostate on 18-fluoro-2-deoxyglucose positron emission tomography CT images. BJR 2010;83:915-920
FOCAL FDG UPTAKE IN PROSTATE

Risk of Malignancy: **HIGH** *

- original ‘definitive’ study
  - 55 cases of focal FDG uptake
  - 3 cases of biopsy proven malignancy
    ‡ 5.4% risk of malignancy
- more likely represents...
  - prostatitis
  - benign prostatic hypertrophy (BPH)

* **BUT**
  • most of 52 ‘benign’ cases were path proven
  • in two separate cancer screening studies (2487 & 1629 men), four foci of FDG avidity in prostate found ‡ all were cancer

13. Han EJ, Choi WH, Yoo IR, Chung SK. Significance of incidental focal uptake in prostate on 18-fluoro-2-deoxyglucose positron emission tomography CT images. *BJR* 2010;83:915-920
FOCAL FDG UPTAKE IN PROSTATE

Subsequent studies:

Hwang I, et al. 2013
• 12,037 FDG PET/CTs
• 184 (1.5%) focal prostate uptake
• 38 underwent biopsy
‡ 61% cancer (Gleason scores 7-10)

Bhosale P, et al. 2013
• 1440 FDG PET/CTs
• 124 (8.6 %) focal prostate uptake
• 26 underwent biopsy
‡ 58% cancer

13. Han EJ, Choi WH, Yoo IR, Chung SK. Significance of incidental focal uptake in prostate on 18-fluoro-2-deoxyglucose positron emission tomography CT images. BJR 2010;83:915-920
63 yo male with history of melanoma. Focal FDG avidity seen in right base of prostate without anatomic correlate (red arrow).
FOCAL FDG UPTAKE IN PROSTATE

Mimics:
• central prostatic FDG activity
  ‡ likely urine activity in prostatic urethra
• activity at superior margin of prostate
  ‡ possible adjacent bladder/ureteral activity

False Positives:
• Recent biopsy
• Focal prostatitis
• Granulomatous prostatitis
  ‡ History of bladder cancer
  ‡ Intravesicular BCG therapy

77 YEAR-OLD MAN UNDERGOING SURVEILLANCE EXAM FOR HEAD AND NECK CANCER
FOCAL FDG UPTAKE IN CENTRAL PROSTATE 💩 URINE IN URETHRA

PRONOUNCED FDG IN CENTRAL PROSTATE DUE TO PRIOR TURP

ABNML FDG UPTAKE IN LEFT APEX OF PROSTATE
FOCAL FDG UPTAKE IN PROSTATE

Discussion:
• second most common cancer in men
• generally, adenocarcinoma of prostate shows no/mild FDG avidity
  -- very low (4%) sensitivity of FDG PET
• PSA does not differentiate benign vs. malignant focal FDG uptake
• risk of malignancy cannot be determined by SUV
• but... given often indolent nature of prostate cancer, a ‘missed’ prostate cancer may be clinically irrelevant in men with other primary malignancy

Focal hypermetabolic activity in the periphery of prostate has high risk of malignancy and should be referred for urologic consult

FOCAL FDG UPTAKE IN UTERUS
FOCAL FDG UPTAKE IN UTERUS

Frequency: 4% pre-menopausal, <1% post-menopausal women

Appearance:
- focal FDG uptake in uterus, higher intensity than surrounding myometrium
  - often corresponds to high T2 SI on MRI which indicates abundant cellularity
- FDG avidity can change significantly in intensity between exams

FOCAL FDG UPTAKE IN UTERUS

Risk of Malignancy:  LOW

- study of 502 fibroid uteri by co-registered PET/MR
  - 22 cases of FDG avid myoma
    † no cases concerning for malignancy
  - 18/164 (10%) leiomyomas in pre-menopausal women had FDG avidity
  - 4/338 (1%) leiomyomas in post-menopausal women had FDG avidity
  - new FDG avidity on serial exams seen in B9 fibroids

50 YEAR-OLD WOMAN WITH BREAST CANCER UNDERGOING EXAM FOR RESPONSE TO THERAPY ASSESSMENT
FOCAL FDG UTERUS† BENIGN FIBROIDS
30 YO WOMAN WITH THIGH SARCOMA UNDERGOING STAGING EXAM
FOCAL FDG UTERUS† BENIGN FIBROID
FOCAL FDG UPTAKE IN UTERUS

Mimics:
• Physiologic
  - Diffuse
• Endometrial carcinoma
  - Localizes to endometrium
• Cervical carcinoma
  - Localizes to cervix

30 YEAR-OLD WOMAN WITH MEDIASTINAL MASS. 2 WEEKS POST-PARTUM.

30 YEAR-OLD WOMAN WITH MEDIASTINAL MASS.
2 WEEKS POST-PARTUM.

DIFUSE FDG UTERUS‡  BENIGN POST PARTUM REACTIVE CHANGES

36 YO WOMAN WITH LIVER MASS

FDG AVID LIVER MASS
FOCAL FDG CERVIX ≠ CARCINOMA

FDG AVID LIVER MASS

FDG AVID Mass in Cervix
FOCAL FDG UPTAKE IN UTERUS

Discussion:
• leiomyomas are most common uterine neoplasm
• most commonly minimal FDG uptake, but highly variable
  ‡ SUVs 3.5-16.0 in largest case series
• SUV cannot differentiate benign from malignant
• leiomyosarcoma can have intense FDG uptake
  • but... rare
  • cannot differentiate on PET ≠ new FDG uptake
  not specific for malignant transformation
• must likely rely on classic clinical/anatomical findings
  such as rapid, massive uterine enlargement
FOCAL FDG UPTAKE IN UTERUS

Discussion:

• leiomyomas are most common uterine neoplasm
• most commonly minimal FDG uptake, but highly variable
  ‡ SUVs 3.5-16.0 in largest case series
• SUV cannot differentiate benign from malignant
• leiomyosarcoma can have intense FDG uptake
  • but... rare
  • cannot differentiate on PET ≠ new FDG uptake not specific for malignant transformation
• must likely rely on classic clinical/anatomical findings such as rapid, massive uterine enlargement

※ Focal hypermetabolic activity of uterine fibroid has LOW risk of malignancy and does not warrant further evaluation
FOCAL FDG UPTAKE IN PROXIMAL AERODIGESTIVE TRACT
FOCAL FDG UPTAKE IN PROXIMAL AERODIGESTIVE TRACT

Frequency: very high, up to 60% 18, 19

Appearance:
- focal FDG uptake in oral floor, Waldeyer’s ring, pharynx, larynx without anatomic correlate
- symmetric or asymmetric
- most often at sites of lymphoid tissue

FOCAL FDG UPTAKE IN PROXIMAL AERODIGESTIVE TRACT

Risk of Malignancy: LOW

- study of 590 patients w/o head & neck malignancy
- mean follow-up of 2.5 years
- 2 occult cancers found
  - 1 oral floor (max SUV 3.7), 1 palatine tonsil (max SUV 3.2)
  ‡ benign sites FDG uptake up to max SUV 7.2

FOCAL FDG UPTAKE IN PROXIMAL AERODIGESTIVE TRACT

Risk of Malignancy: **LOW**

- 818 patients with lung cancer \(^{19}\)
- 42 (5.1%) with focal uptake in pharynx or larynx
  - 36 w/o mass \(^{‡}\) 1 BOT cancer found

66 YO MAN WITH H/O COLON CANCER. RISING CEA.
NEGATIVE DIRECT VISUALIZATION EXAM BY ENT

No mass or other anatomic correlate on CT ‡ likely physiologic or inflammatory
54 YO WOMAN WITH BREAST CANCER
NEGATIVE DIRECT VISUALIZATION EXAM BY ENT
FOCAL FDG UPTAKE IN PROXIMAL AERODIGESTIVE TRACT

Mimics:
• misregistration artifact
  ‡ should see malalignment of PET and CT on fused data set
• vocal cord paralysis
  • may see metabolic & anatomic asymmetry of cords
  • history of chest malignancy and/or XRT should be sought
FOCAL FDG UPTAKE IN PROXIMAL AERODIGESTIVE TRACT

Discussion:
• one of most common sites of incidental FDG avidity
• frequency related to abundance of lymphoid tissue
• presence of lesion on CT should prompt further evaluation
FOCAL FDG UPTAKE IN PROXIMAL AERODIGESTIVE TRACT

Discussion:
• one of most common sites of incidental FDG avidity
• frequency related to abundance of lymphoid tissue
• presence of lesion on CT should prompt further evaluation

Focal hypermetabolic activity of proximal aerodigestive tract has LOW risk of malignancy and recommendations for further evaluation should generally be limited to cases with corresponding CT abnormalities
FOCAL FDG UPTAKE IN LUNG
FOCAL FDG UPTAKE IN LUNG

Frequency: Unknown, but rare

Appearance: Focal FDG uptake in lung WITH NO ASSOCIATED ANATOMIC ABNORMALITY

Risk of Malignancy: LOW

FOCAL FDG UPTAKE IN LUNG

No mass or other anatomic correlate on CT
No mass or other anatomic correlate on CT
FOCAL FDG UPTAKE IN LUNG

Discussion:
- True pathology invariably has anatomic/structural change \(^{20}\)
- FDG microemboli thought to be from pre-existing inflammatory thrombus or iatrogenic from injection \(^{20,22}\)
- Reported in patients with peripheral venous abnormalities, difficult phlebotomy, usage of old intravenous cannula, hypercoagulable state \(^{21}\)

FOCAL FDG UPTAKE IN LUNG

Discussion:
- True pathology invariably has anatomic/structural change
- FDG microemboli thought to be from pre-existing inflammatory thrombus or iatrogenic from injection
- Reported in patients with peripheral venous abnormalities, difficult phlebotomy, usage of old intravenous cannula, hypercoagulable state

Focal hypermetabolic activity in lung without anatomic correlate has NO risk of malignancy and does not warrant further evaluation
FOCAL FDG UPTAKE IN OVAIRES
FOCAL FDG UPTAKE IN OVARIES

Frequency: Variable
  Premenopausal: 4.2 – 33% (varies with menstrual cycle)
  Postmenopausal: Exceedingly rare

Appearance:
- Physiologic uptake mostly unilalateral, spherical or discoid, smooth margins
  - Near uterus, superior to bladder

Risk of Malignancy:
  Premenopausal: LOW
  Postmenopausal: HIGH

26 YO FEMALE WITH LYMPHOMA

UNILATERAL PHYSIOLOGIC OVARIAN ACTIVITY

23 YO FEMALE WITH OSTEOSARCOMA
UNILATERAL PHYSIOLOGIC OVARIAN ACTIVITY
FOCAL FDG UPTAKE IN OVARIES

Mimics:
- Pelvic lymph node
  - More peripheral and near pelvic wall
- Ureter
- Malignancy → postmenopausal
- Ovarian torsion

PHYSIOLOGIC FOCAL URETERAL ACTIVITY IN A POSTMENOPAUSAL FEMALE
FOCAL FDG UPTAKE IN OVARIES

Discussion:
- “Normal postmenopausal ovaries have no visible FDG uptake” ²³
  - Ovarian or adnexal activity in this population should be considered pathologic
- Physiologic ovarian activity in premenopausal patients varies with menstrual cycle
  - Activity seen midcycle (late follicular/early luteal phase)
  - Due to increased metabolic demands from growing follicle ²³
FOCAL FDG UPTAKE IN OVARIES

Discussion:
- “Normal postmenopausal ovaries have no visible FDG uptake”
  - Ovarian or adnexal activity in this population should be considered pathologic
- Physiologic ovarian activity in premenopausal patients varies with menstrual cycle
  - Activity seen midcycle (late follicular/early luteal phase)
  - Due to increased metabolic demands from growing follicle

Focal hypermetabolic activity of ovary(ies) has LOW risk of malignancy in premenopausal women, BUT does not warrant further evaluation with Pelvic US in postmenopausal patients
CONCLUSION

– Occult secondary primary of greatest concern in...
  • Breast
  • Colon
  • Thyroid
  • Prostate
– In certain sites, most frequently inflammatory, physiologic, or iatrogenic
  • Uterus
  • Proximal aerodigestive tract
  • Lung
– Occasionally, risk affiliated with menopausal status
  • Ovaries
  • Endometrium

1. In absence of an anatomic correlate on CT, which of the following sites of focal FDG avidity is most likely benign?
   a. Breast
   b. Lung
   c. Colon
   d. Prostate
   e. Thyroid
2. 54 year-old women with renal cell carcinoma. Based upon the PET-CT images, what is the most likely etiology for the patient’s focal uptake?
   a. DCIS
   b. Fat necrosis
   c. Invasive ductal carcinoma
   d. Invasive lobular carcinoma
   e. Metastasis
3. The most common malignancy associated with focal FDG uptake in the thyroid is?
   a. Medullary carcinoma
   b. Anaplastic carcinoma
   c. Papillary carcinoma
   d. Lymphoma
   e. Metastasis
4. Focal FDG activity in the central prostate likely represents which of the following?
   a. Urine in urethra
   b. Adenocarcinoma
   c. Benign prostatic hypertrophy
   d. Prostatitis
   e. Focal fibrosis
5. When encountering a focus of FDG avidity in the lungs without anatomic correlate, what is the most appropriate management?
   a. Repeat FDG PET-CT in 3-6 months
   b. No further imaging
   c. Per Fleischner Society Recommendations
   d. CT pulmonary angiogram
CONCLUSION

- Incidental foci of FDG avidity are frequently encountered
- 1.2 – 4.8% risk of underlying 2nd primary 1,3,4
- Occult secondary primary of greatest concern in...
  - Breast ‡ DX MMG
  - Colon ‡ Colonoscopy
  - Thyroid ‡ US
  - Prostate ‡ Urology
- In certain sites, can most frequently be inflammatory, physiologic, or iatrogenic
  - Uterus
  - Proximal aerodigestive tract
  - Lung >>> NO RISK
- Occasionally, risk affiliated with menopausal status
  - Ovaries
  - Endometrium

HIGH RISK

LOW RISK

KNOWLEDGE OF RISK OF MALIGNANCY ESSENTIAL IN ORDER TO GUIDE FURTHER EVALUATION/ MANAGEMENT OF PET INCIDENTALOMAS