RC511

Nuclear Medicine Series: Non-FDG PET Radiotracers in Oncology

Wednesday, Dec. 2 8:30AM - 12:00PM Location: S505AB

CT  NM  OI

ARRT Category A+ Credits: 3.50
AMA PRA Category 1 Credits ™: 3.25

FDA  Discussions may include off-label uses.

Hossein Jadvar, MD, PhD, Los Angeles, CA, (jadvar@med.usc.edu) (Moderator) Nothing to Disclose
David A. Mankoff, MD, PhD, Philadelphia, PA (Moderator) Speaker, Koninklijke Philips NV; Consultant, General Electric Company

Sub-Events

RC511-01  Proliferation Imaging: FLT/PET in Oncology

Wednesday, Dec. 2 8:30AM - 9:00AM Location: S505AB

David A. Mankoff, MD, PhD, Philadelphia, PA (Presenter) Speaker, Koninklijke Philips NV; Consultant, General Electric Company

LEARNING OBJECTIVES

1) Describe the kinetics of thymidine relevant to FLT PET imaging. 2) Discuss approaches to FLT image interpretation. 3) Describe studies that have tested FLT PET as a marker cancer response to treatment.

Honored Educators

Presenters or authors on this event have been recognized as RSNA Honored Educators for participating in multiple qualifying educational activities. Honored Educators are invested in furthering the profession of radiology by delivering high-quality educational content in their field of study. Learn how you can become an honored educator by visiting the website at: https://www.rsna.org/Honored-Educator-Award/

David A. Mankoff, MD, PhD - 2013 Honored Educator

RC511-02  Positron Emission Tomography (PET) Imaging of Chemokine Receptor CXCR4 in Patients with Solid Cancers: Initial Results

Wednesday, Dec. 2 9:00AM - 9:10AM Location: S505AB

Tibor Vag, MD, PhD, Munich, Germany (Presenter) Nothing to Disclose
Carlos Gerngross, Munich, Germany (Abstract Co-Author) Nothing to Disclose
Hans-Jurgen Wester, Munchen, Germany (Abstract Co-Author) CEO, SCINTOMICS GmbH
Markus Schwaiger, MD, Munich, Germany (Abstract Co-Author) Nothing to Disclose

PURPOSE

CXCR4 is a chemokine receptor that is overexpressed in various human cancers and is involved in tumor metastasis. In this feasibility study we performed Positron Emission Tomography (PET) imaging of CXCR4 expression in patients suffering from various solid cancers.

METHOD AND MATERIALS

21 patients with histologically proven solid tumors underwent PET imaging using the novel CXCR4 nuclear probe [68Ga]Pentixafor. Maximum standardized uptake values (SUVmax) of the liver, spleen and bone marrow were measured for determination of physiological tracer distribution. For evaluation of in vivo CXCR4 expression on tumors, SUVmax and tumor-to-background ratios (T/B ratio) were determined in a total of 43 malignant lesions including 8 primary tumors, 3 local recurrent tumors and 32 metastases. When available, SUVmax of malignant lesions was compared to corresponding SUVmax measured in standard routine [18F]FDG PET.

RESULTS

Moderate tracer uptake was detectable in the liver, bone marrow and spleen with a mean SUVmax of 3.1, 3.7 and 5.6, respectively. By visual interpretation criteria, 9 of 11 primary and local recurrent tumors were detectable, exhibiting a mean SUVmax of 4.7 (range 2.1 to 10.9) and a mean T/B ratio of 2.9. 20 of 32 evaluated metastases were visually detectable (mean SUVmax of 4.5, range 3.2 to 13.8; mean T/B ratio of 2.8). Spearman’s correlation revealed a low correlation between SUVmax and number of lesions per patient (r=0.3). Compared to [18F]FDG PET obtained in 10 patients, tracer uptake in [68Ga]Pentixafor PET revealed a lower SUVmax in all measured lesions.

CONCLUSION

PET Imaging of CXCR4 in patients with solid cancers is feasible. Based on the experience gained within this small number of patients, SUVmax of malignant solid tumors seems to be lower in [68Ga]Pentixafor PET compared to [18F]FDG PET. Moreover, CXCR4 expression in solid malignancies seems to be highly heterogeneous depending on factors, that have to be elucidated in further studies.

CLINICAL RELEVANCE/APPLICATION

Once the areas of Pentixafor imaging are more clearly defined, PET imaging of CXCR4 might prove as a valuable modality, either as a stand alone diagnostic tool, or in combination with [18F]FDG PET, i.e. when considering [68Ga]Pentixafor for monitoring CXCR4
Mean tumor blood flow decreased within 1-2 days after administration of BEV. Large decrease in blood flow early after treatment of BEV was associated with short time to tumor progression.

**REFERENCES**

Bevacizumab (BEV) is a humanized monoclonal antibody that targets circulating vascular endothelial growth factor. The purposes of this study were to evaluate tumor blood flow in patients with non-small cell lung cancer (NSCLC) before and after treatment of BEV. ACT PET/CT has a high sensitivity for both primary and metastatic GIST, particularly for lesions with low mitotic rate and non-avid FDG. ACT PET/CT was positive in all metastatic lesions (11/11: 100%). The incremental value of ACT over FDG is significant for primary and metastatic GIST with low MiR (both P<0.05). By ROC curve analysis, a FDG SUVmax cut-off value>=4.4 and 3.1 could differentiate lesions of high from low MiR for primary and metastatic GIST, respectively (AUC=0.905 vs 0.875, both P<0.05).

**CONCLUSION**

Metabolic avidity of GIST for FDG has a predictive value for cellular mitotic behavior, but with the disadvantage of FN for lesions having low MiR. ACT PET/CT has a distinct incremental value over FDG for detecting primary/metastatic GIST, but appears to be independent of mitotic behavior.

**CLINICAL RELEVANCE/APPLICATION**

ACT PET/CT has a high sensitivity for both primary and metastatic GIST, particularly for lesions with low mitotic rate and non-avid for FDG. FDG avidity, however, predicts mitotic behavior of GIST.
BEV correlated with short time to tumor progression.

**CLINICAL RELEVANCE/APPLICATION**

The antiangiogenic therapy might not have a benefit for patients with large decrease in blood flow early after treatment of BEV.

**RC511-05 68Ga-PSMA-PET/CT in Patients with Renal Cell Cancer: Initial Results**

**PURPOSE**

68Gallium (68Ga) labelled prostate specific membrane antigen (PSMA) positron emission tomography / computed tomography (PET/CT) has been shown to be a reliable imaging method for the detection of prostate cancer and its metastases. Immunohistochemical studies revealed that PSMA is also expressed in the neovascularity of other solid tumors, especially renal cell cancer (RCC), making these cancers a potential target for 68Ga-PSMA-PET imaging. The aim of this study was to explore the feasibility of 68Ga-PSMA-PET/CT for detection of RCC in patients.

**METHOD AND MATERIALS**

Three male patients (mean age 66 years; range 52 - 74) with primary or metastatic RCC (n=2 clearcell RCC; n=1 papillary RCC) prospectively underwent whole body 68Ga-PSMA-PET/CT (mean M bq: 179,3; Scanner: Siemens Biograph mCT, Siemens Healthcare, Erlangen, Germany). Quantitative assessment of tracer uptake was performed 1 hour after injection (p.i.) by measuring maximum standard uptake values (SUVmax) using isocontour VOIs in histopathologically proven tumor lesions. Additionally, for each lesion tumor-to-background ratios were calculated.

**RESULTS**

All primary RCCs and known metastatic sites were detected by 68Ga-PSMA-PET/CT. Average SUVmax in clear cell and papillary RCC tumour lesions was 16.7 and 4.1, respectively. Mean tumor-to-background ratio was 18.6 for clear cell RCC lesions and was 4.1 for papillary RCC lesions.

**CONCLUSION**

Detection of primary tumors and metastases in RCC patients using 68Ga-PSMA-PET/CT is feasible. 68Ga-PSMA uptake is high in clear cell RCC but rather weak in papillary RCC. Thus the promising diagnostic potential of 68Ga-PSMA-PET/CT rather has to be investigated in clear cell RCC patients.

**CLINICAL RELEVANCE/APPLICATION**

Since RCCs have high metastatic potential exact staging is crucial. Imaging with CT, MRI but also 18F-FDG-PET/CT offers limited sensitivity. PET/CT using 68Ga-PSMA seems to be a promising alternative.

**RC511-06 Hypoxia Imaging: FMISO PET Imaging in Oncology**

**ABSTRACT**

The physiological microenvironment for a tumor is largely dictated by abnormal vasculature and metabolism. Many solid tumors develop areas of hypoxia during their evolution caused by unregulated cellular growth, resulting in greater demand on oxygen for energy metabolism. Hypoxia induces a cascade of changes that reflects the homeostatic attempts (highly conserved evolutionally) to maintain adequate oxygenation that may result in tumor cells to adapt by developing more aggressive survival traits; mediated by Hypoxia Inducible Factor (HIF1α) part of the cellular oxygen sensing mechanism. Hypoxic tumors are not effectively eradicated with conventional doses of radiation and show resistance to several chemotherapeutic drugs. Hypoxia may also result in angiogenesis (itself a marker of tumor aggressiveness) mediated by Vascular endothelial growth factor (VEGF). While angiogenesis is a frequent consequence of hypoxia, some tumors develop extensive angiogenesis without the presence of hypoxia and vice versa. Advances in PET imaging instrumentation, coupled with the development of an increasing array of novel molecular probes, provide opportunities for imaging and selection of appropriate therapies to overcome the cure limiting effects of these two fundamental aspects of tumor microenvironment. The biology of tumor hypoxia microenvironment related to hypoxia and its effect on patient outcome and developments in imaging technology and novel radiotracers for hypoxia imaging with a focus on F-18 FMISO would be reviewed. Challenges and novel treatments to overcome the cure limiting ability of hypoxia will be discussed.

**RC511-07 Prostate Cancer Choline PET Imaging and Other PET Tracers**

**LEARNING OBJECTIVES**

1) Review the major biological targets that may be useful for imaging in prostate cancer. 2) Understand the need for tailoring the imaging technique to the particular clinical phase of disease. 3) Analyze the current evidence with the potential utility of PET with various radiotracers in the imaging evaluation of prostate cancer.
ABSTRACT

Recent advances in the fundamental understanding of the complex biology of prostate cancer have provided increasing number of potential targets for imaging and treatment. In this presentation, I review the experience with a number of major PET radiotracers for potential use in the imaging evaluation of men with prostate cancer.

RC511-08 Primary Tumor Detection in CUP of Neuroendocrine Origin: Additional Value of 68Ga-DOTATATE-PET/CT Compared to Contrast-enhanced CT

Wednesday, Dec. 2 11:00AM - 11:10AM Location: SS05AB

Philipp M. Kazmierczak, MD, Munich, Germany (Presenter) Nothing to Disclose
Axel Rominger, Munich, Germany (Abstract Co-Author) Nothing to Disclose
Christine Spitzweg, Munich, Germany (Abstract Co-Author) Advisory Board, Novartis AG; Advisory Board, Pfizer Inc; Advisory Board, Ipsen SA; Speaker, Novartis AG; Speaker, Pfizer Inc; Speaker, Ipsen SA
Christoph Auerhammer, MD, PhD, Munich, Germany (Abstract Co-Author) Research Grant, Novartis AG; Speaker, Novartis AG; Research Grant, Ipsen SA; Speaker, Ipsen SA; Advisory Board, Novartis AG
Maximilian F. Reiser, MD, Munich, Germany (Abstract Co-Author) Nothing to Disclose
Clemens C. Cyran, MD, Munich, Germany (Abstract Co-Author) Research Grant, Bayer AG Research Grant, Novartis AG Speakers Bureau, Bayer AG
Carsten Bisst, MD, Munich, Germany (Abstract Co-Author) Nothing to Disclose

PURPOSE

To evaluate the additional value of 68Ga-DOTATATE-PET/CT compared to contrast-enhanced CT for primary tumor detection in cancer of unknown primary (CUP) of neuroendocrine origin.

METHOD AND MATERIALS

Patients (n=38, 27 male, 11 female, mean age 62 years) with histologically proven metastatic disease of neuroendocrine origin undergoing contrast-enhanced 68Ga-DOTATATE-PET/CT (Biograph 64, Siemens Healthcare, Erlangen, Germany) for primary tumor detection and staging were consecutively included in this retrospective study. Two blinded readers independently evaluated the separated contrast-enhanced CT and 68Ga-DOTATATE-PET data sets and noted from which of the two imaging modalities they suspected a primary tumor. In case of divergent blinded reading results, a consensus was reached. The final diagnosis, confirmed by either histopathology (n=24) or clinical follow-up (n=14), served as standard of reference.

RESULTS

Primary tumors were suspected in n=33 patients, localized in the small bowel (n=19), the pancreas (n=12), the lung (n=1), and the thyroid gland (n=1) (mean tumor-to-spleen ratio 1.10±0.69; PET/CT: true positive n=30, true negative n=3; CT: true positive n=20, true negative n=5). In n=4 patients, no primary tumor was identified (true negative n=3). N=10 primary tumors were correctly detected by PET but not contrast-enhanced CT, resulting in a diagnostic accuracy of 87% for the fused 68Ga-DOTATATE-PET/CT, compared to 66% for the contrast-enhanced CT alone. High interobserver agreement was noted regarding the localization of the primary tumor (Cohen's k 0.90, p<0.001).

CONCLUSION

68Ga-DOTATATE-PET/CT provides a significantly higher diagnostic accuracy for primary tumor detection in CUP of neuroendocrine origin as compared to contrast-enhanced CT alone.

CLINICAL RELEVANCE/APPLICATION

The present study provides evidence for the routine use of 68Ga-DOTATATE-PET/CT in neuroendocrine CUP, allowing for a comprehensive tumor staging at improved diagnostic accuracy as compared to standard whole-body imaging.

RC511-09 Do we Need High-Dose Contrast-enhanced CT in the Detection of Extra-hepatic Metastases using Gallium-68-DOTATATE-PET/CT in Patients with Neuroendocrine Tumors (NET)?

Wednesday, Dec. 2 11:10AM - 11:20AM Location: SS05AB

Jonas C. Apitzsch, MD, Marburg, Germany (Presenter) Nothing to Disclose
Dirk R. Albanus, Aachen, Germany (Abstract Co-Author) Nothing to Disclose
Z. Erdem, Zonguldak, Turkey (Abstract Co-Author) Nothing to Disclose
Okay Erdem, MD, Zonguldak, Turkey (Abstract Co-Author) Nothing to Disclose
Anton F. Verburg, Aachen, Germany (Abstract Co-Author) Nothing to Disclose
Florian F. Behrendt, MD, Aachen, Germany (Abstract Co-Author) Nothing to Disclose
Felix Mottaghy, MD, PhD, Ulm, Germany (Abstract Co-Author) Nothing to Disclose
Andrews H. Mahnken, MD, Aachen, Germany (Abstract Co-Author) Nothing to Disclose
Alexander Heinzel, Aachen, Germany (Abstract Co-Author) Nothing to Disclose

PURPOSE

Previous studies have shown that PET/CT with 68Ga-labeled somatostatin analogues is useful in the assessment of metastatic disease in patients with neuroendocrine tumors especially with regard to extra-hepatic lesions. It has to be noted that PET in combination with full-dose contrast-enhanced CT (ceCT) exposes the patients to a high dose of radiation whereas the non-contrast-enhanced low-dose CT (ldCT) might reduce the radiation and may in addition avoid side effects such as allergic reactions. Thus, we aimed to determine whether ceCT can be omitted from assessment for extra-hepatic metastases in patients with NET.

METHOD AND MATERIALS

We retrospectively compared the performance of PET/ldCT and PET/ceCT in 54 patients (26 male, 28 female) who underwent a Gallium-68-DOTATATE-PET/CT in our clinic. Selection criteria were as follows: available ldCT and ceCT; histologically confirmed NET; available follow-up of at least 6 months (median 12.6 months; range 6.1-23.2). PET/ldCT and PET/ceCT images were analyzed separately by four experienced physicians. The review process focused on metastases to lungs, bones and lymph nodes. Afterwards, the PET/ldCT and PET/ceCT results were compared to the reference standard consisting of clinical follow-up data to
evaluate the diagnostic accuracy.

RESULTS
In PET/ceCT 139 true positive bone-lesions were detected compared to 140 in PET/idCT, 106 true positive lymph node metastases (PET/ceCT) vs. 90 (PET/idCT) and 26 true positive lung lesions (PET/ceCT) whereas PET/idCT found ?? true positive lung lesions. On a per patient basis id and ce PET-CT achieved similar sensitivity (both 100%) however, specificity was lower for PET/idCT (89% vs. 77%). For lymph nodes PET/ceCT showed superior sensitivity and specificity (sensitivity 92% vs. 80% and specificity 83% vs. 65%). For the detection of pulmonary lesions the sensitivity of PET/idCT was also clearly inferior (23 vs 100%) while specificity was similar (94% vs. 93%).

CONCLUSION
These results represent first evidence that ceCT should not be omitted for extra-hepatic staging using Gallium-68-DOTATATE-PET/CT in patients with neuroendocrine tumors. However, the results need to be confirmed in a prospective trial.

CLINICAL RELEVANCE/APPLICATION
PET/idCT is sufficient in the detection of extrahepatic metastatic disease in NET. There is no further need for high-dose CeCT.

RC511-10  PSA and PSA Kinetics in Predicting 18F-NaF PET Positivity for First Bone Metastases in Patients with Biochemical Recurrence after Radical Prostatectomy

Wednesday, Dec. 2 11:20AM - 11:30AM Location: S505AB

James Yoon, BA, Los Angeles, CA (Presenter) Nothing to Disclose
Leslie Balas, MD, Los Angeles, CA (Abstract Co-Author) Nothing to Disclose
Bhushan Desai, MBBS, MS, Los Angeles, CA (Abstract Co-Author) Nothing to Disclose
Lingyun Ji, MS, Los Angeles, CA (Abstract Co-Author) Nothing to Disclose
Susan Groshen, PhD, Los Angeles, CA (Abstract Co-Author) Nothing to Disclose
Hossein Jadvar, MD, PhD, Los Angeles, CA (Abstract Co-Author) Nothing to Disclose

PURPOSE
To evaluate PSA and PSA kinetics in addition to other pathologic factors to determine their predictive value for 18F-NaF PET positivity for first bone metastases in patients with biochemical recurrence after radical prostatectomy.

METHOD AND MATERIALS
All 18F-NaF PET scans that were performed at USC between 2010 and 2014 were queried to find patients who demonstrate biochemical recurrence after radical prostatectomy. Patients with known metastatic disease at the time of 18F-NaF PET were excluded. Records were reviewed to obtain data on PSA at the time of 18F-NaF PET, PSA kinetics, and pathologic features of the prostatectomy specimen, which were then used for receiver operating characteristic (ROC) analysis to determine predictability for 18F-NaF PET positivity.

RESULTS
36 patients met our inclusion criteria. Of these, 8 (22.2%) had positive 18F-NaF PET scans. Mean values for PSA, PSA doubling time, and PSA velocity were 2.02 ng/mL (range 0.06-11.7 ng/mL), 13.2 months, and 1.28 ng/mL/yr for 18F-NaF PET negative patients and 4.11 ng/mL (range 0.04-14.38 ng/mL), 8.9 months, and 9.06 ng/mL/yr for 18F-NaF PET positive patients (p=0.07, 0.47, and 0.02 respectively). ROC analysis for 18F-NaF positivity gave AUC values of 0.634 for PSA, 0.598 for PSA doubling time, and 0.688 for PSA velocity. ROC analysis with combined models gave AUC values of 0.723 for PSA and PSA doubling time, 0.689 for PSA and PSA velocity, and 0.718 for PSA, PSA doubling time, and PSA velocity. There was no significant association found between 18F-NaF PET positivity and Gleason score, TN staging, and status of surgical margins.

CONCLUSION
18F-NaF PET detected first time osseous metastases in 22.2% of patients with PSA relapse. PSA velocity was the best single variable for predicting 18F-NaF PET positivity. Combining PSA with PSA doubling time or PSA with PSA doubling time and PSA velocity resulted in higher predictability than any variable independently.

CLINICAL RELEVANCE/APPLICATION
18F-NaF PET can detect early prostate cancer bone metastases in the post-prostatectomy setting.

RC511-11  Bone PET Imaging: NaF PET in Oncology

Wednesday, Dec. 2 11:30AM - 12:00PM Location: S505AB

Baris Turkbey, MD, Bethesda, MD (Presenter) Nothing to Disclose

LEARNING OBJECTIVES
1) To identify the advantages of F-18 NaF PET/CT in oncology 2) To understand the importance of a standardized imaging protocol and reporting for F18-NaF PET/CT 3) To become comfortable in differentiating benign lesions from malignant ones on F18-NaF PET/CT

ABSTRACT
F-18 NaF PET/CT has been shown to have higher sensitivity than planar 99m-Tc MDP bone scanning in several studies. The concomitant acquisition of anatomic images permits immediate correlation of any abnormal findings. Additionally, F-18 NaF PET/CT bone imaging can be quantitated, allowing bone disease to be ‘measureable’, increasing its utility therapy monitoring. When a consistent F-18 NaF uptake period is used, the SUV values are highly reproducible, and due to the high extraction fraction, high quality images can be obtained with a radiation dose exposure similar to that of Tc-99m MDP (including the low dose CT scan). This presentation will discuss the benefits and challenges of F-18 NaF PET/CT in oncology.

ABSTRACT
F-18 NaF PET/CT has been shown to have higher sensitivity and specificity than planar 99m-Tc MDP bone scanning in several small
studies. The concomitant acquisition of anatomic images permits immediate correlation of any abnormal findings. Additionally, F-18 NaF PET/CT bone imaging can be quantitated, allowing bone disease to be "measureable", increasing its utility in therapy monitoring. When a consistent F-18 NaF uptake period is used, the SUV values are highly reproducible, and due to the high extraction fraction, high quality images can be obtained with a radiation dose exposure similar to that of Tc-99m MDP (including the low dose CT scan). This presentation will discuss the benefits and challenges of F-18 NaF PET/CT in oncology.