**PET Quantification—The Devil Is in the Details**

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**LEARNING OBJECTIVES**

1) Understand the factors that affect measurement of Standardized Uptake Values (SUVs)
2) Recommend technical steps that can be taken to maximize quality of SUV measurements

**ABSTRACT**

A growing application of PET imaging is evaluation of response early during the course of therapy. This can confirm that the current therapy is effective or allow ineffective therapies to be changed early in the course of treatment. While response can be dramatic and assessed visually for some malignancies (e.g. Hodgkins lymphoma), early response in many other tumors can be subtle, requiring some form of quantification. Standardized uptake values (SUVs) are the most commonly used measurements in PET to quantify tracer accumulation. These measurements are convenient to perform and widely available, but highly dependent on technical and biological factors.

Understanding the limitations and technical considerations for obtaining valid SUV measurements is essential, since these measurements are now being used for therapeutic decisions. The technical factors contributing to the SUV calculation will be reviewed, and recommendations made on how to minimize the potential sources of measurement error that are controllable.

**Diffusion-weighted Magnetic Resonance Imaging for Follow-up and Treatment Response Assessment of Lymphoma: Results of an 18F-FDG-PET/CT-controlled Prospective Study in 64 Patients**

Marius Erik Mayerhoefer MD, PhD (Presenter): Nothing to Disclose, Georgios Karanikas MD: Nothing to Disclose, Helmut Prosch MD: Nothing to Disclose, Barbara Kiesewetter MD: Nothing to Disclose, Michael Weber: Nothing to Disclose, Thomas Knogler MD: Nothing to Disclose, Markus Raderer MD: Nothing to Disclose

**PURPOSE**

To determine the value of diffusion-weighted magnetic resonance imaging (DWI-MRI) for treatment response assessment in fluorodesoxy-glucose (FDG)-avid lymphoma.

**METHOD AND MATERIALS**

Patients with FDG-avid Hodgkin (HL) or Non-Hodgkin lymphoma (NHL) at pre-therapeutic 18F-FDG-PET/CT, who had also undergone pre-therapeutic whole-body DWI-MRI, were included in this prospective study. Depending on the histological lymphoma subtype, patients received different treatment regimens, and follow-up DWI-MRI and 18F-FDG-PET/CT were performed at one or more time points, depending on the clinical course. For each follow-up DWI-MRI, region-based sensitivity/specificity and agreement in terms of treatment response (complete remission, partial remission, stable disease, or progressive disease), relative to the corresponding 18F-FDG-PET/CT, were calculated.

**RESULTS**

64 patients were included: 10 with HL, 22 with aggressive NHL, and 32 with indolent NHL. Overall region-based DWI-MRI sensitivity and specificity were 97.6% (95% confidence interval (CI), 91.7-99.3%), and specificity was 99.5% (95% CI, 99.0-99.9%). For the 51 interim DWI-MRI examinations (performed after 1-3 therapy cycles) region-based sensitivity and specificity were 95.1% (95% CI, 83.9-98.7%) and 99.4% (95% CI, 98.9-99.9%), and for 48 end-of-treatment DWI-MRI examinations, sensitivity and specificity were 100% (95% CI, 89.6-100%) and 99.8% (95% CI, 99.4-100%). With regard to treatment response assessment, DWI-MRI agreed with 18F-FDG-PET/CT in in 99/102 follow-up examinations (97.1%), with a kappa value of 0.94 (P

**CONCLUSION**

In patients with FDG-avid lymphoma, DWI-MRI is a feasible alternative to 18F-FDG-PET/CT for follow-up and treatment response assessment, regardless of the histological subtype (i.e., Hodgkin lymphoma, aggressive NHL, indolent NHL).

**CLINICAL RELEVANCE/APPLICATION**
VSNM21-04  
**Predictive Value of FDG PET/CT prior to Allogeneic and Autologous Stem Cell Transplant for Lymphoma**

Gary Allan Ulaner MD, PhD (Presenter): Research support, General Electric Company Research support; Seragen Pharmaceuticals, Inc.  
Debra A. Goldman MS: Nothing to Disclose  
Joshua Lilienstein MD: Nothing to Disclose  
Mithat Gonen PhD: Nothing to Disclose  
Jocelyn Maragulia BA: Nothing to Disclose

**PURPOSE**

Determine the value of FDG PET/CT prior to allogeneic and autologous stem cell transplant (SCT) of lymphoma patients in predicting outcome following transplant.

**METHOD AND MATERIALS**

A retrospective review was performed under IRB waiver. Patients who underwent allogeneic or autologous SCT for lymphoma at our institution from 2005-2010, and had FDG PET/CT within 3 months before transplant, were included. PET/CT examinations were evaluated for suspicious lesions with FDG-avidity greater than liver background (Deauville 4/5). Clinical records were used to document overall survival (OS), disease specific survival (DSS), and progression free survival (PFS). The relationship between pre-transplant PET/CT and outcome was assessed using Kaplan-Meier methods and log-rank test separately for each group. The relationship between SUVmax and PFS was assessed using a piecewise linear univariate Cox regression in time.

**RESULTS**

273 patients were identified, 114 with FDG PET/CT prior to allogeneic SCT and 159 with FDG PET/CT prior to autologous SCT. Prior to SCT, 33 of 114 (29%) allogeneic patients and 21 of 159 (13%) autologous patients had suspicious FDG-avid lesions. For both allogeneic and autologous SCT patients, there was a significant relationship between suspicious FDG avid lesions and PFS (p=0.01 and p=0.001, respectively).

**CONCLUSION**

The presence of suspicious FDG-avid lesions on PET/CT prior to both allogeneic and autologous SCT identifies lymphoma patients where transplant has a low likelihood of sustained success. The higher the SUVmax of lesions, the greater the risk of recurrence is for the first 12 months following transplant.

**CLINICAL RELEVANCE/APPLICATION**

FDG PET/CT prior to both allogeneic and autologous SCT predicts the likelihood of transplant success in aggressive lymphomas. PET/CT can help guide selection of patients for both of these procedures.

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VSNM21-03  
**FDG-PET/CT Response Assessment Criteria for Hodgkin's and Aggressive Non-Hodgkin's Lymphoma at Completion of Therapy**

Ur Metser MD (Presenter): Nothing to Disclose  
Grainne Mairead Murphy MB BCH, MMedSc: Nothing to Disclose  
Ravi Michael Mohan MD, DPhil: Nothing to Disclose  
Vaughan Beckley: Nothing to Disclose  
David Christopher Hodgson MD, MPH: Nothing to Disclose

**PURPOSE**

Based on the International Harmonization Project (IHP) criteria, PET response assessment of residual nodal masses in patients with lymphoma after completion of therapy is performed visually using mediastinal blood pool (MBP) as the reference. The purpose of this study was to define the optimal reference for PET response assessment and to determine whether visual inspection or semiquantitative measures are the preferred method of assessment.

**METHOD AND MATERIALS**

The study included 137 patients (age range: 18-94 years; median: 50), with Hodgkin’s (n=43) or non-Hodgkin's lymphoma (n=94) assessed for residual masses after completion of therapy. Two experienced readers independently assessed response by IHP criteria, and on a separate read used Deauville-adapted scoring system with liver as reference for residual disease. Pathology and clinical and imaging surveillance data (mean: 19 months) was used as standard of reference. Inter-reader agreement and performance of visual versus semiquantitative analysis was performed. Comparison between methods was performed using McNemar test, with a p-value <0.05 considered significant. Kappa coefficients assessed level of agreement between readers.

**RESULTS**

Based on the standard of reference, 36 patients (26.3%) had residual lymphoma, while 101 patients (73.7%) had complete response. For IHP and Deauville-adapted criteria, sensitivity was 97.2% (p=0.001), specificity was 79.2% and 92.1% (p<0.001), and overall accuracy was 83.9% and 93.4% (p=0.001), respectively; with strong interobserver agreement for both methods (Kappa = 0.858 and 0.854, respectively). For both, visual assessment performed better than uptake-based analysis with overall accuracy of visual and SUV-based analysis was 85.4% and 68.2% for MBP (p<0.001) and 93.8% and 89.8% (p=0.039) for liver.

**CONCLUSION**

Response Assessment Recommendations in Solid Tumors: RECIST vs PERCIST

Heather Jacene MD (Presenter): Nothing to Disclose

LEARNING OBJECTIVES

1) To compare anatomic and metabolic imaging for response assessment. 2) To discuss limitations of current widely used criteria for assessing response. 3) To discuss the benefits and limitations of metabolic imaging for response assessment.

Utility of 18F-FDG PET/MR in Differentiation of Recurrent High-grade Intra-axial Neoplasm from Radiation Changes: A Comparison of PET/CT to PET/MR

Jesse Montagnese DO (Presenter): Nothing to Disclose, Andrew Sher MD: Research Grant, Koninklijke Philips NV; Salim E. Abboud MD: Nothing to Disclose, Lisa Rogers MD: Nothing to Disclose, Norbert Avril MD: Nothing to Disclose, Leo John Wolansky MD: Nothing to Disclose

PURPOSE

Advanced imaging is often utilized in the post-treatment period of high-grade intra-axial neoplasm to better characterize enhancing lesions. Our study compares the diagnostic accuracy of 18F-FDG PET/CT and 18F-FDG PET/MR in differentiating progressive disease (PD) from radiation change (RC).

METHOD AND MATERIALS

We evaluated 12 patients with high-grade intra-axial neoplasm whom had undergone radiation therapy and developed MR evidence of PD per RANO criteria. 13 lesions were evaluated: 10 glioma; 2 metastatic patients (3 lesions). All patients underwent 18F-FDG PET/CT, 18F-FDG PET/MR (with MR attenuation correction, PET/MRAC), conventional diagnostic MR (PET/MRD), and perfusion MR in a single exam. Four separate interpretations were performed of the PET/CT, PET/MRAC, PET/MRD, and perfusion PET/MR with consensus readings by two fellowship-trained radiologists (1 neuroradiology; 1 nuclear). A qualitative subjective rating was given to each lesion (1 = definite RC; 2 = probable RC; 3 = equivocal; 4 = probable PD; 5 = definite PD). The fourth interpretation session was considered the reference standard (11 PD, 2 RC). Sensitivity, specificity, and accuracy were determined for the three interpretation sessions (PET/CT, PET/MRAC, PET/MRD) via ROC analysis after binary reclassification, with a rating of 1-3 defined as RC and 4-5 as PD. Wilcoxon-rank test was used for rating comparison between the three interpretations.

RESULTS

PET/CT yielded a sensitivity, specificity, and accuracy of 0.64, 1.00, and 0.82 (p=0.17), respectively. PET/MRAC demonstrated a sensitivity, specificity, and accuracy of 0.91, 1.00, and 0.96 (p

CONCLUSION

In this small series, 18F-FDG PET/MR utilizing either diagnostic or attenuation-only MR sequences was more accurate in differentiating radiation change from progressive disease compared to 18F-FDG PET/CT, with a statistically significant difference in interpretation between 18F-FDG PET/MR with diagnostic MR and 18F-FDG PET/CT.

18F-FDG PET/CT as an Indicator of Survival in Bone Primary Ewing Sarcoma

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PURPOSE

The existing literature of 18 F-FDG PET/CT in Ewing sarcoma investigates heterogeneous populations of patients with both soft tissue and bone primary tumors. The aim of our study was to evaluate whether the (SUV (max)) using 18 F-FDG PET/CT before and after initiation of chemotherapy, can be used as an indicator of survival in patients with primary Ewing sarcoma of bone.

METHOD AND MATERIALS

A retrospective database search was conducted from 2004 - 2011 and 178 patients with pathologically proven bone primary Ewing sarcoma were identified. Patients who received treatment before the initial PET/CT or underwent PET/CT at other institutions were excluded. Twenty-nine patients underwent 18F-FDG PET/CT before and after starting chemotherapy at our institution. The study included 10 females and 19 males, with a median age of 18 years. One female patient was excluded from the analysis because she underwent partial tumor resection before the initial PET/CT as a symptomatic treatment to relieve nerve compression. Median follow up time for patients alive was 6.2 years (range: 2.6-9.8 years). Univariate Cox proportional hazard model was used to assess effects of baseline SUV (max), post-chemo SUV (max), and the change of SUV (max) on overall survival (OS) and progression-free survival (PFS). OS started from chemo start date, and PFS started from the date of first evidence of progression.
RESULTS

SUV max ranged from 37-2.2 with a median of 8.7 for baseline and from 16.6-1.4 with a median of 3.2 post chemotherapy. High SUV (max) before (HR = 1.1, 95% CI: 1.0-1.2, P = 0.008) and after (HR = 1.2, 95% CI: 1.0-1.4, P = 0.04) chemotherapy was associated with worse overall survival. No significant cut points for SUV (max) were identified.

CONCLUSION

Baseline and post chemotherapy SUV (max) can be used as a prognostic indicator for overall survival in bone primary Ewing sarcoma.

CLINICAL RELEVANCE/APPLICATION

18F-FDG PET/CT can be used as a prognostic indicator for overall survival in bone primary Ewing sarcoma.

VSNM21-08

A Phase II Prospective Trial of Triphasic PET/CT: Delta Slope of SUVmax Differentiates True Positive from False Positive Scans at the Primary Site after Radiation in Head and Neck Squamous Cell Carcinoma

Tangel Chang DO (Presenter): Nothing to Disclose, Carryn Anderson MD: Nothing to Disclose, Michael M. Graham MD, PhD: Nothing to Disclose, Gerry Funk MD : Nothing to Disclose, Anna Button MPH : Nothing to Disclose, Yusuf Menda MD : Research Grant, Advanced Accelerator Applications, Wenqing Sun MD, PhD : Nothing to Disclose, Michael Marquardt BS : Nothing to Disclose, John M. Buatti MD : Nothing to Disclose

PURPOSE

FDG-PET/CT is used for response assessment post-radiotherapy (RT) in head and neck squamous cell carcinoma (HNSCC), but the false positive (FP) rate is approximately 50%. The positive predictive value (PPV) remains low due to inability to differentiate between inflammation and malignancy. We hypothesize that the SUVmax slope when imaged at 60-, 90-, and 120- min after FDG injection (Triphasic PET/CT) would better predict recurrence because tumors should increase uptake between 60- and 120-min whereas nonmalignant, inflammatory uptake will plateau or decrease. The goal is to improve the diagnostic accuracy of FDG-PET/CT as a post-RT response assessment tool.

METHOD AND MATERIALS

Patients with HNSCC were prospectively enrolled to undergo Triphasic 3-month post-RT PET/CT. In addition to our standard whole-body PET scan at 90-min, enrolled patients had a PET of the head and neck with low-dose CT at 60- and 120-min. SUVmax was measured for the three time points and the delta change in SUVmax, [(SUVmax 120-SUVmax 90)-(SUVmax 90-SUVmax 60)], was calculated. Standard outcomes are defined by the 90 min PET/CT as equivocal (EQ), false negative (FN), true negative (TN), true positive (TP), and FP, and the delta change in SUVmax slope between 60-, 90-, and 120-min was evaluated to differentiate between TP and FP.

RESULTS

57 HNSCC patients were eligible for analysis. Median follow-up post-RT was 15.4 months. 16% recurred at the primary site. There were 8 EQ, 3 FN, 38 TN, 4 FP, and 4 TP scans. In those with positive scans, (TP + FP) defined by the 90 min time point, the delta change in SUV max slope could differentiate TP from FP in all cases and was statistically significant using the Wilcoxon Rank Sum Exact test as a predictor of outcome (p=0.02).

CONCLUSION

Analysis of the prospective Triphasic FDG-PET/CT trial demonstrated that the delta change in SUVmax slope at the 60-, 90-, and 120- min post FDG injection allows improved differentiation between inflammation and malignancy in HNSCC patients. Utilizing the SUVmax slope along with the standard SUVmax at a single time point, the FPs induced by inflammation may be better identified. This method improves the PPV, and enhances the accuracy of FDG-PET/CT.

CLINICAL RELEVANCE/APPLICATION

PET/CT post-RT for HNSCC has PPV of 50%, resulting in significant anxiety and morbidity from biopsy/dissection. Delta change in SUVmax slope of triphasic PET/CT may accurately differentiate TP vs FP.

VSNM21-10

Value of Simultaneous PET MR Mammography in Patients with Breast Cancer Undergoing Neoadjuvant Chemotherapy – Preliminary Results

Sonja Kinzer MD (Presenter): Nothing to Disclose, Johannes Grueiiesen : Nothing to Disclose, Oliver Hoffmann : Nothing to Disclose, Ann-Kathrin Bittner : Nothing to Disclose, James Nagarajah : Nothing to Disclose, Thorsten D. Poeppel : Nothing to Disclose, Agnes Bankfalvi : Nothing to Disclose, Kai Nassenstein : Nothing to Disclose

PURPOSE

To assess if simultaneous 18F-Fluorodeoxyglucose (FDG) positron emission tomography (PET) magnetic resonance mammography (MRM; PET/MRM) performed before and after neoadjuvant chemotherapy (NAC) can discriminate between responders and non-responders and predict response to therapy in patients with invasive breast cancer compared to PET and MRM alone.

METHOD AND MATERIALS

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Patients with initial diagnosis of invasive breast cancer underwent simultaneous PET/MR mammography (Biograph mMR, Siemens, Erlangen, Germany) before and under NAC. Two readers evaluated in consensus i) MR mammography concerning size difference, ii) PET concerning changes of standard uptake value and iii) simultaneous PET/ MRM concerning both features to determine response. Image ratings were correlated with histopathology (complete response: CR; non-complete response: non-CR) and regression score after Sinn (0: no effect; 4: no residual tumor detectable) after breast conserving surgery or mastectomy.

RESULTS

Overall, MR mammography alone diagnosed CR in 8 patients and non-CR in 7 patients while PET alone diagnosed CR in 9 patients and non-CR in 6 patients. With PET/MRM readers were able to diagnose CR in 8 patients and non-CR in 7 patients. One patient with no definable tracer uptake on PET (rated as CR) showed a residual contrast enhancing lesion on MRM (non-CR) and was diagnosed correctly as non-CR on PET/MR with a Sinn score of 2 on histopathological examination. On the other hand, in another patient with a reduction of SUV (PET: non-CR but responder) and no change in size (MRM: non-CR, non-responder) histopathology showed partial reaction with a Sinn score of 2. PET/MRM correctly diagnosed this patient as non-CR, responder.

CONCLUSION

In this preliminary study we could show that simultaneous PET/MR mammography in breast cancer patients under NAC is feasible. Both imaging modalities complement one another and can help to distinguish responders from non-responders as well as predict complete response or non-CR.

CLINICAL RELEVANCE/APPLICATION

The combination of PET and MRM helps to discriminate responder and non-responder as well as those with CR and non-CR. PET/ MRM can therefore be a valuable diagnostic tool for breast cancer patients undergoing NAC.

The Bone Scan Index (BSI) Is a Prognostic Factor in Breast Cancer Patients with Bone Metastasis Treated with Zoledronic Acid

Yukinori Okada MD (Presenter): Nothing to Disclose, Yasuo Nakajima MD : Nothing to Disclose, Itsuko Okuda MD : Nothing to Disclose, Yasuyuki Kojima : Nothing to Disclose

PURPOSE

Artificial neural network-based bone scan index (BSI) has been used to quantify the spread of bone metastasis. Currently, BSI has been used as a prognostic indicator in prostate cancer. However, the utility of BSI in breast cancer patients who has bone metastasis is not clear. To elucidate the role of BSI in breast cancer patients with bone metastasis used zoledronic acid, we examined the relationship between BSI, their tumor maker and survival.

METHOD AND MATERIALS

Fifty-four female patients, ranging from 32 to 78 years of age with average of 54.4 years old, were treated for bone metastasis of breast cancer between 1 January 2006 and 27 October 2012. Bone scintigraphies were analyzed using BONE NAVI version 1 (FUJIFILMRI pharma, Co. Ltd. Tokyo Japan; EXINI BoneExini Diagnostics, Sweden) and BSI were calculated at the time whose bone metastasis were found, and the time after 6 months (range 3 months to 9 months) and 12 months (range10 months to 17 months). At the same time, the serum marker of CA15-3 (51 patients) or CEA (49 patients) were examined. Survival rates were compared with BSI and tumor makers using the Kaplan-Meier method.

RESULTS

Survival was significantly better in patients with a BSI change rate =1 after 6 months and 12 months than in patients with a BSI change rate >1 after 6 months and 12 months (6 months, p=0.028; 12 months, p=0.005). Survival was significantly better in patients with a tumor marker change rate =1 after 12 months than in patients with a tumor marker change rate >1 after 12 months (CA15-3; p=0.041, CEA; p=0.048), but there were no significant intergroup differences of there survival between patients with a tumor marker change rate =1 and a tumor marker change rate >1 after 6 months (CA15-3; p=0.507, CEA; p=0.585). There were no significant intergroup differences between patients with a BSI = median and BSI > median (median; 0.67, p=0.67), with a BSI = mean and BSI > mean (mean; 1.414, p=0.421).

CONCLUSION

The BSI change rate after 6 months and after 12 months, and the tumor marker change rate after12 months after onset of bone metastasis are a prognostic factor in breast cancer patients with bone metastasis. The BSI can predict patient’s prognosis earlier than tumor makers.

CLINICAL RELEVANCE/APPLICATION

The BSI change is a useful prognostic factor in breast cancer patients with bone metastasis.