estradiol (FES), [F-18]-fluorodihydrotestosterone (FDHT), and [Ga-68]-labeled F(ab′)2 fragments of trastuzumab.
PET can measure tumor hypoxia using probes such as [F-18]-fluoromisonidazole. Hypoxia is a well-established resistance factor for radiotherapy, increasingly also recognized as a factor that mediate resistance to systemic therapy through the activation of pathways, such as the VEGF pathway, that mediate tumor growth and metastasis. PET can also measure drug resistance arising from barriers to drug delivery to the tumor, for example, by using [C-11]-verapamil to measure regional P-glycoprotein transport.
Finally, PET can detect early changes in response to therapy, for example by measuring tumor proliferation, using tracers such as [F-18]-fluorothymidine and/or cell death, using [F-18]-fluoroannexin. This approach can identify at an early stage which drugs have had a pharmacokinetic effect on the tumor and likely response, and importantly, which drugs are not likely to be effective.
Conclusions: These new radiopharmaceuticals, combined with conventional imaging and established PET procedures using FDG, hold great promise for directing effective, targeted cancer therapy. Further development of the new PET imaging probes will require development of rigorous and robust methods of image quantification, and careful study design to validate the information provided by PET imaging compared to both in vitro assay and to well-defined patient outcomes [5].
Supported by NIH Grants CA42045 and Ca72064

References

[1] Hartwell L, Mankoff D, Paulovich A, Ramsey S, Swisher E. Cancer biomarkers: a systems approach. Nature Biotechnology 2006; 8:905–908.
[2] Weber WA. Positron emission tomography as an imaging biomarker. J Clin Oncol 2006; 24(20): 3282−92.
[3] Kelloff GJ, Krohn KA, Larson SM, et al. The progress and promise of molecular imaging probes in oncologic drug development. Clin Cancer Res 2005; 11(22): 7967−85.
[4] Mankoff DA, Eary JF, Link JM, Muzi M, Rajendran JG, Spence AM, Krohn KA. Tumor-specific imaging in patients: FDG and beyond. Clin Cancer Res 2007; 13: 3560−9.
[5] Mankoff DA, O'Sullivan F, Barlow WE, Krohn KA. Molecular imaging research in the outcomes era: measuring outcomes for individualized cancer therapy. Acad Radiol 2007; 14: 398–405.

S10
DCE-MRI as a biomarker of tumor angiogenesis

G. Jayson. *Christie Hospital and University of Manchester, Manchester, UK*

Introduction: Several randomized trials have demonstrated in a range of tumours the clinical benefit associated with augmenting conventional chemotherapy with inhibitors of Vascular Endothelial Growth Factor (VEGF). This class of drug has been extensively evaluated with Dynamic Contrast Enhanced Magnetic Resonance Imaging (DCE-MRI), largely during trials conducted in the phase I/II setting.
Main Message: DCE-MRI is an attractive biomarker for drugs that inhibit VEGF because the cytokine is the major mediator of vascular permeability. Thus agents that inhibit VEGF should reduce vascular permeability, a feature of the malignant vasculature, and this impacts on the rate of egress of contrast from the vasculature into the interstitial space. This transfer of contrast has been measured in several studies as the Ktrans, the endothelial surface area $\times$ permeability constant. By far the majority of studies have demonstrated that broad spectrum VEGF inhibitors impact on Ktrans and that the degree of change of this parameter correlates with the dose of the drug and with clinical benefit. However, in a recent phase I study of a pure VEGFR2 inhibitor we have seen evidence of an active drug that does not impact on Ktrans, suggesting that the latter parameter is regulated by a more widespread effect on the VEGF system. We have therefore carried out a detailed time course study of patients receiving the monoclonal anti-VEGF antibody, bevacizumab and the data will be presented.
Conclusions: One of the difficulties with DCE-MRI and imaging in general is heterogeneity. We have demonstrated that the vascular enhancing fraction of ovarian cancer and the histographical distribution of other MRI parameters have clinical significance, highlighting the importance of detailed and comprehensive image analysis. This is of continued relevance as the new targets of anti-angiogenic drugs are likely to have effects that are detected through DCE-MRI, confirming the importance of this biomarker in early clinical trial evaluation of new drugs.

References

Jackson A, et al., Clin Cancer Res. 2007; 13: 3449−59.
O'Connor JP et al., Br J Cancer. 2007; 96: 189−95.

S11
The functional diffusion map (fDM): an early predictive biomarker of tumor response

B. Ross. *University of Michigan, Ann Arbor MI, USA*

Introduction: Diffusion MRI measurements can be used to quantify water diffusion values within tumors. Diffusion of water molecules are sensitive to celluar density/structures and as such, therapeutic-induced changes in tumor architecture can be detected through alterations in tumor diffusion values thus the diffusion imaging approach can be used as a sensitive surrogate for early detection of treatment response. Applications of this technology in grade III/IV gliomas, head and neck tumors, breast and metastatic prostate cancer to the bone will be shown.
Main Message: Diffusion MRI (D-MRI), which measures changes in cellular water mobility, has been proposed as an early surrogate for treatment response. Previously we reported that using a functional diffusion map (fDM) at 3 weeks D-MRI was closely associated with RR, time to progression, and OS. Data on fDM in 60 patients with MG are now reported. Sixty patients were recruited for this study. There were no differences in pre-treatment variables between groups (age, KPS, pathologic grade, or surgical resection (all $p > 0.05$, Fisher's Exact Test)). Mean change in ADC, as well as the percentage of