Conclusions: These results highlight the importance of QA in routine tissue banking for research. However, it should not be forgotten that biomarkers that will prove to be clinically useful must be reliable on less than perfect specimens, and, preferably, on formalin fixed, paraffin embedded tissue. This may limit the clinical utility of some biomarkers discovered in the research setting.

S7

Are size-based response criteria appropriate in the era of targeted therapy?

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Introduction: The standard way to assess a patient's response to chemotherapy is to use computed tomography (CT) to measure tumor size using uni-dimensional (RECIST) or bi-dimensional (WHO) criteria. This methodology has changed little in the past 30 years despite the emergence of new therapies and advances in imaging technology.
Main Message: We and others have found that measuring the changes in the size of tumors in one or two dimensions does not adequately capture the effects of novel therapies on primary tumors and metastases. Radiographic changes in the size of tumors treated for instance with epidermal growth factor receptor tyrosine kinase inhibitors such as gefitinib or erlotinib or inhibitors of angiogenesis such as bevacizumab do not necessarily occur at the same magnitude or speed as observed in those individuals treated with standard cytotoxic therapies. With these newer agents, tumors respond by undergoing cystic change, central necrosis, and density changes that may not be captured by conventional measurements of the largest lesion diameter.
Conclusions: In summary, our early experience with volumetric CT calculations, measurements of necrosis or cystic change, "ghosting" of tumors as they change with therapy suggests that these may be promising biomarker technologies to measure response and could replace be an adjunct to other surrogates such as unidimensional tumor measurements, or even more functional biomarkers.

S8

Value of FDG-PET as a marker of treatment response

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PET imaging with the glucose analog fluorodeoxyglucose (FDG-PET) has been evaluated in numerous studies to monitor tumor response in patients undergoing chemo- and radiotherapy. The clinical value of FDG-PET for differentiation of residual or recurrent viable tumor and therapy-induced fibrosis or scar tissue has been documented for malignant lymphomas and various solid tumors. Furthermore, there are now several reports suggesting that quantitative assessment of therapy-induced changes in tumor FDG-uptake may allow prediction of tumor response and patient outcome very early in the course of therapy. Thus treatment may be adjusted according to the individual chemo- or radiosensitivity of the tumor tissue. Since the number of alternative treatments is continuously increasing, early prediction of tumor response to therapy by FDG-PET has an enormous potential to "personalize" treatment and to reduce the side effects and costs of ineffective or unnecessary therapy. Recent studies have demonstrated the feasibility of PET-guided chemotherapy in lymphoma and esophageal cancer. In addition, FDG-PET imaging may shorten clinical trials of new drug candidates, by providing an earlier and more accurate readout for tumor response to therapy. The usefulness of FDG-PET in drug development has been demonstrated in the development of c-kit inhibitors for treatment of gastrointestinal stromal tumors, where metabolic changes preceded a reduction of tumor size by several weeks.
Patient preparation and acquisition of PET have been standardized and simplified in recent years allowing FDG-PET studies for treatment monitoring to be performed outside of specialized research centers. Furthermore, criteria for assessment of tumor response by FDG-PET have been defined by the "International Harmonization Project in Lymphoma". Response assessment by FDG-PET is now an integral part of the "International Working Group Criteria" for response assessment in lymphomas.

S9

PET Biomarkers: beyond FDG

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Introduction: Molecularly targeted therapy holds great promise for improving cancer treatment; however, it creates new demands for tools to guide treatment selection. While treatment selection has traditionally depended upon tissue-based biomarkers, functional and molecular imaging can play an important and complementary role in directing targeted cancer therapy and monitoring early response [1]. PET imaging is modality that is well suited to this task, given its ability to probe multiple facets of pharmacology and tumor biology, and it quantitative capabilities. Most clinical imaging to date has been done using [F-18]-fluorodeoxyglucose (FDG) PET, which has demonstrated its value as a biomarker for measuring response [2]. However, other PET radiopharmaceuticals beyond FDG will also play an important role in directing therapy [3,4].
Main Message: Energy metabolism is associated with tumor growth, but also with a variety of other biological processes, including inflammation and tissue repair in response to damage. As cancer treatment becomes more targeted and individualized to patient and tumor characteristics, more specific PET radiopharmaceuticals will help guide treatment selection by (1) quantifying the therapeutic target, (2) identifying resistance factors, and (3) measuring early response to therapy [4]. Early studies has shown the ability of PET to measure the regional expression of therapeutic targets such as the estrogen receptor (ER), androgen receptor (AR), and HER2 molecule, all established therapeutic targets for breast or prostate cancer, using radiopharmaceutical such as [F-18]-fluoro-