standards in the management of tumour banks (and most generally biobanks), in order to guarantee some degree of homogeneity in biological materials obtained from different hospitals and institutions, (ii) to establish and make publicly available catalogues of "validated" collections of biological materials obtained from patients with cancers, usually treated at several or numerous institutions, (iii) to promote the prospective constitution of new collections, based on a minimal definition of a scientific project that justifies this effort, as an alternative to the retrospective re-qualification of already existing collections.

S5

The "Blood Donor Biobank" – A new approach for identifying and validating biomarkers

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Introduction: The recently established "Blood Donor Biobank" at the blood transfusion service of the Bavarian Red Cross (BSD) offers a unique resource for biomarker researchers. By using blood samples from patients collected and cold stored under standardized procedures before the onset of a certain disease the prognostic value of known biomarkers could be investigated or new biomarkers identified.
Main Message: 400,000 registered blood donors at the BSD are the basis for this innovative project. 250,000 donors donate approximately 500,000 whole blood units each year. A small amount from every blood donation is stored for a possible follow up test at a later date. Today there are already over 3.5 million plasma samples stored in a fully automated cold room at −42ºC.
The "Blood Donor Biobank" which was officially announced in 2006 provides access to some of the samples for diagnostic research and development projects. The responsible ethics committee and data protection board have agreed on the project and the participating blood donors have given their written informed consent that their blood samples and data can be used for medical research. The fact that there are so many blood donors at the BSD is key to having a sufficient number of potential biobank participants. Each year approx. 1200 donors develop a disease that is of interest for the "Blood Donor Biobank" such as cancer, diabetes, CNS or heart disease. On average these blood donors donated blood at least twice a year for several years before the diagnosis. These samples taken from one person over a period of several months or years before the onset of a disease could be used for biomarker research and give new insights in the development of a disease.
Plasma samples from the "Blood Donor Biobank" are currently being used in several collaborations with both academic and industrial research institutes. Various diagnostic techniques are applied to screen for potential biomarkers in particular in the field of cancer research.
Conclusions: The "Blood Donor Biobank" maintains a continuous collection of samples and related data before the diagnosis of a disease. Whereas worldwide similar biobank projects are currently being set up, this biobank is already in existence and contains a sample and data collection that has been continuously build up under standardized procedures during the past seven years and comprises data from approximately 10,000 participants and in excess of 100,000 plasma samples.

S6

Development of clinical biomarkers – the importance of SOPs and quality assurance

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Introduction: Timely development of novel biomarkers for clinical use depends on access to high quality material collected in a uniform manner, with proper regard for ethics relating to the use of human material in research. Quality assurance (QA) is an essential component of research tissue banking. Biological material should be subject to pathological and molecular biological QA prior to release which validates the SOPs used for collection and storage. The Wales Cancer Bank (WCB) has been collecting different types of biosamples (blood, frozen and paraffin embedded tissue) from patients in NHS hospitals in Wales since 2005, and has developed a series of QA procedures for use in the diagnostic setting.
Main Message: Researchers should be aware that priority must always be given to patient diagnosis. In the UK, all human tissue from operative specimens may only be released with agreement of the pathologist, so as not to prejudice its use for diagnosis. Tissue banks that collect material in the routine clinical setting therefore do not have control over all aspects of tissue management. Ethically, the patient's operation must be the same whether he/she has agreed to donate material excess to that used for diagnosis to a tissue bank or not. It is therefore important to put in place measures for QA post collection. H&E sections should be taken from each frozen block and paraffin embedded and stored digitally. A pathology audit revealed that frozen blocks taken from 80% of samples breast and head and neck cases contained more than 80% tumour epithelium. This figure rose to 90% in colon and renal cancer cases. In prostate, 60% of blocks contained less than 20% tumour epithelium. The percentage of tumour epithelium present may affect the sensitivity of some molecular biological tests (e.g. mutation analysis). Molecular biology QA was carried out in a total of 266 frozen tumour blocks from breast, head and neck, renal and colon cancer. In 86% of cases, RNA with an Agilent RNA Integrity Number (RIN) of >7 was extracted. This percentage varied among individual tumour types – head and neck and prostate most reliably producing high quality RNA. High quality (>10 kb) DNA was obtained in all cases using the WCB SOPs. Although extracted RNA may not always reach the QA required for Affymetrix arrays, it may still be useful for studies using RT-PCR. In a recent study conducted for the Chernobyl Tissue Bank, which compared RT-PCR for different sized amplimers of the housekeeping gene PBGD, amplimers of 942 kb were still present 74% of samples with a RIN of less than 5.5.

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-