patient preparation, data acquisition and image analysis including the calculation of quantitative parameters such as standardized uptake values (SUVs). Furthermore, criteria for classifying patients as responders or nonresponders on PET have been proposed (PET response criteria in solid tumors, PERCIST). When following these guidelines reproducible measurements of changes in FDG uptake during therapy are feasible. Comparison of tumor FDG uptake across different patients is more challenging, especially when different scanners are used at different sites. Another challenge when using different PET/CT scanners is a clinical trial is the definition of a "FDG positive" lesion. Since sensitivity and spatial resolution of PET/CT scanners have significantly improved over the years, lesions can easily be "negative" on an older scanner, but "positive" on a newer scanner.
Standardization of FDG PET scans and response criteria have made considerable progress in recent years. Challenges remain when qualitative observations or absolute measurements of tumor FDG uptake need to be compared across different scanners.

References

[1] Shankar LK et al. National Cancer Institute. Consensus recommendations for the use of 18F-FDG PET as an indicator of therapeutic response in patients in National Cancer Institute Trials. J Nucl Med. 2006; 47: 1059−66.
[2] Boellaard R et al. EANM procedure guidelines for tumour PET imaging: version 1.0. Eur J Nucl Med Mol Imaging. 2010; 37: 181–200.
[3] Wahl RL, et al. From RECIST to PERCIST: Evolving Considerations for PET response criteria in solid tumors. J Nucl Med. 2009; 50(Suppl 1): 122S–150S.

SP 109
Meta-analysis of genomic datasets for robust signature discovery and disease characterization

L. Wessels. *The Netherlands Cancer Institute, The Netherlands*

Here we evaluate (1) the prognostic value of available gene signatures; (2) the benefit of integration of clinical and gene expression data for prognostication and (3) the extent to which collaborating gene interactions can be revealed from copy number and expression data.
We performed a comprehensive analysis of the performance of nine gene expression signatures on seven different breast cancer datasets. To better characterize the functional processes associated with these signatures, we enlarged each signature by including all probes with a significant correlation to at least one of the genes in the original signature. In addition we also combined data from different modalities. We generate and evaluate a single prediction model based on both expression and clinical data. We compare three different integration strategies using five classifier types. Finally we employed copy number data from breast cancer samples to detect co-occurring aberrations. Such aberrations could point to genes that collaborate in oncogenesis.
The overall classification performance of the nine gene expression signatures is very similar but show low concordance at the sample level. Functional analysis of the enlarged signatures revealed 11 functional modules with prognostic ability. Of these, proliferation is the most dominant signature. The combination of the RNA-splicing and immune modules resulted in a classifier with high prognostic performance. On NKI 295 breast cancer series, the late OR integration strategy significantly outperformed all other classifiers. Independent datasets also showed that integration resulted in clear benefits, with the intermediate and the late OR integration strategies performing the best. In the co-occurrence analysis we discovered several regions that show interactions and are associated with outcome and breast cancer subtypes. When combining these findings with gene expression data and clinical outcome data, we identified several genes that show co-occurences both at the copy number and gene expression levels and show a significant interaction effect with regard to outcome.
Integration of clinical and expression data improves prognostication, and clinical features can achieve performance comparable to gene expression signatures. Thus, there is no longer a significant performance argument to choose one data source over the other. Finally, co-occurring gene aberrations are a powerful way to reveal oncogenic pathways and stratify cancer.

SP 124
Debate on strategies for data release: controlled access

D.L. Wickerham. *National Surgical Adjuvant Breast and Bowel Project (NSABP), USA*

The National Surgical Adjuvant Breast and Bowel Project (NSABP) is one of the National Cancer Institute of the United States cooperative trials groups with a 50+ year history of conducting large scale adjuvant therapy trials in primary breast and colon cancer. In 1992 the group expanded its research agenda to include chemoprevention trials in breast and colorectal cancer. The NSABP Biospecimen Banks contain formalin-fixed, paraffin-embedded (FFPE) tumor blocks from more than 90,000 breast and colorectal cancer tumor cases and sera from 20,000 treatment trial cases. Lymphocytes and sera are also banked from 33,000 healthy high-risk women from two breast cancer prevention trials. In addition to the centrally reviewed data for participant entry, treatment, recurrence, and death, copies of protocol consent forms are collected for all trial participants. Biospecimens and the corresponding clinical data are provided, on an as needed basis, to qualified investigators from both academia and the private sector on the basis of the scientific merit of proposals. In order to preserve participant confidentiality, the final analysis file which contains the laboratory results from the qualified investigator, and the clinical data from the NSABP Biostatistical Center, is prepared by an independent third party ("Honest Broker") and contains no participant identifiers except for a new randomly assigned number that is generated by the honest broker so the file is anonymized and neither the investigator nor the NSABP can identify any particular participant. Since 2003, 54 projects have been approved, including the development and initial validation of the Oncotype DX® 21 Gene Assay. The approach described here provides access to the specimens and the clinical data while allowing participant consent limitations to be respected, assuring that the privacy and confidentiality of the patients will be maintained, and that the trial data sets will be accurately interpreted.