tumor with increasing ADC (VI), decreasing ADC (VD), or the total percentage of tumor unchanged (VU) were assessed by ROC Analysis to predict the probability of being alive one year from diagnosis. VI and VU were significant predictors (p=0.0001 and 0.0025, respectively). Overall survival of patients stratified by the median VI of the total population at 3 weeks was found to be significant (Kaplan Meier p=0.0046, log rank; hazard ratio 2.4 (95% C.I., 1.3 –4.8)). Similar results were observed by McDonald Criteria at 10 weeks (Kaplan Meier 0.0006; log-rank test; hazard ratio 2.9 (95% C.I., 1.7– 7.2)). Significant results were not observed for fDM at 1 and 10 weeks. These data support fDM as a validated early marker for treatment response in MG and reveal that fDM adds further prognostic value to conventional radiographic assessment. Preliminary examples will also be shown in non-CNS tumor types as well revealing the general extrapolation of this approach to a wide variety of clinical oncological applications.

**Conclusions:** The capability of acquiring fDM data in a wide variety of tumor types in the clinical setting provides the opportunity to pursue the validation of this approach as an early imaging surrogate of treatment response. The successful outcome of these studies would allow for individualization of patient care based upon this early, quantifiable imaging biomarker.

## S12
## MR spectroscopy for patient stratification and tumor monitoring

J. Griffiths. *Cancer Research UK – Cambridge Research Institute, Cambridge, UK*

**Introduction:** Magnetic Resonance Spectroscopy (MRS) is the only non-invasive modality that can monitor body chemistry in the living patient, so it can generate a unique class of biomarkers. MRS can be performed as part of a routine imaging examination on most hospital MRI instruments after minor modifications, and specialised laboratory instruments can be used for animal studies. I shall briefly describe two on-going multi-national studies on patients that are developing biomarkers for (i) diagnosing and grading brain tumours and (ii) predicting response to chemotherapy.

**Main Message:** Brain tumours are currently diagnosed by stereotactic biopsy – unpleasant and risky for the patient. Two EU programmes, INTERPRET (FP5) and eTumour (FP6, ongoing) [1], have developed a computer-based Decision Support System (DSS) that recognises the characteristic MR spectra of brain tumours, giving a non-invasive diagnosis and also the grade of malignancy. A database of >600 quality-controlled spectra, along with their associated images and clinical data, is available. A spectrum from a new case is compared with those in the database by a pattern recognition algorithm, and plotted in a data-space showing its relationship to spectra of tumours in the various classes [2]. The prototype DSS is surprisingly robust and has "learned" to ignore characteristics of different pulse sequences or instruments. In a prospective study it significantly improved the diagnostic accuracy of radiologists, even though many rarer tumour types are as yet insufficiently represented in the database.

A biomarker for predicting response to chemotherapy in individual patients would enable physicians to choose the most appropriate drug and avoid expensive administration of ineffective (but still toxic) agents. CoGMAC, an on-going, NCI-funded project, is developing a $^{31}$P MRS biomarker for predicting response to chemotherapy. After studying several tumour types the project focussed on non-Hodgkin's lymphomas (NHLs) [3]. Initially, CoGMAC tested the hypothesis that the $^{31}$P spectrum would change after a single round of chemotherapy to which the tumour responded, and this was, indeed, observed. However, it was shown that an even better prediction of response to chemotherapy could be obtained from the initial, pre-chemotherapy spectrum, by measurement of the ratio of the area of the PME peak to that of the NTP peak. This PME/NTP ratio was a better predictor of NHL response than the International Prognostic Index (IPI) which is currently used to predict response of NHLs to chemotherapy. When PME/NTP is combined with the IPI prediction is still better. This biomarker, too, has proved to be robust: it seems to work for all types of NHL and several chemotherapy regimes.

**Conclusions:** MRS-based biomarkers, which can already improve the diagnosis and treatment of cancer, could also be used to provide pharmacodynamic information in trials of novel anticancer drugs.

### References

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## S13
## Meta-analysis of gene-expression profiles: towards a unified understanding of breast cancer sub-typing and prognosis

C. Sotiriou. *Jules Bordet, Brussels, Belgium*

**Introduction:** It is evident that even though several breast cancer studies have generated a large number of arrays with complex genomic data, numerous questions remain unanswered. What is the relationship between the molecular classification and several prognosis signatures? What is the role of individual genes in a signature and what is their biological meaning? How are different prognostic signatures related with respect to prognostication and should clinical, pathological and currently used biomarkers be integrated in this process?

**Main Message:** To address these issues, our group, in collaboration with a team at the Swiss Institute of Bioinformatics, undertook a comprehensive meta-analysis of publicly available gene-expression and clinical data totaling 2833 breast tumors. In this meta-analysis we