Changes in metabolic profile of colorectal cancer undergoing chemoradiation therapy assessed by high-resolution magic angle spinning spectroscopy

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Purpose: Prediction and early monitoring of tumor response is a prerequisite for individualized cancer therapy. For locally advanced rectal cancer, preoperative chemoradiation therapy (CRT) has demonstrated to increase survival significantly for some of the patients; yet there are no ways to predict how individual patients will respond. Knowledge about the detailed biochemical and metabolic profile of the untreated tumor and the early changes could possibly predict the tumor's response to therapy. This first study examines the grouping of MR spectra from pretreatment tumor tissue and tumor tissue obtained after 6 Gy of CRT.

Materials and methods: Ten patients with locally advanced rectal cancer (T3-4,N0-2) underwent CRT. During radiation therapy, concomitant chemotherapy was administered as oxaliplatin (50 mg/m^2 once every week) and capecitabine (825 mg/m^2 x 2 daily). Surgery was performed 6-8 weeks after CRT completion. Pretreatment and following 6 Gy CRT, biopsies were snap frozen in liquid nitrogen and stored until high-resolution magic angle spinning spectroscopy (HRMAS) examination. The spectra were obtained using a Bruker Avance DRX600 instrument at 4°C and a spinning rate of 5kHz. Standard pulse-acquired spectra were obtained as previously described[1]. The MR spectra were mean normalised before scaling by the variable stability scaling method (VAST)[2]. This is a supervised scaling method, which utilize a priori knowledge of the samples and down-weights the least stable variables within each group of interest (in our case pre-treatment vs. treatment). Principal component analysis (PCA) with mean-centering and full cross validation was applied for the further analysis of the spectra.

Results and discussion: Representative HR-MAS spectra from tumor tissue from a patient with colorectal cancer before onset of therapy and after 6 Gy CRT are shown in Figure 1. The spectra show changes in several resonances, including lipids, glucose and creatine. In Figure 2, the score plot of principal component 1 and 2 from PCA of standard pulse-acquired spectra are presented. The spectra of biopsies taken pre-treatment (•) are clearly different from those taken after onset of therapy (■), and the two groups form two distinct clusters, mainly due to the variations described by PC1. These PCs describes 87% of the total variation in the original data. The histopathology will be correlated with the tumor's metabolic profile when the resection specimens have been analysed.

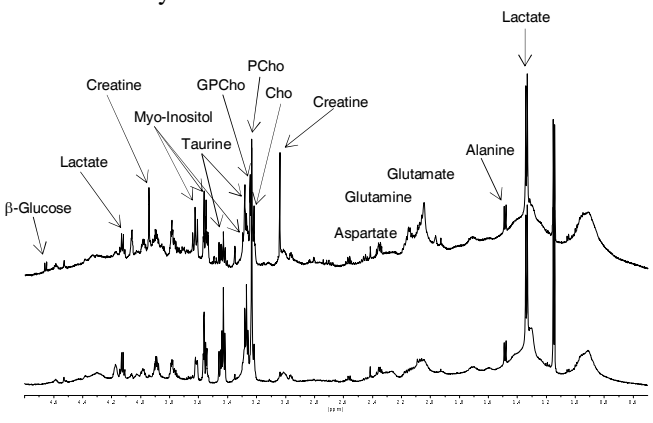

Figure 1: HR-MAS spectra from a tumor before (bottom) and after 6 Gy CRT (top)

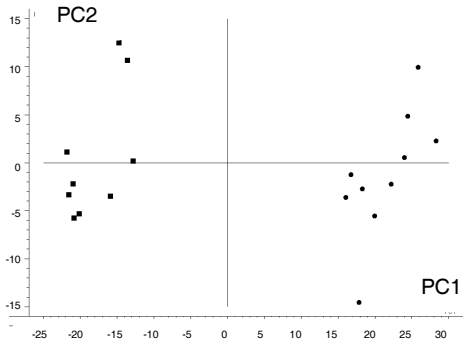

Figure 2: PC1 and PC2 from PCA of pretreatment and treatment tumor biopsies

Conclusion: MR tissue phenotyping reveals distinct changes in the metabolic pattern following CRT treatment of human colorectal cancer.

References: Sitter B et al, NMR Biomed 2006, 19, 30-40 2. Keun HC et al. Analytica Chimica Acta , 2003, 490:265-276