Prediction of response to chemo/radiation therapy of squamous cell carcinomas of the head and neck by ^{1}H MRS studies of choline

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Introduction

Higher choline levels have been observed in the primary tumor and metastatic lymph nodes of the head and neck squamous cell carcinoma (HNSCC) compared to normal muscle tissue using ex vivo ^{1}H MRS (1). It has also been reported that choline levels from tissue biopsy of patients exhibiting treatment failures were higher than the specimen of patients who exhibited treatment response (2). However, the use of in vivo ^{1}H MRS of HNSCC has been limited due to the presence of susceptibility and motion artifacts in this region. In this study we performed ^{1}H MRS in the metastatic cervical lymph nodes of HNSCC to assess the potential of choline as a biomarker for treatment response.

Materials and Methods

Single-voxel ^{1}H MR spectroscopy was performed with 32 patients using PRESS sequence at 1.5T (n=24) and 3T (n=8) Siemens scanners. All HNSCC patients were treatment naïve at the time of MRS study and had palpable metastatic cervical lymph node masses. A neuroradiologist identified these masses using routine multi-slices T1 and T2 weighted images. The MRS voxel was placed in the center of the metastatic node, based on the fat saturated T2 weighted images. The size of the voxel was varied according to the size of the tumor with a minimum voxel dimension of 10 mm in any one dimension in order to achieve spectra with decent SNR. Up to six outer volume saturation bands were placed around the voxel to suppress fat signals from the surrounding normal tissue. Water suppressed single voxel spectrum was acquired using a TR of 1.5 s, TE of 135 ms and 256 acquisitions. The use of intermediate TE (135 ms) allows for detection of choline, while serving as an additional "T2-filter" to suppress unwanted signals from mobile lipids. In order to compare the spectra from different patients and for longitudinal studies, an additional spectrum from the same voxel was acquired without water suppression. The integrals of total choline and water resonances were computed using a Siemens Leonardo workstation. The patients were categorized as complete responders (CR, with no evidence of disease), or partial responders (PR, with evidence of residual disease) based on clinical or pathological (if surgery was performed) assessment at the end of chemo-radiotherapy. The difference between the groups was tested using Mann Whitney U Test with 95% significance level. The institutional review board approved this study, and written informed consent was obtained from all subjects before the study.

Results and Discussion

Figure 1a shows an example of ^{1}H spectrum acquired from a metastatic cervical lymph node. At an echo time of 135 ms, the presence of lactate is indicated by an inverted peak at 1.3 ppm, as shown in Fig.1a. However, lactate signal was not consistently observed in all patients, partly due to lipid contamination. As such, we only analyzed total choline (tCho) in this study. Peak integrals from tCho peak were normalized to the integral of unsuppressed water peak to account for difference in voxel size used from these different patients. Figure 1b shows a scatter plot of tCho and residual tumor volume at the end of treatment. A negative correlation (although not significant) was observed between two measures. As emphasized by the exponential upper envelope of the scatter plot (dashed line), higher pre-treatment tCho appears to be associated with lower residual tumor volume at the end of the treatment. Although paradoxical to general belief that high choline levels correlate with higher malignancy (3) and treatment failure (2), these preliminary results suggest that higher pre-treatment tCho levels are suggestive of complete response, which can also be seen by the difference in the medians of CRs and PRs in Fig.1c. A higher level of hypoxic/necrotic regions in partial/non-responding patients may have contributed to the lower tCho signals from these tumors. These studies indicate that pre-treatment choline levels can be used as a marker for prediction of treatment response in patients with Head and Neck cancer, however, the study needs to be performed in a larger patient population to confirm this hypothesis.
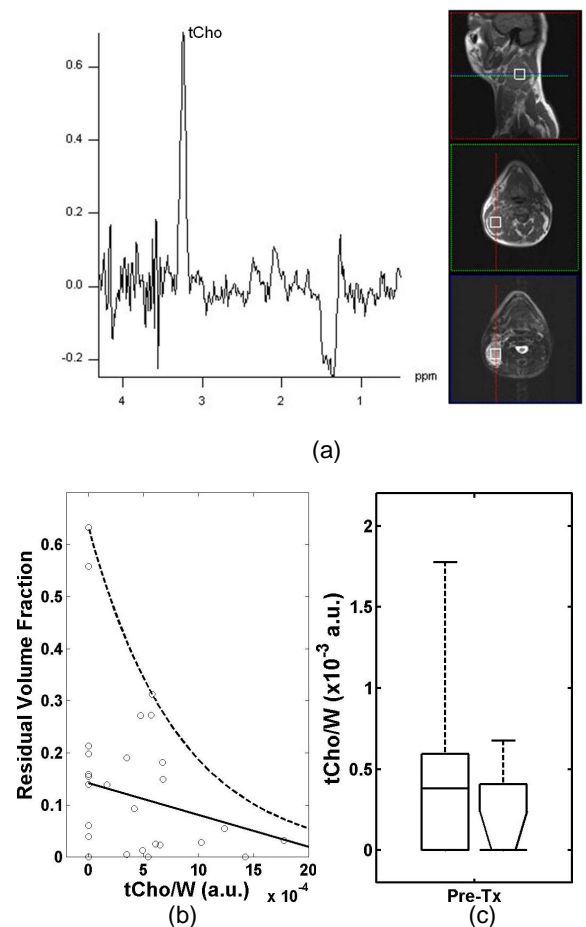

(a)

(b)

(c)

Figure 1. Representative ^{1}H spectrum (TE=135 ms) from a patient with HNSCC (a). A plot of the residual tumor volume versus pretreatment tCho/water ratios from all patients is shown in (b). Circles represent measured data and the solid line is the linear least-square fit whereas the dashed line shows the upper envelope of the data using an exponential function. An increased pre-treatment tCho/water ratio was observed from CR patients (rectangular box in Figure 1c) as compared to the median values from the PR group (box with notch).

Reference

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