Correlation of the Phospholipid-Related Signatures in ^{31}P and ^{1}H Spectra: An Approach to Increase the Sensitivity of the Prediction of Therapeutic Outcome in non-Hodgkin's Lymphoma by *In Vivo* MRS

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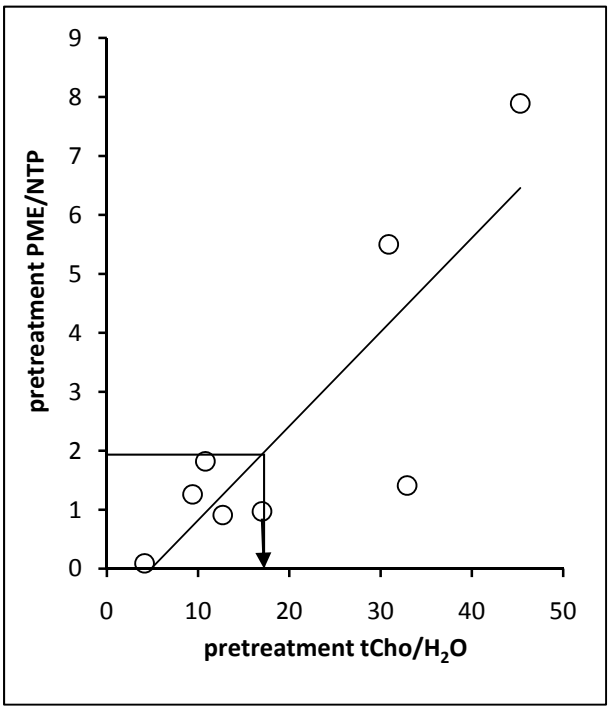
Our previous cooperative work using ^{31}P MRS to study non-Hodgkin's lymphoma (NHL) patients prior to the start of standard treatment has indicated that the sum of the phospholipid-related intermediates, phosphoethanolamine plus phosphocholine normalized to nucleoside triphosphates (PME/NTP) can successfully predict both the long-term response to treatment and the drug-free survival.[1] However, our cooperative results have been hindered by the inherent lack of sensitivity of ^{31}P MRS. Our previous work, which was carried at 1.5 T, was unable to study tumors below 15 milliliters of nominal volume (i.e., a cubic voxel of 25 millimeters per side) which raise two issues with regard to our results. First, a data selection bias might prevent our results from being generalized to the rest of the population if smaller tumors behave differently than larger ones. Second, the significant group of patients with smaller tumors that could not be studied under our protocol limits the clinical application of the technique.

The aim of our present work is to increase the sensitivity of our measurements and concomitantly increase the sensitivity of the prediction of therapeutic outcome in NHL patients. Our initial approach was to include ^{1}H MRS, which increases overall spectral acquisition time by only ten minutes. The rationale for this has been fourfold: the increased sensitivity of the MR determination of ^{1}H in comparison to ^{31}P, the more widely available ^{1}H measurement technology, the reported total choline (tCho) increase in ^{1}H MRS of several tumors that could serve as a marker of treatment response, and the fact that our ^{31}P MRS includes in the determination phosphocholine which is part of the tCho signal in ^{1}H MRS.

We report here our initial results correlating the pretreatment PME/NTP ratio determined by *in vivo* ^{31}P MRS, which we have shown predicts therapeutic outcome in NHL, with the tCho-to-water (tCho/H_2O) ratio determined by ^{1}H MRS.

Procedures & Patients, This work has been approved by the offices in charge of overseeing humans as subjects of research at each institution. Three dimensionally-localized, ^{1}H-decoupled, nuclear Overhauser enhanced, ^{31}P MRS using the chemical shift imaging (CSI) algorithm and a water-suppressed/not-water-suppressed pair of PRESS single voxel ^{1}H MR spectra using a TE of 135 ms were acquired *in vivo* in the tumors of eight NHL patients prior to start treatment, and the PME/NTP and tCho/H_2O ratios determined from the ^{31}P and ^{1}H tumor spectra respectively.

Results, The correlation of the PME/NTP *vs.* the tCho/H_2O ratios determined on each of the NHL patients prior to receive treatment is shown in the Figure. The correlation showed a statistically significant linear regression ($y = 0.16x - 0.77$, $r^2 = 0.7$, $p < 0.005$).



Discussion, We have previously reported that a lower pretreatment tumor value of the PME/NTP ratio predicts complete long-term response to cancer treatment in NHL patients, mainly in diffuse large B-cell and follicular lymphomas under anthracycline-based combination chemotherapy.[1] The PME/NTP cutoff found to differentiate between complete responses and all the other treatment responses was set at 1.9. Using this PME/NTP cutoff, the regression analysis shown in the Figure predicted that the cutoff for tCho/H_2O would be 16.7. This correlation suggests that prediction of treatment outcome may also be possible using the tCho/H_2O ratio determined by ^{1}H MRS. This will enable us to study tumors with volumes as small as 1 milliliter, based on the increased sensitivity of the MR observations of ^{1}H in comparison to those of ^{31}P. In addition the simultaneous determination of *in vivo* ^{31}P and ^{1}H MRS could provide additional information to carry out a more adequate evaluation of the NHL patient undergoing treatment.

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Reference, 1. Arias-Mendoza F, Payne GS, Zakian KL, et al: Pretreatment Phosphorus Magnetic Resonance Spectroscopy of non-Hodgkin's Lymphoma: improving the predictive value of the International Prognostic Index to therapeutic response. submitted to the Clin Cancer Res, 2009.