Prediction of Treatment Response in Follicular and Mantle Cell Lymphomas using *In Vivo* ^{31}P MRS before Treatment

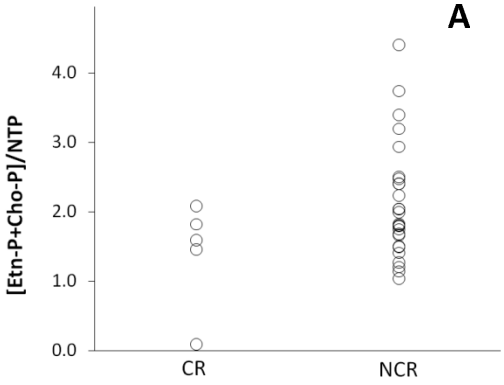
F. Arias-Mendoza[1], G. Payne[2], K. Zakian[3], M. Stubbs[4], H. Mojahed[1], A. Shukla-Dave[3], N. R. Maisey[2], D. Cunningham[2], H. Poptani[5], M. R. Smith[6], O. A. O'Connor[7], J. Zain[7], S. J. Shuster[8], A. D. Zelenetz[9], G. A. Follows[10], J. Raemaekers[11], M. MacKenzie[11], M. O. Leach[2], J. A. Koutcher[3], J. R. Griffiths[4], A. Heerschap[12], J. D. Glickson[5], and T. R. Brown[1]

[1]Radiology, Columbia University, New York, NY, United States, [2]Radiology, Royal Marsden Hospital, London, United Kingdom, [3]Radiology, Memorial Sloan Kettering Cancer Center, New York, NY, United States, [4]Radiology, Cambridge University, Cambridge, United Kingdom, [5]Radiology, University of Pennsylvania, Philadelphia, PA, United States, [6]Clinical Oncology, Fox Chase Cancer Center, Philadelphia, PA, United States, [7]Clinical Oncology, Columbia University, New York, NY, United States, [8]Clinical Oncology, University of Pennsylvania, Philadelphia, PA, United States, [9]Clinical Oncology, Memorial Sloan Kettering Cancer Center, New York, NY, United States, [10]Clinical Oncology, Addenbroke's Hospital, Cambridge, United Kingdom, [11]Clinical Oncology, Radboud University Nijmegen Medical Center, Nijmegen, Netherlands, [12]Radiology, Radboud University Nijmegen Medical Center, Nijmegen, Netherlands

Introduction: Non-Hodgkin's lymphoma (NHL) is a heterogeneous group of more than 20 histologically distinct malignancies. It is the fifth most common cause of adult cancer in the US with the fourth largest economic impact of all cancers. Our international multi-institutional research program has previously demonstrated that the *phosphoethanolamine* plus *phosphocholine* [Etn-P + Cho-P] to total nucleotide triphosphates (NTP) ratio acquired prior to treatment predicts treatment failure and drug-free survival in the most commonly observed NHL variant, Diffuse Large B-Cell Lymphoma (DLBCL) (F Arias-Mendoza, et al Proc. ISMRM, 2008). These tumors are conventionally treated with cyclophosphamide, hydroxydoxorubicin, oncovin and prednisone (CHOP) or similar treatments. We have also recently reported that addition of rituximab to the treatment protocol did not alter the predictive benefit of [Etn-P + Cho-P]/NTP in DLBCL.

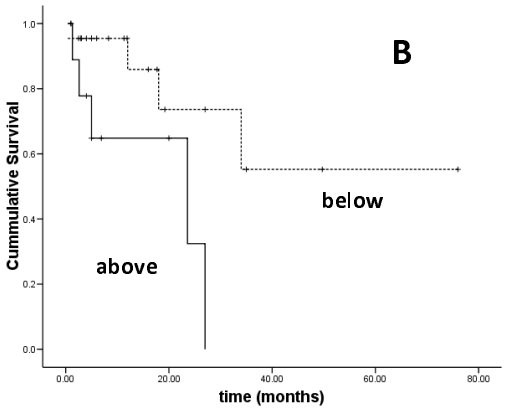
In this work, we studied less frequent histological subtypes of NHL (mainly follicular and mantle cell lymphomas) to test the utility of the [Etn-P + Cho-P]/NTP ratio in predicting treatment failure and drug-free survival in these patients.

Procedures & Patients: 3D-localized, ^{1}H-decoupled, nuclear Overhauser enhanced, ^{31}P MR spectroscopy was performed in the tumors of all patients. Selection of patients was based on clinical data completeness and adequate spectral quality, which resulted in a total of 32 patients including 19 with Follicular Lymphoma (FL), 6 with Mantle Cell Lymphoma (MCL) and 7 with other types (excluding DLBCL). Long-term treatment response was assessed six-months after treatment completion using bidimensional radiological measurements in serial CT scans following the WHO criteria. The patients were grouped as those with either a complete response (CR) and those without a complete response (NCR). The latter group included patients with partial responses, and stable or progressive disease. In addition, drug-free survival (DFS) was defined as the time in months between the end of treatment and initiation of new treatment.



Results & Discussion: The pre-treatment [Etn-P + Cho-P]/NTP mean ± standard error (number of cases in parenthesis) for the CR and NCR cases were 1.41 ± 0.35 (5) and 2.11 ± 0.16 (27) respectively. A t-test demonstrated significant differences between the CR and NCR values ($p < 0.04$). However, a Fisher test did not show any significant difference due in part to the low number of patients exhibiting complete response (n = 5).

We have previously shown that increased sensitivity of the [Etn-P + Cho-P]/NTP ratio can be achieved by combining our measurements with the international prognostic index (IPI), a clinical prognosis parameter c ommonly utilized in DLBCL. Using the IPI information, the 32 patients from the present study were divided into low and high risk groups and their pre-treatment [Etn-P + Cho-P]/NTP values were plotted accordingly. A cutoff for each IPI group was generated using ROC curves correctly classifying as many cases as possible. The combined cutoffs identified as the IPI-dependent pre-treatment [Etn-P + Cho-P]/NTP threshold divided the cohort of patients studied into two groups. These two groups were analyzed for their drug-free survival using Kaplan-Meier curves and evaluating the test differences using the Tyrone-Ware procedure (Figure **B**). In these tests, a significant drug-free survival difference exists amongst the patients above (solid line in Fig. **B**) and below (dotted line in the figure) the IPI-dependent threshold ($p < 0.04$), The patients divided by cutoffs based on IPI or [Etn-P + Cho-P]/NTP alone did not show significance.



Conclusion: In previous studies we have shown that we can predict treatment response and disease-free survival in both a full cohort of NHL patients and the subset of patients with DLBCL using the [Etn-P + Cho-P]/NTP ratio. Our purpose in the current study was to test if this parameter was only sensitive in prediction of treatment response to DLBCL tumors or if it could be used as a more generalized marker for prediction of treatment response in the less common forms of NHL as well.

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