# Biochemical Characterization of Lymphadenopathy in Tuberculosis, Sarcoidosis and Metastasis using In vitro MRS

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## OBJECTIVE

To evaluate the potential of in vitro MR spectroscopy in the differential diagnosis of lymphadenopathy in patients with tuberculosis, sarcoidosis and metastasis.

## INTRODUCTION

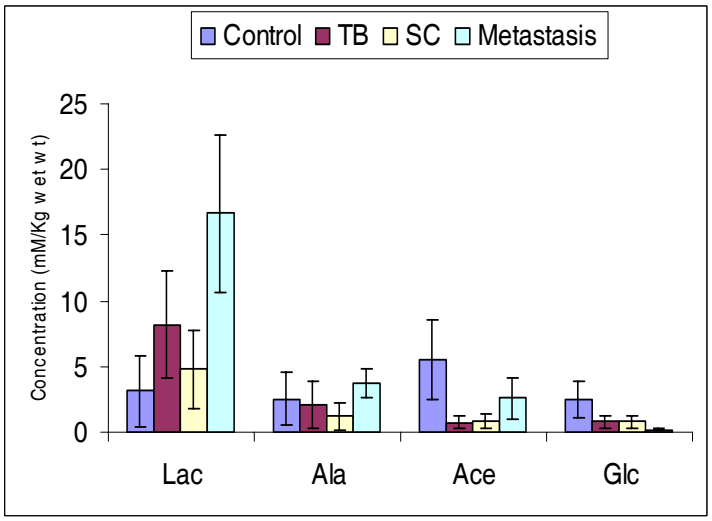
Lymphadenopathy occurs in diseases like tuberculosis (TB), carcinoma and sarcoidosis (SC). Distinguishing the cause is often challenging especially the differentiation of TB from SC and also can be confused with malignant diseases. Based on the node size, the extent of lymphadenopathy may be assessed using radiological imaging procedures like computed tomography, ultrasonography and chest radiography. However, to determine the exact cause, histopathology is necessary which also fails to differentiate between TB and SC. Recently, we reported detection of axillary metastasis in breast cancer patients using in-vitro MR spectroscopy (1,2). In present study, the biochemical profile of enlarged lymph nodes of patients with tuberculosis, sarcoidosis and metastasis was investigated using in vitro MRS and compared with normal lymph nodes to understand the metabolic changes accompany these diseases and to evaluate whether such biochemical markers would assist in the differential diagnosis of lymphadenopathy.

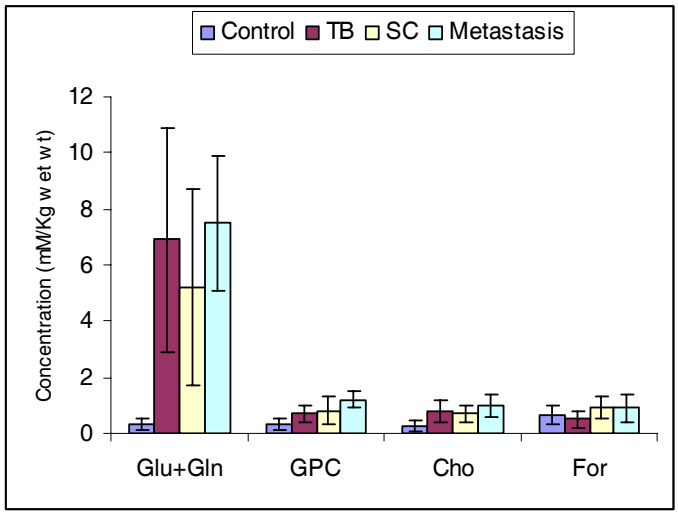
## MATERIAL AND METHODS

Thirty nine patients (age range 14-73 yrs, mean age 35 yrs) with lymphadenopathy due to suspected diagnosis of tuberculosis, sarcoidosis, or metastasis over a period of two years from November 2004 to November 2006 were included in the study. Of the 39 nodes, 20 were tubercular, 8 had metastatic deposits, and in 11 were sarcoidosis as per histopathological evaluation. Clinical evaluation, hemogram, liver and kidney function tests, chest X-ray, CECT chest (if chest X-ray is abnormal), fundus examination and angiotensin converting enzyme level in suspected sarcoid patients and investigations for fitness for surgery were carried out in all these patients. Lymph nodes were considered as sarcoid nodes only after clinical correlation, fundus examination, measuring angiotensin converting enzyme levels, and ruling out the possibility of tuberculosis or any other granulomatous disease. Histopathological normal nodes (n=10) from breast cancer patients served as controls. The surgically dissected nodes were bisected. One half was immediately frozen and stored in liquid nitrogen for MRS study while the other was sent for conventional histopathological evaluation. The perchloric acid extracts of the lymph nodes were prepared using the standard protocol and lyophilized powder obtained was dissolved in 0.6 ml of $D_2O$ solvent. Sodium trimethyl silyl- (2,2,3,3-H4) propionate (TSP) was added as a standard for chemical shift and quantification of concentrations of metabolites. 1D proton spectra with water suppression were acquired at 400 MHz (DRX-400, BRUKER, Switzerland) with a relaxation delay of 14s. Concentration of metabolites were determined by comparing the integrated intensity of isolated resonances of the compounds of interest with that of the TSP signal. The concentration of metabolites in various diseases was compared using one-way ANOVA test for multiple comparisons.

## RESULTS

Figures below show the graphic representation of the concentration of metabolites in nodes with tuberculosis, sarcoidosis, metastasis and controls. Significant difference was observed in the concentration of Lac, Ace, Glu+Gln, Cho and Glc ($p < 0.05$) in nodes from patients with TB and SC compared to controls. Elevated levels of concentration of Lac, Ace, Glu+Gln, Cho, Glc and GPC ($p < 0.05$) metabolites were observed in nodes with metastatic deposits compared to control nodes. Nodes from patients with tuberculosis showed higher concentration of Lac ($p < 0.05$) compared to patients with sarcoidosis.




## DISCUSSION

To the best of our knowledge, this is the first study to evaluate the biochemical profile of lymph nodes in tuberculosis, sarcoidosis and its comparison to control and metastatic nodes. Significantly higher concentration of Lac and membrane metabolites GPC and Cho were observed in metstatic compared to control nodes suggesting proliferating activity of cancerous cells. Our results showed higher concentration of Lac in nodes from TB patients compared to the patients with Sarcoidosis indicating higher anaerobic respiration activity in patients with TB. Concentration of formate was found to be higher in sarcoidosis nodes compared to TB. The results provide an insight into the differences in the metabolic activity of cells in lymphadenopathy due to TB and sarcoidosis and suggest the clinical usefulness of in vitro MRS in the differentiation of TB and sarcoidosis.

## REFERENCES

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