

# Pattern recognition methods in $^1\text{H}$ in vivo NMR studies of cerebellum tumors

## 1. INTRODUCTION

Central nervous system (CNS) tumors are frequent childhood malignancies and posterior fossa tumors accounts for two-thirds of all pediatric brain tumors [1-2].

$^1\text{H}$  nuclear magnetic resonance *in vivo* spectroscopy (MRS) is a powerful, noninvasive tool for investigating metabolic changes in intact brain. It is also widely utilized in investigation and classification of brain tumors [3-4]. The present study combines MRS and pattern recognition (PR) method – the partial least squares discriminant analysis (PLS-DA), in order to reveal differences in metabolic profiles of the most common types of cerebellar tumors diagnosed in children. PR methods proved to be useful in metabolomics and complex biological data analysis [5-6], and begin to gain popularity in the analysis of *in vivo* proton spectra [4].

## 2. MATERIALS AND METHODS

The studied group consisted of 21 patients (median age 14) with diagnosed cerebellum tumors. All of them were after brain irradiation with total dose 54 Gy and day fraction 1.8 Gy (median values). Four histopathologically confirmed groups has been distinguished:

- medulloblastoma (MB) (12 cases – 57.14%)
- astrocytoma (AST) (5 cases – 23.8%)
- ependymoma (EPN) (3 cases – 14.3%)
- glioblastoma (GBM) (1 case – 4.76%)

Patients were examined from one to several times in extended time in order to monitor treatment effects (Figure 1). The 121  $^1\text{H}$  MRS spectra were acquired using the whole-body MRI/MRS system operating at a field strength of 2T and a proton resonance frequency of 81.3 MHz. The volumes of interest of  $1.5 \times 1.5 \times 1.5 \text{ cm}^3$  were located in the left and right hemispheres and at the center of the cerebellum. A PRESS sequence was applied with the following parameters: TR=1500 ms, TE=35 ms and 50 Acq.

In order to visualize the metabolic differences between tumor types Partial Least Squares Discriminant Analysis (PLS-DA) supported with the orthogonal signal correction (OSC) [7] spectral filtering was applied to unresolved spectra in the range from 0.2 to 4.0 ppm.

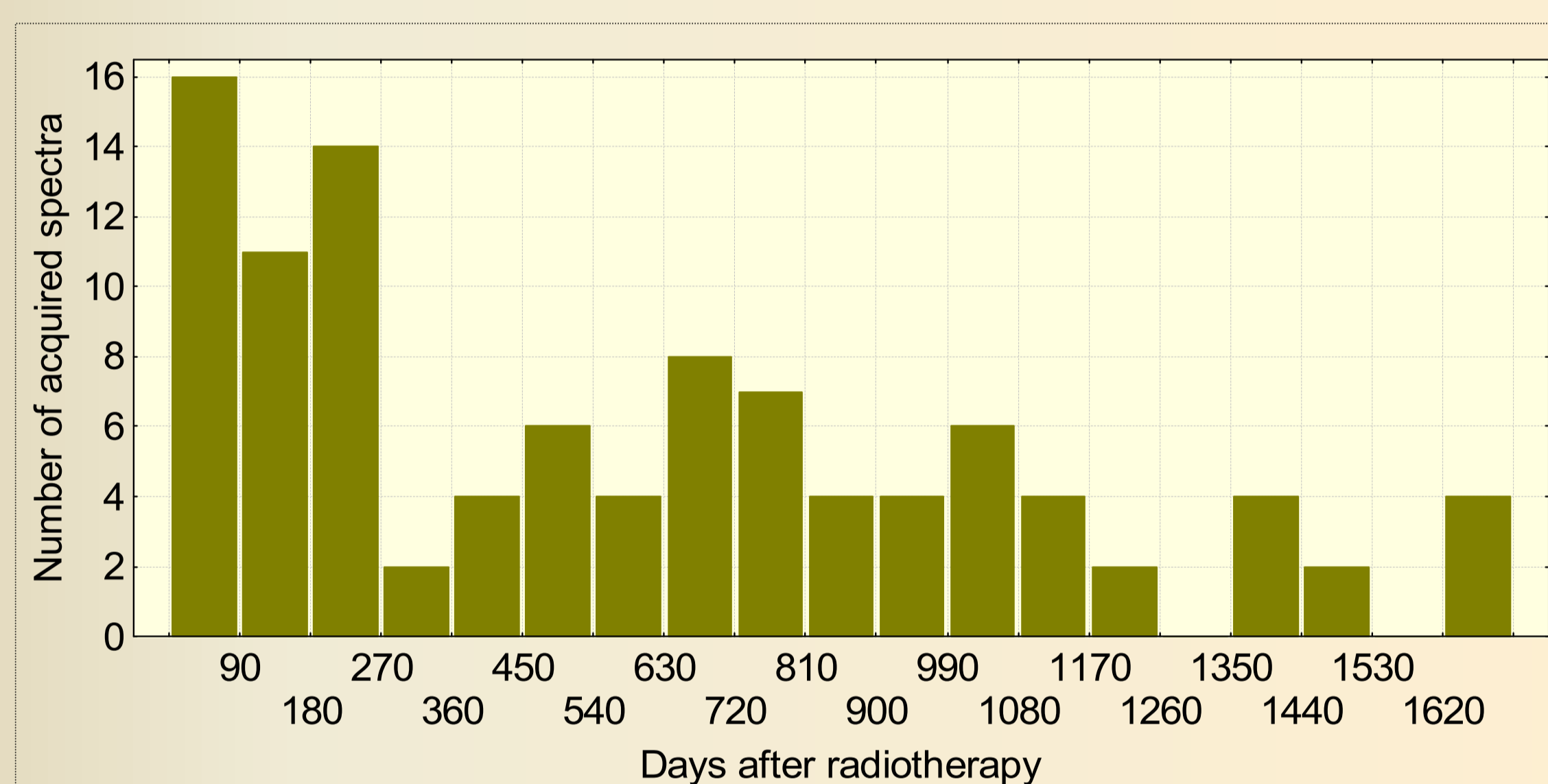


Figure 1. Number of spectra acquired during the treatment monitoring.

## 3. RESULTS AND DISCUSSION

Analysis of all tumor groups resulted in a one-component model with the explained X and Y variance equal  $R^2X=0,353$  and  $R^2Y=0,133$ , respectively, and the predictive ability  $Q^2=0,121$ . This model separates GBM from remaining tumors (Figure 2a). X-weights plot (Figure 2b) shows significant increase of mobile lipids levels at 0.9 ppm and flattening of the rest of the spectra in GBM (Figure 2b).

To achieve more robust separation GBM group was removed from the data. The successive analysis resulted in a two-component model with  $R^2X=0,326$  and  $R^2Y=0,352$ , respectively, and the predictive ability  $Q^2=0,19$ . A clustering according to the histopathological data is apparent (Figure 3a). Mixing of AST and MB spectra indicates some differences between both the groups. However, the first group tends to fill the first and fourth quarter while the majority of the latter group spectra is located in the second quarter of scores plot.

The spectral regions responsible for the clustering are identifiable in the X-weights plot (Figure 3b). EPN is characterized by the elevation of the spectral region between 0.86-1.28 ppm corresponding to mobile lipids and macromolecules. Significant increase of alanine (1.48 and 3.76 ppm), taurine/scyllo-inositol (3.33 ppm), glucose (3.43 ppm) and myo-inositol (ml) (3.56 ppm) observed in AST and the increased creatine/phosphocreatine (Cr) (3.0 and 3.94 ppm), glutamate/glutamine (Glx) (2.1-2.5 ppm) and N-acetyl-aspartate (NAA) (2.0, 2.6 ppm) levels in MB distinguish both the groups.

The early radiation brain damage is found to be characterized by a decrease of Cr and NAA, while increase of lipids and decrease of remaining metabolites' levels is characteristic for the late radiation injury (data not shown).

## 4. CONCLUSIONS

$^1\text{H}$  MRS combined with PR methods effectively differentiate cerebellum tumor types as well as distinguish early and late radiation metabolic changes. Moreover, the PR methods provide information on spectral regions responsible for data clustering.

Such an approach allows raw data to be used in the analysis and gives fast and easily interpretable results presented in a graphical form.

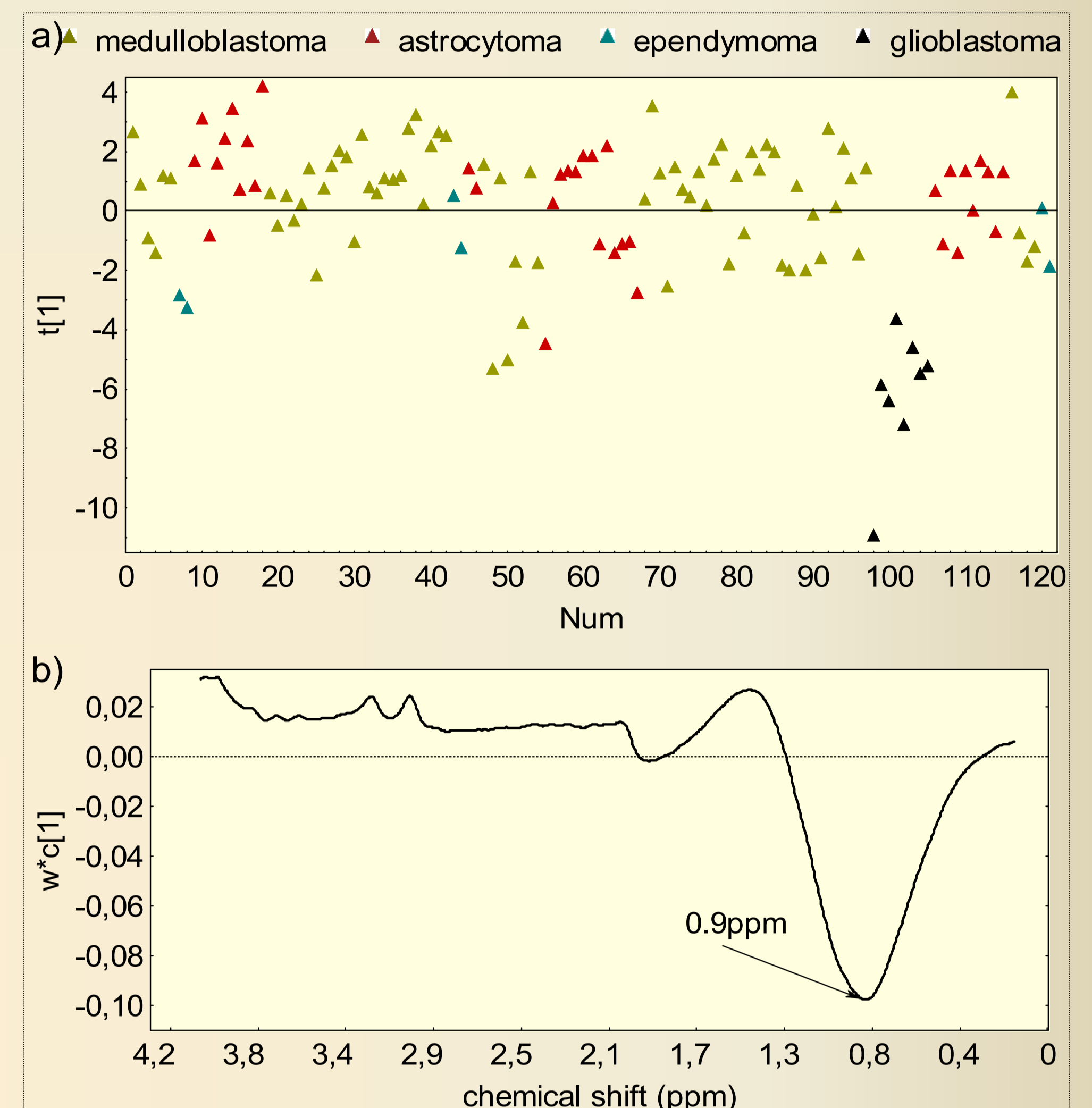


Figure 2. PLS-DA scores (a) and X-weights (b) plots for the model obtained for all the analyzed groups. GBM (▲) is strongly separated.

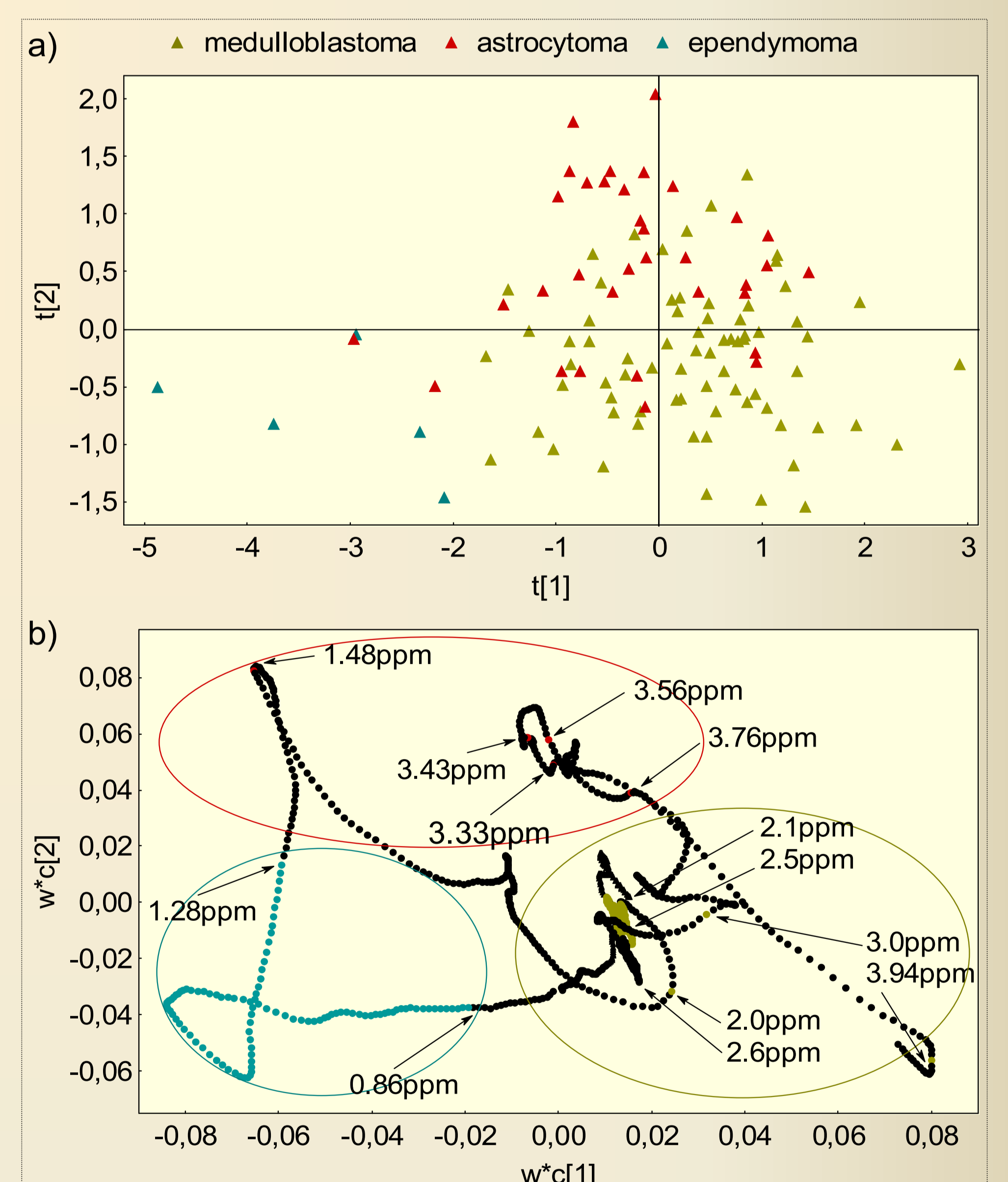


Figure 3. PLS-DA scores (a) and X-weights (b) plots for the model obtained for the data with the GBM group excluded. Clustering is markedly improved, however only the ependymoma group (▲) is clearly separated. X-weights plot shows the spectral regions/peaks positively correlated with the particular group.

## References:

1. Warren KE et al. Proton magnetic resonance spectroscopic imaging in children with recurrent primary brain tumors. *J Clin Oncol.* 2000; 18: 1020-1026.
2. Beebe DW et al. Cognitive and Adaptive Outcome in Low-Grade Pediatric Cerebellar Astrocytomas: Evidence of Diminished Cognitive and Adaptive Functioning in National Collaborative Research Studies (CCG 9891/POG 9130). *J Clin Oncol.* 2005; 23: 5198-5204.
3. Devos A et al. Classification of brain tumours using short echo time  $^1\text{H}$  MR spectra. *J Magn Reson.* 2004; 170: 164-175.
4. Menze BH et al. Optimal classification of long echo time *in vivo* magnetic resonance spectra in the detection of recurrent brain tumors. *NMR Biomed.* 2006; 19(5): 599-609.
5. Bertram HC et al. A metabolomic investigation of splanchnic metabolism using  $^1\text{H}$  NMR spectroscopy of bovine blood plasma. *Analytica Chimica Acta.* 2005; 536: 1-6.
6. Ramadan Z. et al. Metabolic profiling using principal component analysis, discriminant partial least squares, and genetic algorithms. *Talanta* 2006; 68: 1683-1691.
7. Wold S et al. Orthogonal signal correction of near-infrared spectra. *Chemom Intel Lab Sys.* 1998; 44: 175-185.