# AUTOMATED DETECTION OF HUMAN BRAIN TUMORS USING IN VIVO $^1$H MR SPECTRA OF HEALTHY BRAIN TISSUE

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***Abstract:*** *Presence of a brain tumor affects the metabolite concentrations of healthy brain tissue. This study inspects the qualification of MR spectroscopy recordings of this tissue for automatic tumor patient classification with linear discriminant analysis, artificial neural networks and support vector machines. With spectroscopy datasets reduced down to the concentrations of two different metabolites, a classification performance of approximately 80% could still be achieved.*

***Keywords:*** *MR-spectroscopy, brain tumors, classification, multilayer perceptrons, support vector machines*

## Introduction

While the current criterion standard for brain tumor detection is biopsy with subsequent histological assessment, in vivo $^1$H magnetic resonance (MR) spectroscopy has been recognized as a possible non-invasive alternative over the past decades. This radiological method allows localized recordings of relative or absolute metabolite concentrations within the brain, which in turn differ significantly for healthy and pathological brain tissue [1]. Furthermore, it has recently been shown that tumors influence the spectrum of "healthy" tissue localized in the contralateral hemisphere as well [2]. In this study, the feasibility of several machine learning techniques for tumor patient classification based upon such spectra is demonstrated in detail.

Especially the metabolite N-acetylaspartate can serve as a marker for neural integrity as its concentration depletes with most brain lesions. Busch et al. already emphasized its pivotal role for the oncological analysis of MR spectroscopy data [2]. This study additionally addresses the question whether other metabolite concentrations assessable by MR spectroscopy are also eligible for the classification task.

## Materials

In total 264 spectra of 96 different persons were considered. 135 spectra were recorded from 52 patients with the region of interest placed above the ventricle in the hemisphere contralateral to the tumor. The remaining data originated from a healthy control group. Although the patients' data was labeled according to the outcome of histological examinations (Tab. 1) and the tumor types are relevant from a medical point of view, they were not distinguished in this study due to low patient numbers.

Table 1: Number of spectra and patients with regard to the biopsy-based tumor classification.

| Tumor classification | Spectra | Patients |
|---|---|---|
| Astrocytoma II | 17 | 3 |
| Astrocytoma III | 20 | 6 |
| Glioblastoma | 88 | 28 |
| Metastasis | 6 | 4 |
| Without histology | 4 | 3 |

The data comprised relative concentrations of the metabolites N-acetylaspartate (Naa), choline containing compounds (Cho), creatine (Cre), myoinositol (Myo) and the sum of glutamate and glutamine (Glx).

Each test dataset was build using 20% of the overall data, the corresponding training sets contained 60 - 80% depending on validation requirements of the algorithms. All test errors were averaged over 100 experiments to avoid bias which might be introduced by a specific choice of datasets.

## Classification algorithms

Three different supervised learning methods were applied for the automatic distinction between healthy and diseased persons. The regularized linear discriminant analysis (LDA) [3] is a multivariate statistical method based on covariance estimates under the assumption of classwise normal distributed features. It strives to maximize the interclass and minimize the intra-class variances by conducting a linear separation in the input space.

Artificial neural networks (ANNs) consist of units – the so-called neurons – which are arranged in layers. The connections between neurons pertaining to subsequent layers are governed by adaptive weights. During the learning phase, these weights are adjusted by error backpropagation (IRprop+ [4]) employing a cross-entropy function. In this study, feed forward networks with one hidden layer consisting of at most seven neurons were used. The activation for these neurons was modeled by a Fermi function.

Support vector machines (SVMs) [5] are maximum-margin classifiers. They implicitly perform a kernel-induced, not necessarily linear mapping of the input data into a so-called feature space in order to linearly separate the data afterwards. For the benefit of the overall classification performance, the soft-margin SVMs utilized in this study allow certain misclassifications under penalty. Gaussian kernels with diagonal covariance matrices were used as well as

Table 2: Percentaged mean classification error for different metabolite combinations. Exclusively the best results are given for each algorithm. (N) indicates a normalization of all underlying concentrations with respect to Cre. For SVMs, the applied kernel is denoted by (G) for Gaussian, (L) for linear and (P) for polynomial.

| Metabolites | LDA | ANN | SVM | LDA (N) | ANN (N) | SVM (N) |
|---|---|---|---|---|---|---|
| Naa, Cho, Cre, Myo, Glx | 17.4±5.0 | 15.3±4.0 | 12.0±7.2 (P) | | | |
| Naa, Cho, Myo, Glx | 18.0±5.6 | 15.7±4.4 | 14.2±6.0 (P) | 16.6±4.9 | 16.6±4.7 | 14.5±4.3 (P) |
| Naa | 37.5±6.0 | 40.2±5.5 | 43.0±6.5 (L) | 23.1±5.9 | 23.7±4.3 | 21.8±3.0 (G) |
| Naa, Cre | 23.7±5.4 | 24.2±3.9 | 25.7±4.5 (P) | | | |
| Naa (N), Cho, Cre, Myo, Glx | 16.5±4.8 | 14.2±4.8 | 15.4±5.3 (P) | | | |
| Cre | 31.9±6.2 | 31.0±4.6 | 32.7±4.3 (P) | | | |
| Cho, Cre, Myo, Glx | 28.9±5.7 | 22.1±5.4 | 16.6±7.8 (P) | | | |
| Cho, Cre, Myo | 29.1±6.1 | 25.3±4.8 | 20.0±7.2 (P) | | | |
| Cho, Cre, Glx | 29.6±5.3 | 21.4±5.8 | 16.0±7.1 (P) | | | |
| Cre, Myo, Glx | 27.1±5.1 | 22.9±4.7 | 20.8±6.0 (P) | | | |
| Cho, Myo, Glx | 30.6±5.2 | 24.0±5.1 | 20.2±6.4 (P) | 44.0±6.5 | 38.4±7.3 | 36.4±4.9 (P) |
| Cho, Myo | 32.5±5.8 | 34.6±4.2 | 27.0±6.2 (P) | 42.2±5.9 | 45.8±4.8 | 38.8±4.3 (L) |
| Cho, Glx | 31.2±5.4 | 24.5±5.4 | 21.9±5.5 (P) | 45.3±6.5 | 39.5±9.8 | 35.9±5.1 (P) |
| Myo, Glx | 30.3±5.9 | 25.2±5.4 | 18.1±7.5 (P) | 44.7±6.1 | 41.0±6.4 | 32.1±9.0 (G) |

linear kernels and polynomial ones of degree two. The parameters of all Gaussian kernels were chosen via kernel target alignment optimization [6]. The regularization constant was fixed to 1,000 or 10,000 depending on kernel choice.

## Results

The mean error rates of all classification techniques upon different datasets comprised of the concentrations of one or more metabolites are summarized in Tab. 2. The lowest rate of 12.0±7.2% was achieved with SVMs on the full set of metabolites. In general, SVMs outperformed the LDA as well as the ANNs in nearly all classification tasks.

The Naa and Cre values alone contained only enough information to reach an error rate as low as 37.5±6.0% respective 31.0±4.6%. However, under normalization with respect to Cre the Naa-value based tumor detection improved to a rate of 21.8±3.0%. This observation of decline was limited to datasets including Naa and consistent only for LDAs. Elsewise, the normalization usually gave rise to an increased number of erroneous classifications.

Albeit the most accurate classification results were obtained by incorporating the Naa concentrations, tumor detection was also viable with other metabolites only. Without Naa, the lowest mean error of 16.0±7.1% was reached with Cho, Cre and Glx responses. But also combinations of two metabolites provided enough information for sustaining an error rate as low as 18.1±7.5% (Myo, Glx).

## Discussion

Coincident with Busch et al. [2], a strong decrease in classification performance of LDAs was observed if Naa concentrations were discarded. ANNs and SVMs were also affected by the absence of Naa values in a similar way. However, combinations of the remaining metabolite concentrations contained almost an equal amount of information as normalized Naa values, leading to classification results of up to approximately 80%. Remarkably, it was not decisive which metabolites were included in these combinations. This finding is particularly useful for cases where some relative concentrations are missing.

In contrast to our expectations, normalizing the concentration values with respect to Cre generally lead to increased error rates. This indicates the possibility of relations between the unnormalized metabolites, which are found implicitly by the algorithms. Overall, the results show that SVMs employing linear and polynomial kernels in particular are well suited for the tumor patient classification task. This may be especially relevant for early cancer diagnosis since the required data can be collected from apparently healthy tissue and therefore no indication of tumor presence is necessary in advance.

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