In vivo MRS metabolic profiles of human brain metastases from different primary cancers

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Introduction

Recent strategies in oncology are focusing on more individualized treatment depending on the biological characterization of the tumors. Furthermore, the need for early evaluation of response is increasing in order to optimize and avoid ineffective treatment. MR spectroscopy provides biochemical profiles of tumors in vivo and has been reported to differentiate brain tumors in several studies [(1-3)]. Brain metastases are characterized by high lipid and choline content, and lower levels of other metabolites like N-acetyl aspartate [(2)]. The objectives of this study were to characterize brain metastasis originating from different primary cancers, and to correlate the spectra with clinical outcome for the patients.

Experimental

Single volume 1H MR Spectra were obtained from patients (n=21, age 59±12) with brain metastases (n=27) using a 3T clinical MR system (Philips Intera). The patients had primary breast cancer (n=7), lung cancer (n=8), malignant melanoma (n=4) or colon cancer (n=2). Six of the patients had two or more metastases and spectra were then obtained from two of them. The MR examination was performed before any treatment of the metastases was started. The MRI protocol consisted of standard T_1 - and T_2 - weighted images, including contrast enhanced MRI. The volume of interest (VOI) was located within the tumor, with a size of 10x10x10 or 15x15x15 mm^3 using point resolved spectroscopy pulse sequence (PRESS) with repetition time (TR) 2000 ms and echo time (TE) 33 ms. All acquisitions were obtained with 192 measurements. Bandwidth, number of points and sampling interval were 2000Hz/1024/0.5ms. The data was examined using the multivariate method principal component analysis (PCA). Grouping tendency of spectra due to origin of metastases and clinical outcome (grouped in < 3 month survival or > 3 months survival after first MR examination) of the patients were examined.

Results and discussion

Mean spectra of the in vivo 1H MR spectra of brain metastases are shown in Figure 1. Most spectra are dominated of lipid signals. Choline compounds are detected in a majority of the metastases (n=20), while NAA was detected in only three patients (one primary breast and two primary lung metastases). The PCA shows a trend to cluster brain metastases from primary lung and breast cancer, while the metastases from malignant melanomas showed no uniformity (Figure 2). The two colon metastases are clustered in the upper right quadrant of the score plot. The separation is based on PC1 and PC2, which account for more than 77 % of the total variation of the spectra. Samples expressing high score in PC1 are characterized by increased lipid and reduced choline level, as described by the loading profile of PC1 (Figure 3). These results show that the metabolic profiles of brain metastases contain information that can characterize metastases from different origin. There was no clear grouping of MR spectra related to clinical outcome (survival). This correlation will be analyzed further using other multivariate approaches and by including a larger number of patients.

Conclusion

The tumor biology, including MRS determined metabolic profiles, might be valuable clinical information when planning the treatment of brain metastases, and also when deciding to terminate further therapies. These metabolic profiles must be evaluated further to assess the clinical value of in vivo MRS of brain metastases.

References

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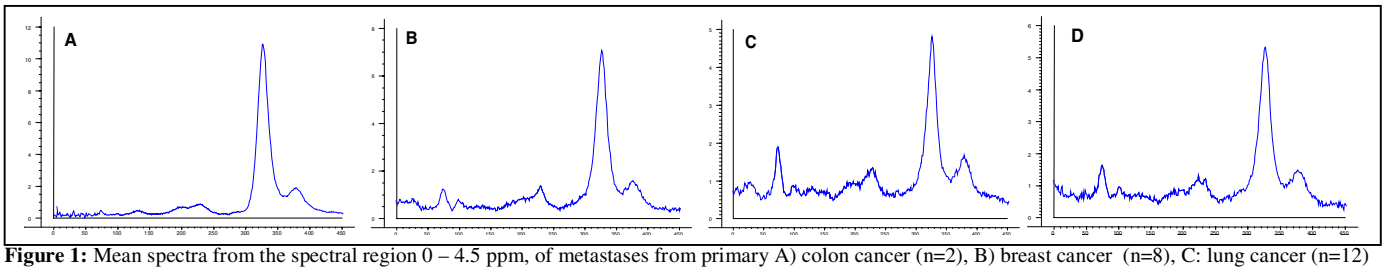

Figure 1: Mean spectra from the spectral region 0 – 4.5 ppm, of metastases from primary A) colon cancer (n=2), B) breast cancer (n=8), C: lung cancer (n=12) and D: malignant melanoma (n=5).

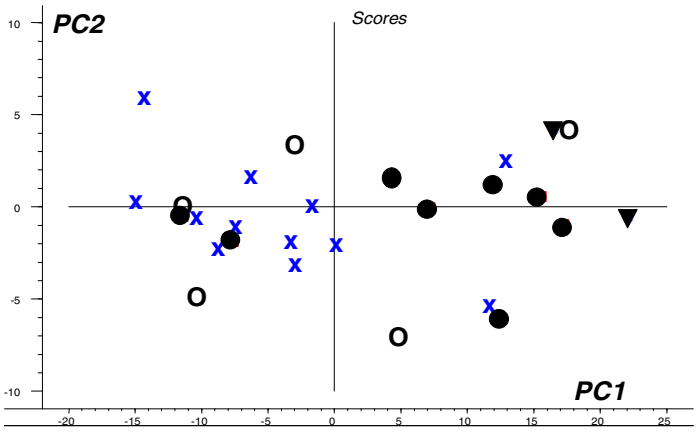

Figure 2: Score plot of PC1 and PC2 from principal component analysis of in vivo spectra (spectrum region 0 – 4.5 ppm) of metastases (n=27) in patients with different primary cancer; ▼ = colon, ● = breast, **X** = lung, **o** = malignant melanoma.

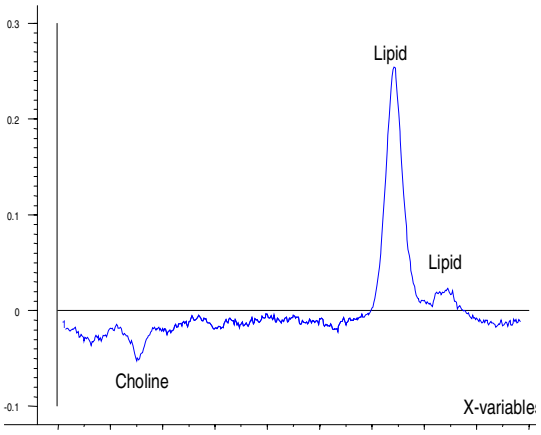

Figure 3: Loading profile of PC1, representing 77% of the spectral variations.