Differential diagnosis of brain tumor recurrence and radiation necrosis using MR spectroscopy

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Target audience

Physicians and Physicists using MR spectroscopy in neurooncology will benefit from this information.

Introduction

MR imaging (MRI) represents a method of choice for non-invasive characterization of human brain lesions, but its specificity is fairly low. In the presence of a new enhancing lesion, for example, MRI does not allow a confident differential diagnosis (DD) between a recurrence of a viable tumor and a reaction to radiochemotherapy (RChT). MR spectroscopy (MRS) can help in these cases as these two types of histopathological lesions are supposed to show different metabolic profile. Nevertheles, the literature confronting this issue has not produced a solid DD protocol yet. Most of the authors suggest using increased Cho/Cr as a marker of tumor recurrence. It is known that tumors show increased total choline (Cho) and unchanged total creatine (Cr). However, RChT is also proved to alter metabolism in the treated area, including Cr levels[1]. On this basis, we decided to compare MRS and histopathology data using stereotactic biopsies navigated by merged MRI and 3D MRS data and to compare different MRS evaluation methods to validate published results.

Subjects and Methods

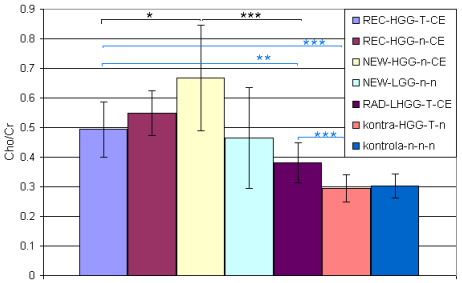
52 patients with a diagnosis of an intracranial tumor and 59 healthy subjects were examined using a 3T imager equipped with a Tx/Rx head coil. 24 patients underwent surgical resection and consequent RChT. 5 patients were examined repeatedly. In 14 patients the diagnosis was assessed on the basis of a specimen obtained by open-frame navigated biopsy during subtotal or total lesion resection; in 9 cases an MRI-3D MRS merged dataset was used for navigation. The diagnosis of radionecrosis was assessed by a physician according to the modified McDonald criteria after at least 6 months of follow-up.

All the subjects provided an informed consent in agreement with local Ethical Committee rules.

The measurement protocol consisted of anatomical T2-weighted MRI, native or T1-weighted CE MRI and 2D and 3D spectroscopic imaging (2D PRESS-SI with and without water suppression, phase encoding 16x16, FOV=160x160x15mm, TR/TE/NA=1510ms/30ms/4 and 3D PRESS-SI with water suppression, phase encoding 14x14x12, FOV 160x160x90 mm, TR/TE/NA=1200ms/135ms/1). SI data were analyzed by a program jSIPRO[2] with LCModel[3]. 2D metabolic data were referenced to the water signal.

5 different methods of data evaluation for DD between tumor recurrence and radionerosis were tested: M1: comparison of lesional Cho/Cr values in patients` group and the mean values over all regions in control group. M2: comparison of Cho between patients and controls. M3: interhemispheral comparison of Cho/Cr in each patient and the assessment of the best threshold for DD. M4: interhemispheral comparison of Cho values in the individual patient and the assessment of the best threshold for DD. M5: M4 + comparison of the same regions in patients and controls if data from contralateral region is not available.

Fig.1: Mean Cho/Cr values over subject groups: HGG-high grade gliomas, LGG-low grade gliomas, REC-tumor recurrence, RAD-radionecrosis, NEW-newly diagnosed tumor T-treated by radiochemotherapy, CE-contrast enhanced lesion on T1-weighted MRI, kontra-contralateral hemisphere to the lesion, kontrola-controls, n-no treatment, no CE
* p<0.01, ** p<0.005, *** p<0.001



Results

Statistically significant different Cho/Cr values were found between group of primary and group of treated recurrent high grade gliomas (HGG), as well as between treated recurrent HGG and radionecrosis (Fig.1). Neither Cho nor Cr showed significant difference between recurrent tumors and radionecrosis. Cr values in treated lesions were significantly lower than in controls or contralateral hemisphere. Interhemispheral comparison of individual patients showed increased Cho values in tumor recurrence and decreased Cho in radionecrosis (Fig. 2). Both groups showed increased Cho/Cr and decreased NAA, NAA/Cr, Cr, Ins. Irradiated tumors with necrotic regions showed significantly increased Cho/Cr, but only slightly increased or decreased Cho levels and increased Lactate. Sensitivity of DD between recurrent tumor and radionecrosis based on generally used M1 reached 78%, but specificity only 43%. M2 reached sensitivity of 63% and specificity of 50%. Threshold of interhemispheral difference in M3 set to 20% reached sensitivity of 78% and specificity of 25%. The threshold in M4 set to 15% reached sensitivity of 78% and specificity of 88%. M5 reached sensitivity of 89% and specificity of 91%.

Discussion

Our data confirmed the significant difference of Cho/Cr between the group of recurrent HGG and radionecrosis. However, interhemispheral comparison showed a reduction of Cr in both lesion types attributable to radiochemotherapy. It results in increased Cho/Cr in both groups and consequently in poor specificity of M1 and M3. We conclude that Cho/Cr is not an appropriate marker for DD in individual subjects. As significant metabolite changes were found in various regions of healthy brain, the use of mean values from all brain regions as a threshold for DD (M1, M2) is insufficient. The most convenient method is the assessment of the parameter difference between ipsi- and contra-lateral region (in %). Moreover, careful interhemispheral comparison can be useful for monitoring treatment response as treated tumors showed significantly lower Cho than primary tumors.

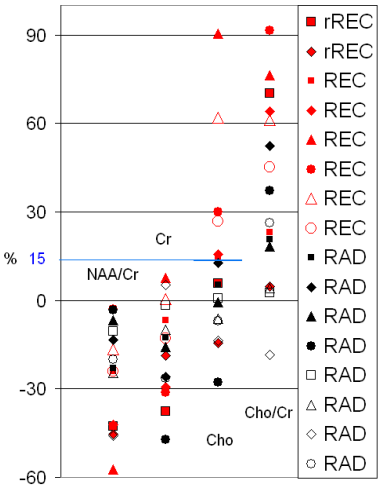


Fig.2: Ipsi- vs contra-lateral differences of selected parameters in individual patients. NAA-total N-acetyl aspartate, Cr-Creatine, Cho-Choline, REC-tumor recurrence, rREC-regressive recurrent tumor, RAD-radionecrosis.

Conclusion

The comparison of MRS results with histopathologic findings showed that the best method for DD between tumor recurrence and radionecrosis seems to be the interhemispheral comparison of Cho values in individual subjects. Tumor recurrence shows interhemispheral Choline increase higher than 15%, while radionecrosis shows Choline reduction or increase up to 15%.

References

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