Potential of Relaxation-Weighted ^{23}Na-MRI for Brain Tumor Characterization

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Introduction

In brain tumors, the average ^{23}Na-concentration is typically increased due to edema and sustained cell depolarization, a precursor of cell division [1]. It was already shown that relaxation-weighted ^{23}Na-MRI can be used to separate tumor compartments [2]. In this work it was evaluated whether relaxation-weighted ^{23}Na-MRI can provide additional information for tumor grading. Therefore, 16 patients suffering from different brain tumors (14 WHO grade I – IV and 2 metastases) were examined at 7 Tesla with ^{23}Na-MRI with different relaxation weightings.

Methods

^{23}Na images were acquired on a 7 T whole body system (Magnetom 7 T, Siemens Healthcare Solutions, Erlangen, Germany) using a double-resonant (^{1}H: 297.2 MHz; ^{23}Na: 78.6 MHz) quadrature birdcage coil (Rapid Biomed GmbH, Rimpar, Germany). Anatomical images, including T_1 weighted (T1w) images before and upon contrast media administration, were acquired in the clinical routine workup using a 3 Tesla MR system (Magnetom Tim Trio, Siemens Healthcare, Erlangen, Germany).

$^{23}NaT_N$: Acquisition of the total sodium concentration with minimized relaxation-weighting (TE/ TR= 0.3/ 120 ms; $\alpha = 90°$, readout length: $T_{RO} = 10$ ms; nominal spatial resolution = (4 mm)^3; acquisition time: $T_{AQ} = 10$ min).

$^{23}NaT_H$: To achieve a higher spatial resolution of (2.5 mm)^3 while maintaining an acceptable image acquisition time, TR was shortened resulting in minor T_1 -weighting (TE/ TR/ T_{RO} = 0.5/ 25 /20 ms; $\alpha = 55°$; $T_{AQ} = 13$ min 20 s).

$^{23}NaR_{IR}$: An inversion recovery (IR) preparation was applied to exploit T_1-differences of ^{23}Na ions. Signal arising from ^{23}Na compartments with longitudinal relaxation times like in CSF ($T_1 = 64$ ms) was suppressed by using an inversion time of TI = 41 ms (TE/ TR/ T_{RO} = 0.6 – 0.8/ 185 /10 ms; (5.5 mm)^3, $T_{AQ} = 10$ min).

$^{23}NaR_{SUB}$: A fast ($T_{AQ} = 2$ min 30s) ^{23}Na multi-echo sequence was applied to exploit differences in T_2^*-relaxation times (TR/ T_{RO} = 30/ 10 ms; $\alpha = 68°$; (5 mm)^3. Images with echo times $TE_A = 0.6$ ms and $TE_B = 13$ ms were subtracted using a weighted difference. The weighting factor $e^{+(TE_B - TE_A)/T_2^{*,CSF}}$ was chosen such that T_2^*-times like in CSF (T_2^* (CSF) = 56 ms) were fully suppressed. All ^{23}Na-MRI measurements used a density-adapted 3D radial projection pulse sequence [3].

To keep the total exam time short, not all sequences were applied for each individual patient ($^{23}NaT_N$, $^{23}NaT_H$, $^{23}NaT_{IR}$, and $^{23}NaT_{SUB}$ imaging were applied to 12, 6, 14, and 10 out 16 patients, respectively). Results from ^{23}Na imaging were correlated with the Mib-1 proliferation rate of tumor cells. For comparability, signal of tumor, edema and CSF ($^{23}NaX_Y$) normalized to healthy brain tissue ($^{23}NaX_{healthy}$) was calculated according to following equation: $^{23}NaX_Y[\%] = (^{23}NaX_Y - {}^{23}NaX_{healthy}) \;/\; {}^{23}NaX_{healthy}$

Results

In 15 out of 16 patients ^{23}NaT imaging revealed elevated total ^{23}Na signals of tumor tissue, whereas an increased relaxation-weighted ^{23}Na tumor signal was found in five out of 16 patients (Fig. 1a). Perifocal edema (present in six patients) exhibited hyperintense signals in ^{23}NaT imaging and hypointense signals in ^{23}NaR imaging (Fig. 1b). The pattern of signal changes in ^{23}NaT and ^{23}NaR was consistent for all WHO grade I – III brain tumors with elevated ^{23}NaT and decreased ^{23}NaR signals of tumor tissue. In all five glioblastomas the ^{23}NaR signal was higher than the maximal ^{23}NaR signal of WHO grade I – III tumors (Fig. 1a). Exemplarily images of a glioblastoma are shown in Fig. 2. Regression analysis revealed a positive correlation between normalized ^{23}NaR signal of tumors and Mib-1 proliferation rate ($R^2 = 0.74$, $p_{corr} < 0.00$) (Fig. 3a), whereas no correlation was found between ^{23}NaT signal and Mib-1 proliferation rate (Fig. 3b). Also, no correlations were found between normalized ^{23}Na signal and other histopathological markers such as mitotic activity, cell density and vascularization.

Discussion

An increased signal in both ^{23}NaT and ^{23}NaR imaging suggests tissue with an elevated concentration of sodium ions with short relaxation times. This signal increase might be due to an increase of the intracellular ^{23}Na concentration indicating a breakdown of the Na+ / K+ - ATPase and / or the Na+ co-transporter, e.g. in tumors with high proliferation rates as indicated by the positive correlation of ^{23}NaR signal and Mib-1 proliferation rate (Fig. 3a). Results from published animal studies also suggest an intracellular weighting of the $^{23}NaR_{IR}$ signal [4]. An elevated signal in ^{23}NaT imaging along with a decreased signal in ^{23}NaR imaging might be compatible with an increased extracellular volume fraction (e.g. due to edema, c.f. Fig. 1b). It should be noted, that a pathologically altered density of the intra- or extracellular matrix might evoke changes in ^{23}NaR signal intensities as well. Although this study is not suited for describing the physiological processes behind the ^{23}NaR signal, our results allowed for a correct separation of all gliomas into WHO grade I – III and WHO grade IV tumors. This indicates that ^{23}NaR imaging reveals valuable physiological tissue characteristics different from ^{23}NaT imaging and might provide significant information for a functional *in vivo* tissue characterization.

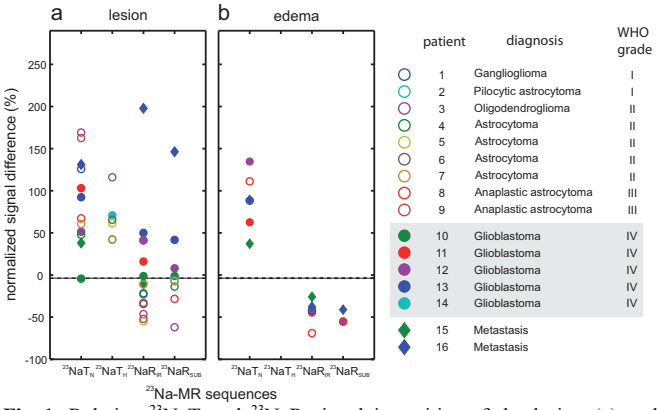

Fig. 1. Relative ^{23}NaT and ^{23}NaR signal intensities of the lesion (a) and perifocal edema (b). All glioblastomas exhibited ^{23}NaR signals higher than the WHO grade I – III tumors (a). Perifocal edema (b) showed hyperintense signals in ^{23}NaT and hypointense signals in ^{23}NaR imaging.

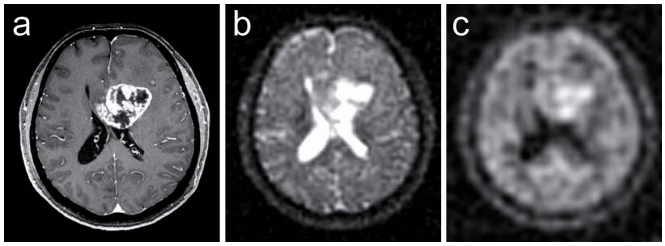

Fig. 2. Glioblastoma (WHO grade IV). (a) T1w imaging revealed rim enhancement upon contrast media administration. b) $^{23}NaT_H$ imaging demonstrated an increased signal of tumor tissue. c) $^{23}NaR_{IR}$ imaging yielded elevated signals mainly of the central tumor portion.

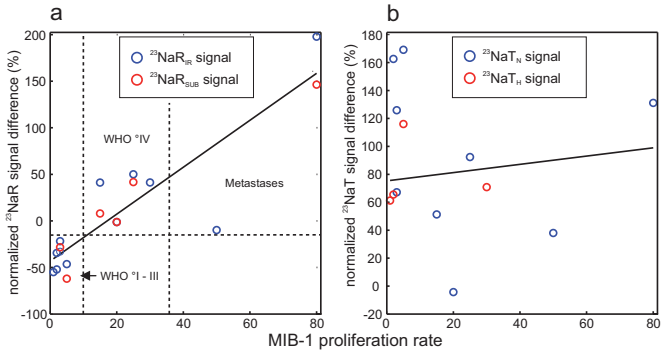

Fig. 3. Linear regression analysis demonstrated a positive association between ^{23}NaR signal and Mib-1 proliferation rate (**a**). There was no association between ^{23}NaT signal and Mib-1 proliferation rate (**b**).

References

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