Separation of Sodium Compartments for Characterization of Tumor Tissue by ^{23}Na-MRI

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Introduction

Sodium (^{23}Na) ions play an important role in cellular homeostasis and cell viability. In brain tumors, the average ^{23}Na-concentration is typically increased due to edema and sustained cell depolarization, a precursor of cell division (1). In this work 12 patients with different brain tumors were investigated with different ^{23}Na-contrasts (spin-density, ^{23}Na-FLAIR) to separate ^{23}Na-signal compartments. Additionally, for one glioblastoma patient ^{23}Na-T_1- and ^{23}Na-T_2^*-maps were acquired.

Methods

^{23}Na-images were acquired on a 7 T whole body system (Magnetom 7 T, Siemens Medical 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). Additionally, T_2-FLAIR- and contrast-enhanced T_1-images were acquired with a 3 T MR system (Magnetom Tim Trio, Siemens Medical Solutions, Erlangen, Germany). All ^{23}Na-MRI measurements used a density-adapted 3D radial projection pulse sequence (2). To visualize the local sodium concentration, T_1 weighting in the gradient echo data sets was minimized by using a long TR of 120 ms (^{23}Na-conc). The other parameters for the concentration measurements were: TE = 0.35 ms, $\alpha = 90°$, spatial resolution (4 mm)^3, acquisition time T_{AQ} = 10 min. To suppress signal from sodium ions in an unrestricted environment, a second 3D data set was acquired with an inversion recovery preparation, exploiting the differences in the T_1 times of the free and restricted sodium ions (^{23}Na-FLAIR; parameters s. fig.).

After image acquisition both sodium data sets were visually compared to the contrast-enhanced T_1-weighted images acquired at 3 T, and ^{1}H-FLAIR images. In total, 12 patients were investigated (7 without therapy; 4 upon surgery, 1 following radiotherapy). The heterogeneity of the lesions concerning the sodium compartments (increased ^{23}Na-concentration with both, suppressed and non-suppressed parts in ^{23}Na-FLAIR images) was visually inspected.

In one glioblastoma patient, T_1/T_2^*-maps were calculated from 5 ^{23}Na-FLAIR / 2 multi echo ^{23}Na acquisitions (^{23}Na-ME). Furthermore, a double echo sequence (^{23}Na-DE) was used where the second echo was subtracted from the first to suppress long T_2^*-components (^{23}Na-DE: TE_1/TE_2 = 0.6 / 13 ms, TR = 30 ms; α = 68°; T_{AQ} = 2 min 30 s; resolution: (5 mm)^3; ^{23}Na-FLAIR: TE/ TR = 0.55/ 251 ms; TI = 3/ 20/ 40/ 60/ 100 ms; resolution (6 mm)^3; Hamming-filtering; T_{AQ} = 5 min 14 s; ^{23}Na-ME: a) TE = 0.45/ 7.2/ 14/ 21/ 28/ 35/ 42/ 49 ms; b) TE = 4/ 11/ 18/ 25/ 32/ 39/ 46/ 53 ms; TR = 65 ms; α = 81°; T_{AQ} = 10 min 50 s; resolution: (4 mm)^3).

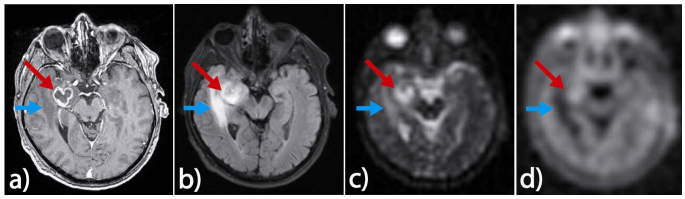

Fig. 1. Images of a glioblastoma patient. a) contrast-enhanced T_1-MPRAGE b) T_2-FLAIR c) ^{23}Na-DA-3DPR-conc. d) ^{23}Na-FLAIR (TE/TR = 0.75/124 ms; TI = 34 ms; resolution: (5 mm)^3; Hamming-filtering; T_{AQ} = 10 min 20 s). One part of the lesion is suppressed in the ^{23}Na-FLAIR image, whereas the other part shows high signal intensity.

Results

In Fig. 1 images of a patient with a right temporo-mesial glioblastoma multiforme (prior to therapy) are shown. The ^{23}Na-conc image shows a high sodium concentration within the tumor lesion. In the frontal part of the tumor a concentration similar to that in the cerebrospinal fluid (CSF) is found, whereas the lateral section shows only a minor ^{23}Na-signal increase (Fig. 1c). In the ^{23}Na-FLAIR images, CSF is well suppressed, as is the signal in the lateral tumor section (Fig. 1d). However, the frontal part of the tumor still shows a high ^{23}Na-FLAIR-signal, whereas both parts of the lesion are hyperintense in the ^{1}H-FLAIR images (Fig. 1b). The frontal region exhibits peripheral contrast media enhancement with central necrosis (red arrows; Fig. 1a).

In Fig. 2, images of a glioblastoma patient after surgical removal of the right fronto-parietal tumor are depicted. Signal arising from the right frontal-parietal resection-cavity is suppressed in the ^{23}Na-FLAIR-image (blue arrow), whereas the contrast media enhancing part (red arrow) of the lesion shows high ^{23}Na-signal intensities.

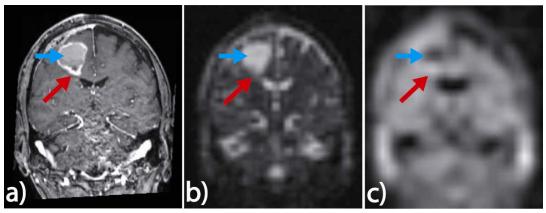

Fig. 2. Images of a glioblastoma patient after tumor-resection. a) contrast-enhanced T_1-image. b) ^{23}Na-conc. d) ^{23}Na-FLAIR (TE/TR = 0.75/190 ms; TI = 37 ms; resolution: (5.5 mm)^3; Hamming-filtering; T_{AQ} = 10 min 20 s). The resection-cavity is suppressed in the ^{23}Na-FLAIR-image (blue arrow), whereas the enhancing part (red arrow) shows a high signal.

In Fig. 3, images of a patient following surgical resection of a right-frontal oligodendroglioma are shown. The rim of the resection-cavity exhibits high signal-intensities in all acquired sodium image-contrasts (Fig. 3a-c), but no contrast media uptake. Within the resection-cavity, T_1 and T_2^* values ($T_1 \approx 55$ ms; $T_2^* \approx 42$ ms) are decreased compared to CSF ($T_1 \approx 61$ ms; $T_2^* \approx 59$ ms). 7 patients (3 patients without therapy, all (4) surgery patients) showed a heterogeneity of the lesions, whereas in 5 patients (4 patients without therapy, 1 radiotherapy patient) no heterogeneity in the ^{23}Na-signal could be detected.

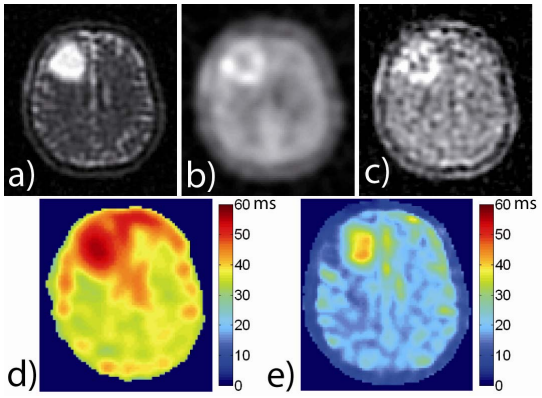

Fig. 3. Images of an oligodentroglioma patient after surgery. a) ^{23}Na-conc. b) ^{23}Na-FLAIR (TE/TR = 0.65/185 ms; TI = 37 ms; resolution: (5.5 mm)^3; Hamming-filtering; T_{AQ} = 9 min 52 s). c) Subtracted image of the ^{23}Na-DE-sequence. d) ^{23}Na-T_1-map; e) ^{23}Na-T_2^*-map.

Discussion

Devoid of contrast media enhancement, the lateral part of the glioblastoma multiforme in Fig. 1 is identified as vascular edema (blue arrow). Here, ^{23}Na-ions exhibit similar T_1-relaxation times as in CSF, indicating a much higher mobility than in healthy brain tissue. In the contrast-enhancing frontal parts the blood brain barrier is disrupted, and an increased cell proliferation is expected. This is consistent with the observed high ^{23}Na-concentration and the increased ^{23}Na-FLAIR signal. The high ^{23}Na-signal at the rim of the resection-cavity (Fig. 3a-c) might also indicate an increased intracellular ^{23}Na-concentration. However, this increase might be caused by increased cell proliferation or alternatively postoperative changes, since all surgery patients showed heterogeneity in the sodium signal.

The observed signal homogeneity in 5 patients might also be due to the limited resolution of ^{23}Na-MRI, which is particularly pronounced in ^{23}Na-FLAIR. A further limitation of ^{23}Na-FLAIR is a the high RF energy deposition due to the 90° and 180° pulses. This SAR-limitation requires long pulses (1 ms – 2 ms), which are then susceptible to off-resonances due to a small bandwidth. Here, a subtraction technique based upon ^{23}Na-DE sequence data (s. Fig. 3) might serve as a fast alternative to ^{23}Na-FLAIR.

Our findings demonstrate that a combination of ^{23}Na-contrasts can separate different ^{23}Na-compartments, which might be of importance for the early detection of tumor malignancy.

References

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