

Predicting and monitoring treatment response with DWI

Harriet C. Thoeny

DWI as predictive parameter for treatment outcome

DW-MRI has been shown to have potential in the prediction and monitoring of treatment response of different tumors (1-7). A strong negative correlation was found between mean pretreatment tumor ADC in patients with rectal cancer and the percentage size change of tumors after chemotherapy and chemoradiation (1). Tumors with higher ADC values had a poorer prognosis, probably due to more necrotic areas.

In patients with brain malignancies undergoing radiation therapy using high b-value DW-MRI, all responding lesions showed an increase in the ADC soon after initiation of treatment whereas all non-responding lesions showed no change or a decrease. These findings suggest the great potential of DW-MRI for noninvasive monitoring of treatment response (5).

The potential that pretreatment ADC maps may indicate the outcome of therapy was shown in an animal tumor model where tumors with the lowest ADC values before treatment with a vascular targeting agent still had viable tumor cells on histology after treatment in contrast to those with higher ADC values (6).

Published data suggest the potential of DW-MRI as predictor of therapy outcome. The findings of the different studies lead to the hypothesis that tumors with a lower ADC and therefore higher cellularity before treatment will be more sensitive to cytotoxic and radiation treatment, whereas tumors with higher ADC levels and therefore more areas of necrosis will be more sensitive to agents that interfere at the vascular level.

Monitoring treatment response

DW-MRI is a promising noninvasive tool for in vivo monitoring of treatment-induced changes and provides information on both vascular changes as well as cellular integrity (6). Noninvasively obtained early knowledge of response to treatment is clinically useful as it helps in making decisions regarding treatment options individual patients at an early time point, thereby preventing unnecessary toxicity from prolonged ineffective treatment of non-responding tumors. By the same token expensive therapies might also be avoided.

Cellular and vascular changes in response to treatment precede changes in size and might therefore be an early surrogate marker for treatment outcome (8; 7). In particular, vascular targeting agents show early intratumoral changes without a decrease in tumor volume in contrast to other anticancer therapies, such as cytotoxic agents and irradiation (7; 9).

DW-MRI provides information about microscopic structures such as cell density and integrity or necrosis (10). Thus, a viable tumor can be differentiated from a necrotic tumor with DW-MRI but not with conventional MR imaging (11).

It has been shown that DW-MRI is able to discriminate between non-perfused but viable and necrotic tumor tissue for early monitoring of therapeutic effects of vascular targeting agents (7). Furthermore, DW-MRI and dynamic contrast-enhanced MR imaging showed similar changes induced by vascular targeting agents, whereas DW-MRI provided initial information about intratumoral cell viability versus necrosis (7). One might therefore speculate that DW-MRI is able to see vascular changes after treatment as well as to discriminate between viable and necrotic tumors at an early stage and would be an indirect biomarker for apoptosis. In most malignant tumors (highly cellular tumors) a response to treatment would be reflected in an increase in ADC. This hypothesis has already been corroborated in several anatomic sites, including breast cancer (12; 13), primary and metastatic cancer to the liver (14; 15),

and primary sarcomas of bone (16; 17). Early after initiation of therapy however a decrease in ADC might be observed due to cellular swelling or reduction in blood flow depending on treatment, tumor type, and timing of imaging. Cellular swelling has been noted to occur in the early phases of apoptosis in response to anticancer treatment (18; 19), whereas later on fibrosis and scarring can be observed after successful treatment as reported for rectal cancer (1). As these two biophysical changes are reflected in a decrease in ADC, the exact time points of imaging during the respective therapies as well as the response of the different tumor types have to be defined in larger scale studies.

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