Combination of perfusion and diffusion-weighted MRI for functional evaluation of therapeutic response of lung cancer

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Introduction:

Magnetic resonance (MR) is widely applied as an important non-invasive tool to investigate tumor angiogenesis. Dynamic contrast-enhanced MRI (DCE-MRI) provides important pharmacokinetic parameters which can measure sensitive pathophysiological characteristics and detect changes in tumor vasculature after injection of contrast agents used for kinetic distribution within the region of interest (ROI). Diffusion-weighted MRI (DW-MRI), which generates an apparent diffusion coefficient (ADC), is the tool to evaluate diffusion of water molecule which is also correlated with the direction of fibers and tumor cellularity. Evidence has shown that alteration of structure and blood perfusion of tumors, including apoptosis, necrosis, fibrosis, etc. occurs after treatment. In addition, increased ADC has been reported to be an indicator of early tumor response to chemotherapy or target therapy. Hence, combination of both DCE-MRI and DW-MRI provides more comprehensive understanding of change of internal tumor composition. Many preclinical studies have indicated that the addition of various types of antiangiogenic or antivascular therapy to single-dose or fractionated radiotherapy can synergistically improve the response of human and murine tumors to treatment.

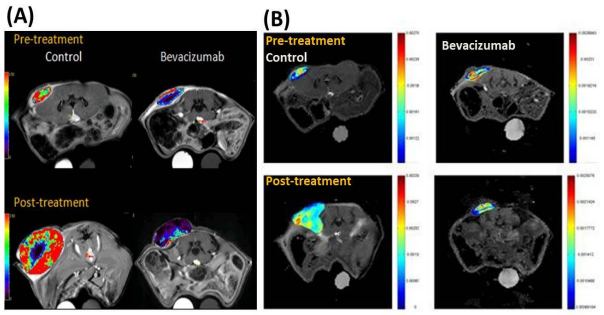

Fig.1.

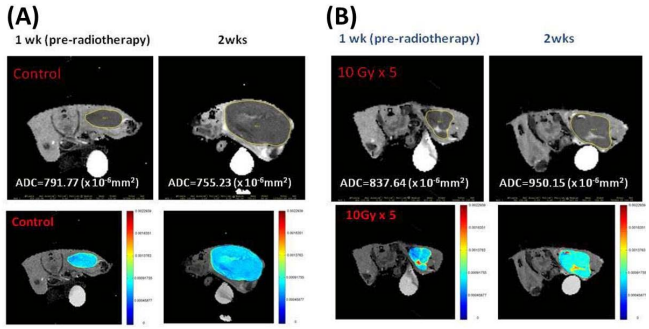

Fig 2.

Fig 1. Comparison of between K^{trans} mapping (A) between mouse treated with intraperitoneal saline injection (control group) and intraperitoneal bevacizumab. Note that apparent smaller tumor size in the bevacizumab group which had smaller values in K^{trans} mapping. More prominent tumor vascularity and K^{trans} values at peripheral portion of the tumor were found as well. Pharmacokinetic analysis of DCE MRI correlated with microvessel density and tumor size. However, ADC mapping (B) was not sensitive to evaluate treatment response as DCE MRI in VEGF-overexpressed NSCLC xenograft model.

Fig 2. Diffusion weighted MRI with ADC mapping (A: control LLC mice and B: Radiotherapy with 10Gy x5). After treatment, there is increased value of ADC compared with control groups.

Results and Conclusions

In this study, percentage reduction of K^{trans} and tumor size were significantly decreased after RT and Bevacizumab treatment. Pharmacokinetic analysis of DCE MRI is proven correlated well with histopathologic evidence of microvascular density, although DWI with ADC mapping was not sensitive to evaluate treatment response as DCE MRI in VEGF-overexpressed NSCLC xenograft model. However, higher values of ADC mapping were found in early evaluation after RT treatment in LLC mice model. ADC is a promising quantitative analysis, with accuracy, and supplementation with DCE MR imaging seems to further improve sensitivity. The findings indicated the significance of combination different MR imaging biomarkers for in vivo evaluation of tumor angiogenesis and therapeutic response of lung cancer applied in the clinical practice in the future.