Assessment of tumor microvasculature in brain metastasis by pharmacokinetic model using dynamic MRI.

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Introduction:
Angiogenesis plays a key element in the pathophysiology of tumor growth and metastasis. Dynamic contrast-enhanced magnetic resonance imaging (DCE-MRI) was proposed to investigate the microvascular structure. The pharmacokinetics of injected contrast agents were tracked by MRI as they pass through the tumor vasculature. Quantitative parameters can be derived, which reflected the treatment responses in primary tumors. The purpose of the study was to explore the induced changes from metastatic tumors, such as in patients with brain metastasis from breast cancer.

Methods and Materials:
Patients of breast cancer with evidence of brain metastasis underwent radiotherapy and/or chemotherapy. Imaging of the brain were performed before and one month after treatment using a 3 Tesla MRI scanner (Trio with TIM,Siemens,Germany). Contiguous 3D volumes were obtained with a gradient echo sequence of TR/TE=13.6/3.8 ms, and a rapid intravenous bolus injection (0.1 mmol/kg) of Gadopentetate dimeglumine (Magnevist; Schering, Germany). 120 volumes were acquired with the temporal resolution of 2.6 seconds. Quantitative DCE parametric maps were reconstructed based on two-compartment model, including the vascular plasma volume (Vp), transcapillary contrast agent transfer constant (Ktrans) and extracellular extravascular volume (Ve). The derived parameters at regions of tumors as well as the tumor volumes were compared before and after treatment.

Results and discussion:
The findings showed that the microenvironment from a metastatic tumor can be modified by radiotherapy and/or chemotherapy. The vascular permeability within the tumor could be decreased, as reflected in the reductions in Ktrans immediately after
the treatment. It could suggest an early sign of the tumor response to the treatment, because of the disruption of vasculatures. The changes of Ve and Vp could be a reflection of the temporal evolutions from the therapeutic intervention. Decreased tumor volume was expected at a later stage. The findings obtained from the DCE derived indices are consistent with the expected biological effect. The underlying mechanism quarantines the worth of further investigation.

**Conclusion:**
Dynamic MRI enables quantification of the tumor vascularity and permeability, hence could serve as a potential surrogating biomarker for treatment response for patients with brain metastasis.