

# IN VIVO ASSESSMENT OF NON-SMALL CELL LUNG CANCER: DETECTION OF EARLY RESPONSE TO CONCURRENT CHEMORADIOTHERAPY BY USING BREATH-HOLD DYNAMIC CONTRAST ENHANCED MRI

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## In Vivo Assessment of Non-Small Cell Lung Cancer: Detection of Early Response to Concurrent Chemoradiotherapy by Using Breath-Hold Dynamic Contrast Enhanced MRI

**Target Audience** This work targets those, who are interested in monitoring lung cancer treatment response by dynamic contrast-enhanced (DCE) MRI.

**Purpose** To investigate the capability of using DCE-MRI parameters to predict response to concurrent chemoradiotherapy (CCRT) in patients with non-small cell lung cancer (NSCLC).

**Introduction** DCE-MRI has been extensively used in monitoring treatment response on many anatomies. However, this technique was not fully explored in lung cancer due to breathing motion. In this paper, we demonstrated by using a mutual information based nonlinear registration scheme and two compartment Tofts model, clinical relevant parameters could be extracted from a breath-hold DCE-MRI to monitor treatment response on NSCLC.

**Methods** This study was approved by the institutional review board, and written informed consent was obtained from all nine subjects. All patients with stage IIIA or IIIB NSCLC, who underwent DCE-MRI before CCRT, 2 weeks after starting therapy (total dose of 20 Gy) and at the end of therapy (total dose of 60 Gy), were enrolled. All MR examinations were performed with a 3.0-T scanner by using an eight-tunnel body phased-array coil. Multi-flip angles were first performed before dynamic scanning to determine pre-contrast T1 mapping. Dynamic sequence was then performed with a 4s tempo and continued for 168s. During dynamic acquisition, patient took a breath for every 12s. All multi-flip angle data and dynamic data were nonlinearly aligned by using registration algorithm [3] before pharmacokinetic analysis by two-compartment Tofts model [1, 2]. Regions of interests (ROI) were outlined on the whole tumor, where the largest area of tumor was observed. The following quantitative parameters were recorded: volume transfer constant ( $K_{trans}$ ), rate constant ( $K_{ep}$ ), fraction of extravascular extracellular volume ( $V_e$ ), and fractional blood plasma volume per unit volume of tissue ( $V_p$ ). Histogram analysis was performed on each ROI of these parameter maps, where mode value and mean value of each parameter was calculated for statistical analysis. The treatment response after CCRT was assessed with Revised Response Evaluation Criteria in Solid Tumors (RECIST1.1), and then the relationship between quantitative parameters and early tumor response to CCRT was evaluated by Spearman's correlation analysis.

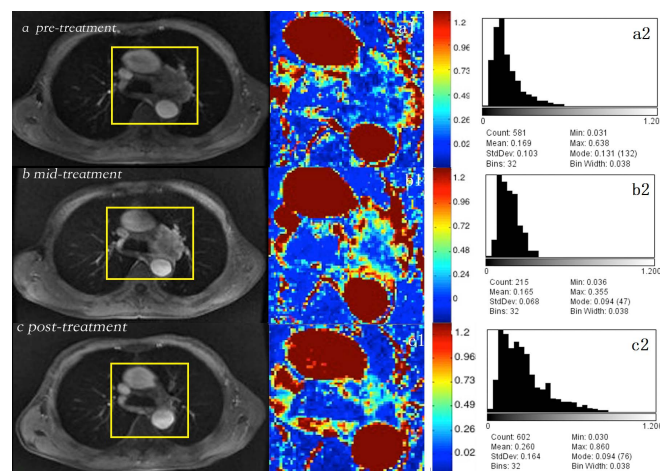
**Result and Discussion** Both DCE-MRI parameters of mode value and mean value (i.e.  $K_{trans}$ ,  $K_{ep}$ ,  $V_e$ ) in tumors showed significant changes in response to CCRT ( $P < 0.05$ ). The mode values of pre-treatment  $K_{trans}$  ( $r = -0.87$ ,  $P = 0.01$ ),  $V_e$  ( $r = -0.80$ ,  $P = 0.03$ ) and mid-treatment  $K_{trans}$  ( $r = -0.87$ ,  $P = 0.01$ ) were inversely correlated with percentage tumor regression and early tumor response to CCRT. However, significant correlations was found only between mean values of pre-treatment  $K_{trans}$  ( $r = -0.79$ ,  $P = 0.04$ ) with early tumor response to CCRT. No significant correlations were observed between parameters calculated from the third scan and tumor regression rate. Fig.1 and Fig.2 shows different response to CCRT of patients with NSCLC. Patients with lower pre-treatment  $K_{trans}$ ,  $V_e$  and decreased  $K_{trans}$  in mid-treatment tend to have a good response.

**Conclusion** DCE-MRI parameters seems to be a promising tool for monitoring the early response to or predicting prognosis after CCRT of NSCLC, and mode value calculated by histogram analysis may more reliable than mean value. Nonetheless, more data are needed.

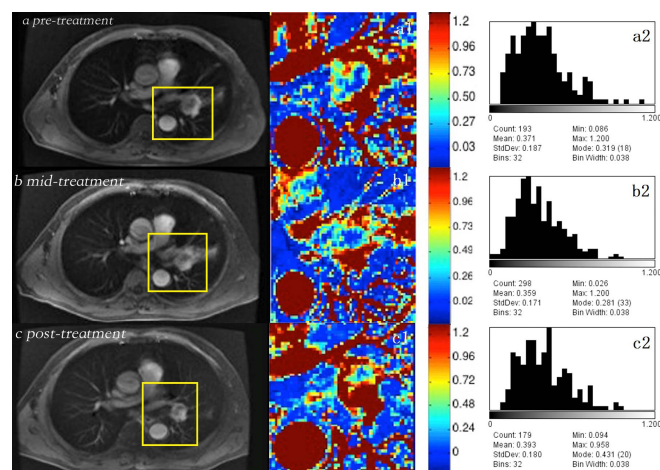
**Reference** 1. Tofts P (ed.). Quantitative MRI of the Brain: Measuring Changes Caused by Disease. Wiley, Chichester, UK, 2003.

2. Tofts PS, Kermode AG. Measurement of the Blood-brain Barrier Permeability and Leakage Space using Dynamic MR Imaging. 1. Fundamental Concepts. Magnetic Resonance in Medicine, 1984; 17(2): 357-367.

3. Rueckert D, Sonoda LI, Hayes C, et al. Nonrigid Registration Using Free-Form Deformations: Application to Breast MR Images. IEEE Transactions on Medical Imaging. 1999 Aug; 18(8):712-21.



**Fig. 1** A 61-year-old man with non-small cell lung cancer, who had a good response of concurrent chemoradiotherapy was shown. a. before therapy (pre-treatment), b. 2 weeks after therapy (mid-treatment) and c. at the end of therapy (post-treatment). Axial color-coded  $K_{trans}$  maps of DCE-MRI at pre-treatment (a1), mid-treatment (b1), and post-treatment (c1). Histogram was shown on a2, b2 and c2, respectively.



**Fig. 2** A 62-year-old man with non-small cell lung cancer, who had a poor response of concurrent chemoradiotherapy was shown. a. before therapy (pre-treatment), b. 2 weeks after therapy (mid-treatment) and c. at the end of therapy (post-treatment). Axial color-coded  $K_{trans}$  maps of DCE-MRI at pre-treatment (a1), mid-treatment (b1), and post-treatment (c1). Histogram was shown on a2, b2 and c2, respectively.