

Evaluation of pretreatment and early response DCE MRI in head and neck cancer: prediction of short-term outcome

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Introduction

For an optimal oncologic treatment strategy, it is important to be able to predict the outcome of treatment as early as possible. For example, patients who have complete pathologic response have longer disease-free and overall survival. Early identification of nonresponders may enable patients to benefit from alternative therapeutic approaches. An advantage of the noninvasive MRI technique is that subjects can be imaged multiple times before, during and, after treatment. Dynamic contrast-enhanced magnetic resonance imaging (DCE-MRI) is a method for characterizing the pathophysiological microenvironment of tumors [1]. With proper compartmental modeling, the data yields results relating to the tumor microenvironment. In this study we assess the value of pretreatment and early response DCE-MRI in predicting the short-term response to therapy in patients with head and neck squamous cell carcinoma (HNSCC) with neck nodal metastases.

Material and Methods

Patients 16 newly diagnosed HNSCC patients with metastatic nodes (M/F: 13/3, age: 58±8y, primary cancer: 10 base of tongue, 5 tonsil, 1 nasopharynx) underwent a clinical MRI examination, which included DCE MRI. Patients were scanned before (Pre-Tx), and 10-14 days into chemo-radiation treatment (Wk2-Tx). Three to four months after completing treatment, a short-term response assessment was performed based on WHO criteria [2]. Patients were divided into 2 groups; complete response (CR; no evidence of disease on clinical and imaging exam) and incomplete clinical response (ICR; measurable disease). **MRI** MRI was performed on a 1.5 Tesla GE Excite scanner using an 8-channel neurovascular phased-array coil. The protocol consisted of MR imaging covering the entire neck or oral cavity/tongue or nasopharynx using T2-weighted and T1-weighted images. DCE MRI studies were acquired on the nodes using a fast multi-phase spoiled gradient echo sequence. Antecubital vein catheters delivered a bolus of 0.1mmol/kg Gd-DTPA (Magnevist) at 2 cc/s, followed by saline flush. The entire node was covered contiguously with 5-7 mm thick slices, zero gap, yielding 3-6 slices with 3.75-7.5 sec temporal resolution. Acquisition parameters included TR 9 ms, TE 2 ms, flip angle 30°, bandwidth 15.63 kHz, FOV 18-20 cm, time course data points 40-80, and matrix 256x128. **Analysis** MRI data was analyzed with Matlab. ROIs were manually drawn by an experienced neuro-radiologist. Quantitative DCE-MRI analyses of the tumor tissue time course data was done using the two compartment Tofts model in all ROIs [3] on a pixel by pixel basis. A population based arterial input function was used [3]. The latter analyses calculated the pixel K^{trans} (volume transfer constant) and v_e (extravascular-extra-cellular volume fraction). A histogram analysis was performed on all pixels within the ROI, which yielded the median and standard deviation (std) of the distribution of all pixels.

Statistical analysis (in SPSS 17.0). The differences between the pretreatment scan (Pre-Tx) and the early response scan (Wk2-Tx) were tested using a paired-samples t-test. To assess the predictive value of DCE-MRI for short-term response, logistic regression analysis was performed using the DCE-MRI parameters from Pre-Tx, Wk2-Tx, and the combined ratio of the 2 time points (Wk2/Pre). The specific parameters included: tumor volume, median(K^{trans}), std(K^{trans}), median(v_e), and std(v_e). The forward stepwise (LR) method of analysis was used (variable entered if $P < 0.10$, variable removed if $P > 0.15$). After creation of the multivariate model the predicted probabilities were saved. An ROC curve was constructed with these probabilities to assess the accuracy of the multivariate model for the prediction of short-term response. Additionally, a non-parametric Mann-Whitney U test was performed to assess differences in parameters between CR and ICR.

Results

None of the DCE-MRI parameters was significantly different between Pre-Tx and Wk2-Tx ($p > 0.06$). At short-term response evaluation, 13 patients had complete response and 3 patients had incomplete clinical response. Figure 1 displays typical Pre-Tx and Wk2-Tx DCE results from a patient that demonstrated CR. The logistic regression analysis of the Pre-Tx indicated that median(v_e) ($p = 0.014$) was a significant pretreatment predictor of short-term response. The short-term responses could be predicted correctly in 15 patients (93.8%, sensitivity is 100%, specificity = 67%) using median(v_e), and the area under the ROC curve was 0.92 [95% CI 0.84 1.00]. No Wk2-Tx parameter was a significant predictor. For the ratio Wk2/Pre, both median(K^{trans}) ($p = 0.035$) and std(v_e) ($p = 0.046$) were significant predictors. The short-term responses could be predicted correctly in 15 patients (93.8%, sensitivity is 100%, specificity = 67%), area under the ROC curve was 0.95 [95% CI 0.89 1.00] (Figure 2). Pre-Tx median(v_e) was the only significantly different parameter between CR and ICR ($p = 0.02$) (figure 3).

Discussion

For pretreatment DCE-MRI parameters, it was found that v_e was a significant predictor of short-term outcome. Lower v_e values (leakage space) are associated with worse prognosis. Interestingly, not the early response DCE-MRI parameters itself, but the ratio of early response over pretreatment values (Wk2/Pre), yielded median(K^{trans}) and std(v_e) as significant predictors. An increase in median(K^{trans}) and std(v_e) was related to worse response. Apparently, an increase in perfusion and heterogeneity during early response is unfavorable for treatment outcome.

Conclusion

Pretreatment v_e was a significant predictor of response. With respect to pretreatment DCE parameters, early response DCE parameters (median(K^{trans}) and std(v_e)) marginally improve prediction of short-term response in advanced head and neck cancer.

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References

[1] Yankeelov, CMIR 2007 3(91); [2] Rengan, Am J Clin Oncol 2008 31(465); [3] Shukla-Dave, BMC Med Phys 2009 9(4).

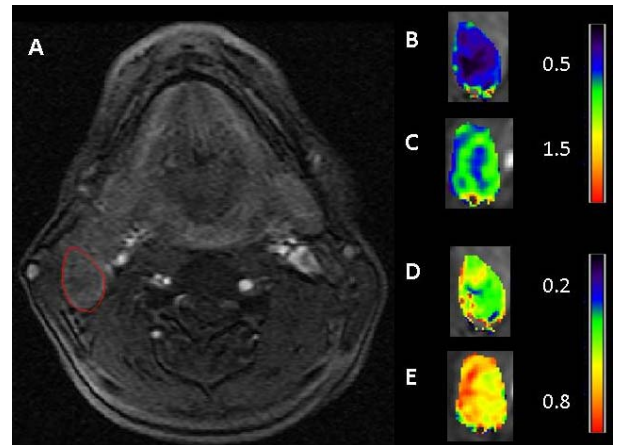


Figure 1: Pretreatment and early response DCE images of a patient with CR (m, 41y, primary tonsil). (A) Pre-Tx postcontrast T1w, node is marked in red. (B) Pre-Tx K^{trans} , (C) Wk2-Tx K^{trans} (both in min^{-1}), (D) Pre-Tx v_e , (E) Wk2-Tx v_e (both dimensionless).

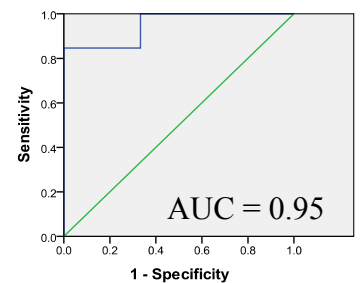


Figure 2: ROC curve constructed using the predicted probabilities of the logistic regression model for the obtained Wk2/Pre imaging parameters (significant predictors: median(K^{trans}) and std(v_e)). AUC: area under the curve.

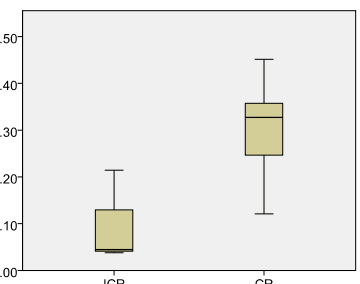


Figure 3: Pretreatment median(v_e) values for patients with complete response (CR, right), and incomplete response (ICR, left). $P = 0.02$, Mann-Whitney U.