Entropy Analysis of Peak Enhancement Ratio from DCE-MRI as a Potential Marker to Assess Brain Tumor Response to Radiotherapy

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Introduction:

Peak enhancement ratio (PER) derived from dynamic contrast enhanced magnetic resonance imaging (DCE-MRI) has been used as an imaging biomarker to monitor tumor response to therapy for years [1]. For patients who cannot benefit from medical therapies, one recognized feature is the changes in tumor composition from homogeneity to heterogeneity. Heterogeneity, such as heterogeneity of the tumor blood supply, has been used to estimate the response to tyrosine kinase inhibitors (TKI) in patients with renal cell cancer by calculating entropy in computer tomographic (CT) imaging [2]. Entropy is a measure of irregularity, and higher entropy represents increased tumor heterogeneity [2]. To our knowledge, the potential of entropy analysis in DCE-MRI has not been fully discussed. The objective of this study was to assess heterogeneity changes in PER stemmed from DCE-MRI by calculating entropy in patients with brain tumors before and after radiotherapy (RT).

Materials and Methods:

Twenty-three patients with brain tumors underwent DCE-MRI before and after RT. Follow-up contrast-enhanced CT or contrast-enhanced MRI were used to judge the tumor response to treatment based on Response Evaluation Criteria in Solid Tumor (RECIST) [3]. Finally, there were 11 patients in the non-responder group and 12 patients in the responder group. DCE-MRI was conducted on a 3T system (Signa; General Electric, Milwaukee, WI). The parameters for the DCE-MRI protocol were 12 slices gradient echo sequence, TR/TE/θ =5.8 msec/2.2 msec/30°, FOV= 256 mm×256 mm, and matrix size=256×192. The definition in region of interest (ROI) of tumor was performed by one experienced radiologist, and curves of signal intensities as a function of time at each pixel were extracted from the series of successive images. Then, the PER calculated for each pixel as $(SI_{max}\text{-}SI_{base})\times 100\%/SI_{base}$ within the ROI could be depicted. SI_{max} was the maximum signal intensity after injecting the contrast agent while SI_{base} was the signal intensity before injecting the contrast agent. Heterogeneity in the ROI was quantified by calculating entropy with the following equations:

$$\text{entropy}=-\sum_{I=1}^{K}[P(I)]\log_2[P(I)]$$

where I is the PER within the ROI, K is the largest PER within the ROI, and P(I) is the probability of the occurrence of the given PER. The ratio of post-RT entropy to pre-RT entropy was defined as therapeutic entropy ratio (TER).

Results:

Figure 1 displays examples of a non-responder and a responder. Color maps of PER showed that non-responder was marked by a coarser tumor composition and increased entropy of PER after RT, and it corresponding TER was 1.08. In contrast, responder was characterized by a change from heterogeneous to homogeneous tumor compositions after RT. With the decrease in entropy of PER, it corresponding TER was 0.71. Averages and standard deviations for TER in the non-responder and the responder group are demonstrated in Fig. 2. With *P* less than 0.05, TER was significantly higher in the non-responder (1.14±0.14) than that in the responder (0.86±0.1). The performance of TER is demonstrated in Fig. 3. With the optimal cut-point of 0.98, the area under the receiver operating characteristic (ROC) curve (AUC) was significant in TER (AUC=0.98, 95% confidence interval: 0.92-1, *P*<0.05). It corresponding sensitivity and specificity were 100% and 91.67%, respectively. Entropy analysis showed the leverage of diagnosing the non-responders accurately in this study.

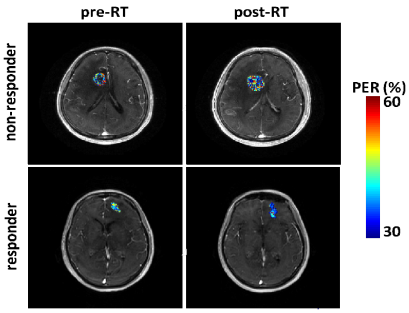

Figure 1. Color maps of peak enhancement ratio (PER) for a non-responder (top raw) and a responder (bottom raw). The corresponding TERs were 1.08 and 0.71 for non-responder and responder, respectively.

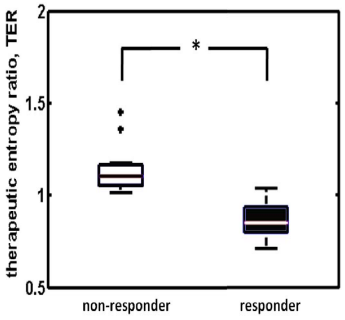

Figure 2. Boxplot showing the distribution of TER. There was a significant difference in TER between the non-responder and responder groups (*: *P*<0.05).

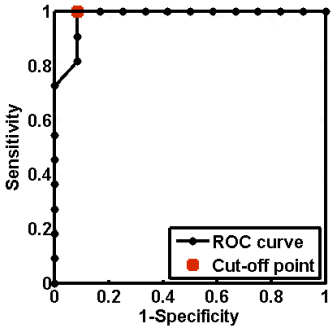

Figure 3. ROC curve for TER. Area under the ROC curve was significant in TER (AUC=0.98, *P*<0.05). The corresponding sensitivity and specificity were 100% and 91.67%, respectively.

Discussion and Conclusion:

In this study, we successfully evaluated the brain tumors response to RT by calculating the entropy of PER distribution acquired from DCE-MRI. For patients in the non-responder group, tumors become more aggressive and exhibited increases in heterogeneities. The degree of heterogeneities could be quantified by calculating entropy to measure the scatter of the PER within the ROI. The increase in entropy after RT would reflect the increase in heterogeneity, and resulted in the larger TER in the non-responder. In conclusion, entropy analysis yields useful information regarding changes in tumor heterogeneity after therapy, while the PER from DCE-MRI gives insightful look into microvasculature without complicated calculation. Combing the advantages of the two, it can improve the diagnosis ability and help monitor response to therapy in clinical.

References:

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