Improving Bladder Cancer Staging by using quantitative DCE-MRI with k-means clustering

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Purpose

Accurate T staging of bladder cancer is still a clinical challenge and limited by cystoscopy and current bladder imaging. This study is aimed at assessing if DCE-MRI using a quantitative pharmacokinetic approach utilizing k-means clustering can be useful in the T staging of bladder tumors.

Methods

Twenty-four (21 males, 3 females; age: 67±12) bladder cancer patients were included in this prospective study. Tumor stage of each patient was determined by the pathological examination of their cystectomy bladder specimen after the completion of MRI. All patients were imaged on a 3T MRI system (Achieva, Philips Healthcare, Cleveland, Ohio, USA) using 2-channel RF multi-transmit and a 32-channel phased-array surface coil. Axial DCE-MRI was performed with a 3D-spoiled Gradient Echo sequence. A single bodyweight-based dose (0.2 mmol per kilogram) of Gd-based contrast agent (Gadopentate dimeglumine) was injected at a constant rate of 0.5 mL/s.

Data post-processing was done on IDL (Exelis VIS)-based software to estimate voxel-wise pharmacokinetic parameters, the amplitude of signal enhancement (Amp) and the AIF-adjusted exchange rate of the contrast agent between EES and the plasma space (k_{ep}) (1). All voxel-wise Amp and k_{ep} values were non-dimensionalized by using their averages.

Based on prior pilot data, k of 3 was found to be the optimal number of clusters. k-means clustering of the non-dimensionalized Amp and k_{ep} values of all twenty-four patients were performed on Microsoft Office Excel with Solver add-in to determine three cluster centers (centroids) (2). The volume fractions (VFs) of three clusters were calculated and correlated with the tumor stage. Student t-test was used to assess the differences in cluster VFs of four groups: stage ≤T1, T2, T3, and T4. $P < 0.05$ was considered to be statistically significant. Receiver operating characteristic (ROC) curve analysis was done to assess the ability of cluster VFs to distinguish different stages.

Results

Out of twenty-four patients, three were found with stage ≤T1, nine with T2, eight with T3, and four with T4.

Staging on stage-by-stage basis: Significant difference in the VF of cluster 2 was found between ≤T1 vs. T2 ($P < 0.02$), ≤T1 vs. T3 ($P < 0.02$), and T3 vs. T4 ($P < 0.01$). The differences in all three cluster VFs were statistically significant ($P < 0.05$ for cluster 1 and 3, $P < 0.001$ for cluster 2) between stage T2 vs. T3.

Assessment of fat infiltration (≤T2 vs. ≥T3): Non-organ-confined (fat-invasive) bladder tumors had significantly higher VFs of cluster 1 and 3 ($P < 0.05$) and a significantly lower VF of cluster 2 ($P < 0.001$) than did organ-confined (non-fat-invasive) tumors. This could be visualized on color cluster maps (Figure 1). Using the VF of cluster 2 to differentiate fat-invasive from non-fat-invasive tumors presented with area-under-the-curve (AUC) value of 0.83 (Figure 2).

Discussion

k-means clustering of DCE-MRI pharmacokinetic parameters was used to quantitatively assess the differences in the distribution of these parameters within a bladder tumor via three cluster VFs. All three cluster VFs in this study were shown to be correlated with T stages of bladder cancer. The VF of cluster 2 was the most potential biomarker with a high AUC value in the differentiation of fat-invasive from non-fat-invasive tumors.

Conclusion

This Phase I clinical trial has demonstrated that k-means clustering of pharmacokinetic parameters appears to be a useful quantitative technique for the assessment of DCE-MRI to improve the accuracy of the T staging of bladder cancer.

References

1. Yang X et al, Magn Reson Med. 2008, 59(6):1448-56.
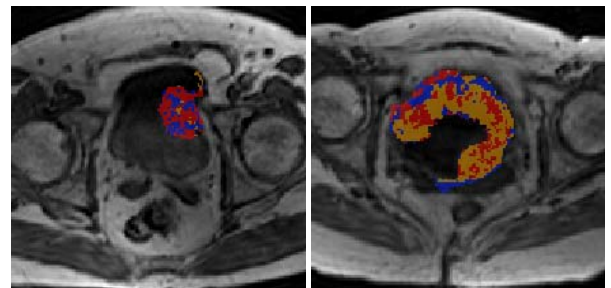2. Aravind H et al, Int J Comput Appl. 2010; 11(7): 19–25

Figure 1: Color cluster maps show the differences in the VFs of cluster 1 (blue), 2 (yellow), and 3 (red) between a fat-invasive bladder tumor (left image) and a non-fat invasive bladder tumor (right image).
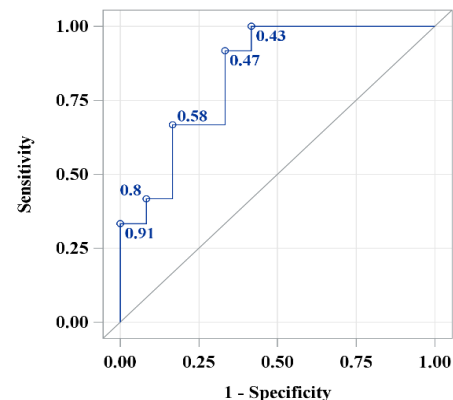

Figure 2: ROC curve analysis of using the VF of cluster 2 to assess the fat infiltration in bladder cancers.