Predicting Gleason Scores of Prostate Cancer Using Combined Trace Apparent Diffusion Coefficient and Tumor Volume

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Introduction

With increasing life expectancy, prostate cancer (PCA) is becoming one of the most common forms of malignancy in men. Clinically, the Gleason Scores (GS) are commonly used to assess the aggressiveness of PCA with grades from 1 to 5. The GS is one of the parameters in a strategy of staging system that predicts prognosis and helps decision of treatment options. Magnetic resonance (MR) imaging has been widely used to detect PCA and to assess cancer staging [1]. Recently, trace apparent diffusion coefficient (tADC) calculated from diffusion MR imaging in tumors is found to have a significant negative correlation with tumor GS [2]. However, there are substantial overlaps of tADC values in GS of 6, 7 and 8. It makes difficult to serve this index as a prognostic indicator by using tADC values only. Since tumor volume (TV) has also been recognized as a relevant predictor of PCA pathologic stage and aggressiveness [3], in this study, we perform a retrospective analysis of tADC and TV in regions which were pathologically confirmed to contain PCA. TV, tADC, and combined parameters were calculated correlated with GS. The goal of the study was to determine an index with stronger correlation with GS.

Materials and Methods

Twenty male patients (55-71 years; average, 62 years; mean PSA: 13.2 ng/ml) with pathologically confirmed PCA were recruited in the study. For each patient, MR acquisition and subsequent TRUS biopsy were performed within two weeks. MR images were acquired on a 1.5T scanner (GE, Echo Speed, Milwaukee, WI, USA) with an endorectal coil. Diffusion tensor imaging (DTI) was acquired using spin-echo echo planar imaging (EPI) with multiple transaxial slices of the prostate from base to apex. Imaging parameters: TR/TE = 17000/79 ms; slice thickness = 1mm; slice gap = 0, in-plane resolution = 1mm x 1mm; six diffusion-sensitive gradients at {±1,0,1}, {0,1,±1},{±1,1,0} with b = 500 s mm-2; number of averages (NAV) = 6. Trace ADC was determined by calculating the mean of the eigenvalues of the diffusion tensor. TV of biopsy-positive regions was calculated by continuous voxels with the tADC values less than 1.2 μm^2/ms, that is, mean + 1 standard deviation from our previous results (Average tADC value of PCA tissues: 1.0 ± 0.2 μm^2/ms). Average radius of cancerous region, noted as R, was calculated from the equation $TV=4\pi R^3/3$. Pearson correlation analysis was performed between each index and GS of cancerous tissues. The statistical analysis was carried out using the program for Graphpad PRISM, version 5.01. A p-value of less than 0.05 was considered statistically significant.

Results

Totally 59 regions out of 20 patients were found to contain PCA by histopathology. In our analysis, tADC values, TV, and R were found significantly correlated with GS with Pearson coefficient of -0.61, 0.62, and 0.64, respectively. ($p<0.0001$) (figure 1). In combined parameters, tADC/TV and tADC/R were found significantly correlated with GS with Pearson coefficient of -0.69 and -0.77, respectively ($p<0.0001$) (figure 2).

Discussion and Conclusions

In this study, our results are similar to previous reports showing moderate correlation between tADC value and GS (r=-0.61) [2]. TV and R are also found having moderate correlation with GS (r=0.62, 0.64, respectively). However, all of these parameters have substantial overlaps in GS of 6 and 7. In our opinion, the overlaps in GS of 6 and 7 are mainly caused from some small PCA nodules with low tADC values and some large PCA nodules with high tADC values. To reduce these overlaps, two combining parameters, tADC/TV and tADC/R, were calculated to correlate with GS and were found having stronger correlations with GS (tADC/TV: r=-0.69; tADC/R: r=-0.77). The nodules with small sizes might be corrected to higher grade of GS owing to have low tADC values. On the other hand, the nodules with large nodule might be corrected to lower grade of GS owing to have higher tADC values. The correlation between tADC/R and GS is better than the correlation between tADC/TV and GS. The reason might be caused from a large range of TV, which may affect too much weighting from TV but not from both tADC and TV. After changing the TV term into R, the effects from tumor size are reduced and the weightings of tADC and tumor size will be balanced. While the unit of tADC/R, μm/s, could be seen as the velocity of water molecules in that area, which might be associated with the cellularity of the cancerous tissues. A cutoff tADC value of 1.6μm^2/ms to measure the TV was reported to have accurate measurement of TV in the peripheral zone [4]. However, it needs additional manual selection of an appropriate region of interest (ROI). Is this study, we choose the cutoff tADC value of 1.2μm^2/ms. It could automatically calculate the TV without selecting ROI, and also determine a meaningful cancerous area to assess the aggressiveness of PCA after combining with tADC value. In conclusion, we have retrospectively analyzed the parameters of tADC and TV in pathologically confirmed PCA regions. We found that a combined parameter of tADC/R (μm/s) had a best correlation with GS.

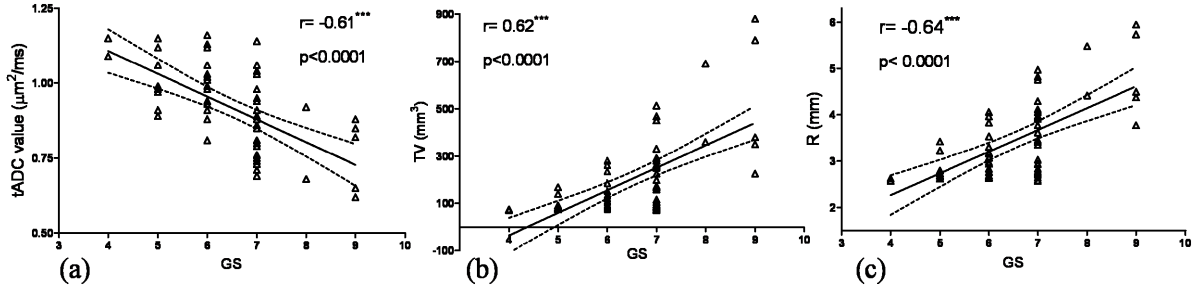

Figure 1. The correlations between (a) tADC and GS, (b) TV and GS, and (c) R and GS

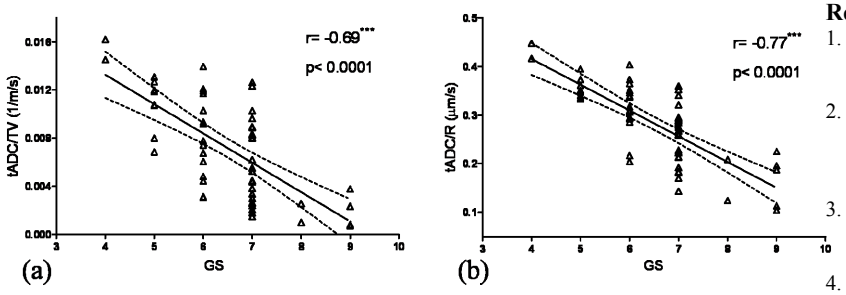

Figure 2. The correlations between (a) tADC/TV, and (b) tADC/R.

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