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Differences between HPV positive and negative oropharyngeal cancer detected by Non-Gaussian IVIM

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Introduction

The apparent diffusion coefficient (ADC) of diffusion weighted imaging (DWI) has been associated with response to treatment for oropharyngeal squamous cell carcinoma (OPSCC). However, recently it has been suggested that ADC value is a surrogate of human papillomavirus (HPV) status, and not an independent prognostic factor. Non-Gaussian Intravoxel Incoherent Motion (NG-IVIM) imaging is a novel extension of conventional DWI that enables simultaneous assessment of microvascular perfusion and inter- and intra-cellular diffusion. This provides a more detailed picture of the tumor microenvironment than ADC only. Recently, we optimized NG-IVIM specifically for the head-and-neck region in volunteers. Here, for the first time, the optimized acquisition was applied in OPSCC patients. The aim of this study is to investigate the differences in NG-IVIM parameters between HPV positive (HPV+) and HPV negative (HPV-) OPSCC and compare NG-IVIM parameters to the ADC derived from conventional DWI.

Materials and methods

Thirty-one consecutive OPSCC patients that underwent a planning MRI including a DWI scan ($b=0, 10, 2 \times 80, 130, 570, 2 \times 770, 2 \times 780, 790$ and 4×1500 s/mm²) between February 2020 and September 2021 were included. The DWI images were corrected for geometric distortion and rigidly registered to the T2w images acquired during the same scan session. With help of T1w images with and without gadolinium contrast, the GTV was segmented on the T2w images by an experienced radiation oncologist, and projected on the DWI. Within the GTV, voxel-wise fitting of the conventional mono-exponential ADC model and the bi-exponential NG-IVIM model (Figure 1a) was performed, and ADC, the free diffusion coefficient D , pseudo-diffusion coefficient D^* , perfusion fraction f , and kurtosis K were estimated. D^* and f are both related to microvascular perfusion, while K is related to restricted diffusion and cellularity. The average D , K , f and D^* , and ADC were compared between HPV+ and HPV- tumors using a Wilcoxon rank sum test. A p -value < 0.05 was considered statistically significant.

Results

In total 19 HPV+ and 12 HPV- tumors were included. The rank sum test revealed a significantly lower ($p=0.015$) ADC in HPV+ compared to HPV- tumors, in line with literature (Figure 1b). Moreover, aside from a significant difference in D ($p=0.043$), also differences in the perfusion related parameters f ($p=0.045$) and D^* ($p=0.0035$) and the cellularity related parameter K ($p=0.026$) were found (Figure 2). Additionally, the range of ADC is larger than the range of D , indicating a contribution of microvascular perfusion in the ADC that is not accounted for in the mono-exponential model.

Conclusion

NG-IVIM revealed differences in both microvasculature and cellularity between HPV+ and HPV- tumors, in addition to the difference in ADC obtained from conventional DWI. So, NG-IVIM is capable of providing a much more detailed picture of the tumor micro-environment and could aid in the understanding of differences between HPV+ and HPV- tumors.

a

$$S_i = S_0 e^{-b_i \cdot ADC} \quad (\text{Eq. 1})$$

$$S_i = S_0 \left((1-f) \left(e^{-b_i D + \frac{1}{6}(b_i D)^2 K} \right) + f e^{-b_i D^*} \right) \quad (\text{Eq. 2})$$

b

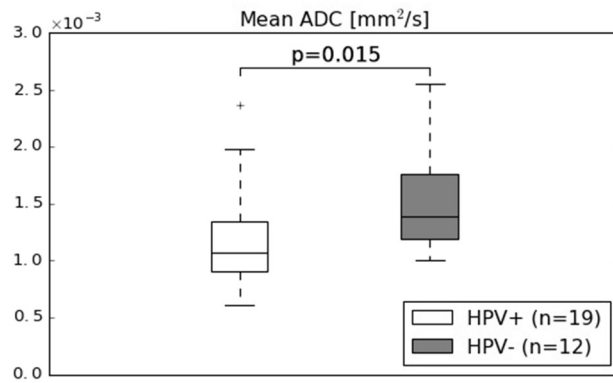


Figure 1. (a) Equations of the mono-exponential ADC model (Eq. 1) and the NG-IVIM model (Eq. 2). (b) Boxplot of the mean ADC values in the GTV for HPV+ (white) and HPV- (grey) tumors. A significantly higher ($p=0.015$) ADC was found in HPV- tumors.

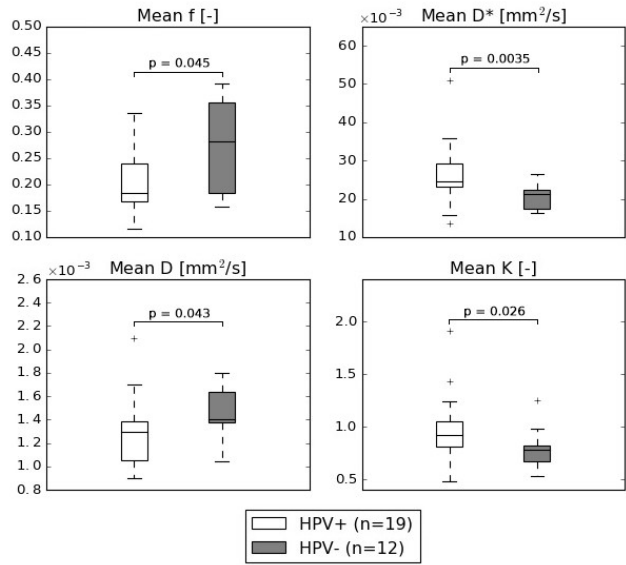


Figure 2. Boxplots of the mean NG-IVIM parameter values in the GTV for HPV+ (white) and HPV- (grey) patients. HPV+ tumors had a higher D* and K compared to HPV- tumors, and a lower D and f.