A multi-level deep learning algorithm to estimate tumor content and cellularity of prostate cancer

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Abstract

Prostate cancer is the most common cause of cancer death in men in the UK, responsible for more than 11,000 UK deaths each year. Diagnosis and grading of prostate cancer is an increasingly complex process and requires a more detailed analysis from pathologists to complete it with accuracy. Such process is not only time-consuming, but also prone to intra- and inter-observer variabilities. We designed a multi-level deep learning algorithm for the estimation of tumor content and cellularity of prostate cancer using fully convolutional neural networks. The approach provides accurate and consistent results, and is applicable across the whole range of computational pathology problems.

1 Introduction

In recent years, deep learning has been widely used within the domain of computational pathology for the analysis of whole slide images, and recent results encouraged its adoption to address a range of challenging problems [1-4]. In males in the UK, prostate cancer is the most common cancer, with around 47,200 new cases per year [5]. Prostate biopsy results can show how aggressive the cancer is, i.e. how likely it is to spread outside the prostate. This is called Gleason grade, Gleason score, or grade group [6]. Identification of prostate cancer grade is carried out at two very different levels of magnification. At low power, the pathologist identifies the right tissue structure. This is followed by examining at a much higher power view to observe the cell morphologies and classify based on this. Such a process is an increasingly complex, time-consuming, and also prone to intra- and inter-observer variabilities. In this work, we aim to build a deep learning approach to estimate tumor content and cellularity of prostate cancer.

2 Methods

In building the deep learning algorithm, our approach is to build two models, one at low power with the responsibility of identifying tissue structures (or tissue-level segmentation), and another at high power with responsibility for segmenting and quantifying the individual nuclei (or nucleus-level segmentation). A major part of building supervised deep learning algorithms is the provision of annotated 'ground truth' labels for all pixels. In this case, annotations were provided by pathologists at the appropriate levels for the two models. The tissue-level and nucleus-level models are fully-convolutional segmentation models, so for every pixel presented, the model predicts a class for that pixel [7]. In order to create models robust to the typical color variations seen in staining of slides, we extensively augment with respect to color variation causing our models to learn color-invariant features [8].

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3 Results

Figure 1 shows the sum of probability obtained from the tissue-level model. As seen in the figure, the model accurately classifies different Gleason patterns as Tumor, and non-tumor tissue (such as stroma, for example) as NonTumor. Figure 2 shows the correlation between nucleus counts, with correlation-coefficient of 0.997. Examples of applying the tissue-level and nucleus-level models to prostate cancer slides with various Gleason patterns can be found in Fig. 3 The figure shows the level of detail which can be obtained from the deep-learning segmentation models.

4 Conclusion

The presented multi-level deep learning algorithm predicts probability maps across the image, which could be used to provide the detail for the macrodissection boundaries and tumor cellularity of prostate cancer. The ability of the approach to identify tumor patterns accurately and consistently would likely be the foundation of the solution of challenging problems, such as grading prostate cancer. This approach is, however, not limited to this particular use case or problem domain, and is applicable across the whole range of computational pathology problems.

References

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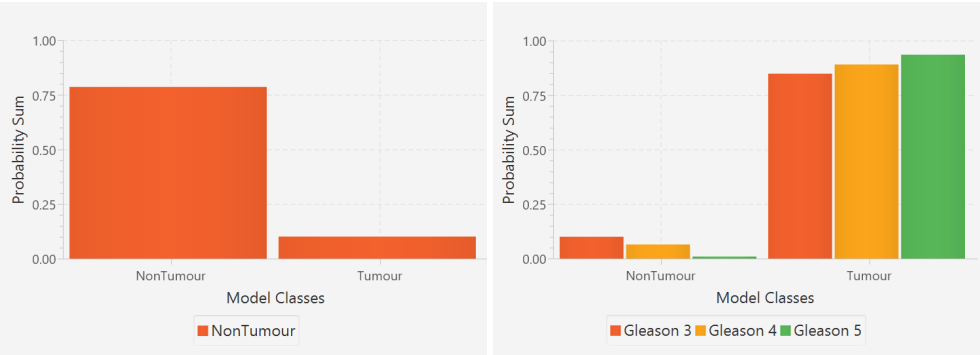

(a) (b)

Figure 1: Sum of probabilities obtained from structure-level model for (a) NonTumor Class, and (b) Tumor Classes (Gleason 3, 4, and 5).

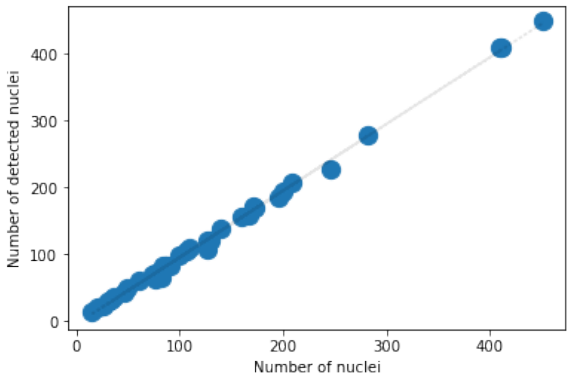

Figure 2: Correlation between nucleus counts (correlation-coefficient=0.997).

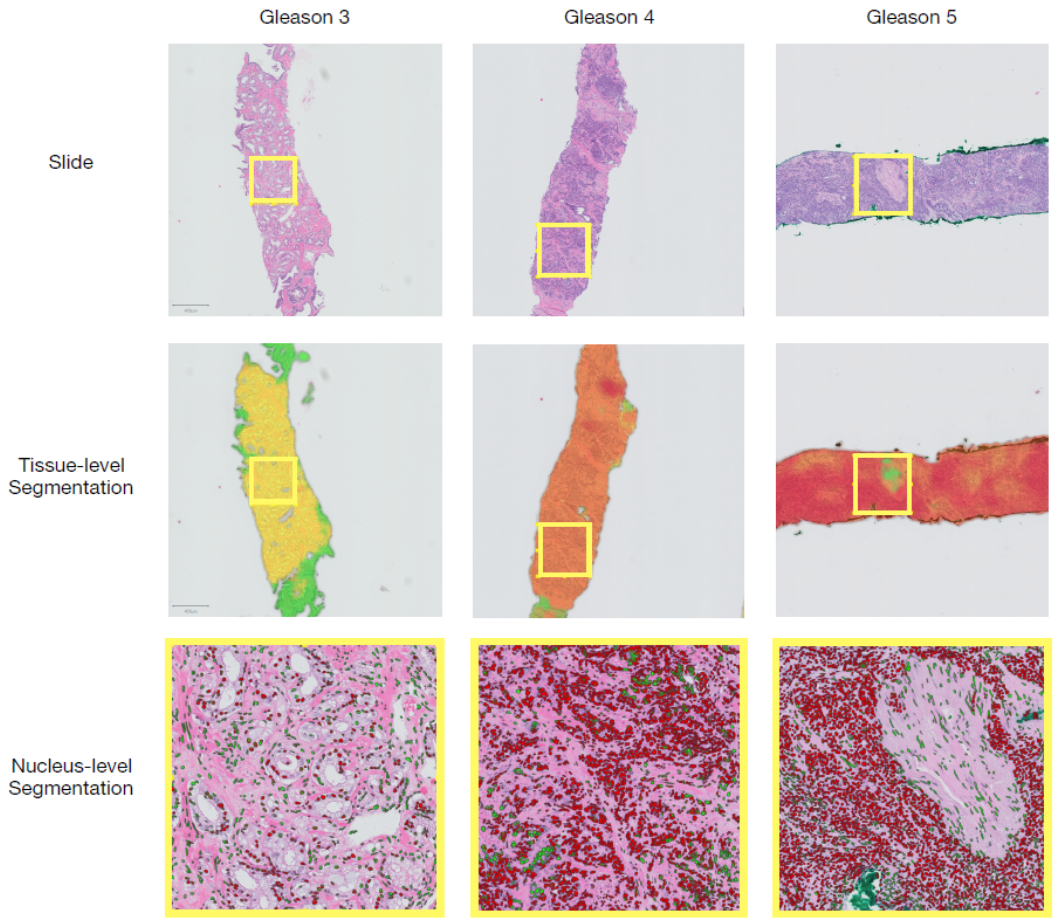

Figure 3: The results of applying the tissue-level and nucleus-level models to prostate cancer slides. The color code for the tissue-level segmentation: NonTumor is green, Gleason 3 is yellow, Gleason 4 is orange, and Gleason 5 is red. The color code for the Nucleus-level segmentation: NonTumor Nucleus is green, and Tumor Nucleus is red.