Optimized Biopsy Procedures for Estimating Gleason Score and Prostate Cancer Volume

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Introduction: Prostate biopsy is the gold standard procedure for estimating Gleason Score (GS) and cancer volume (CV), which are two important surrogate markers for prostate cancer aggressiveness. Currently, biopsy estimates GS based on architectural patterns of the sampled tissue at the *microscopic* level [1] and estimates CV based on the percent positive biopsies. However, underestimations are sometimes observed mainly due to the sampling errors of biopsy [2-5]. This problem is partially alleviated in this paper, where we have developed optimized biopsy procedures that could differentiate between prostate specimens having high and low GS/CV by sampling the spatial cancer distributions at the *macro* level. Differentiation rates of 81.93% (for GS) and 94.79% (for CV) have been obtained under cross validation in a population of prostatectomy specimens. To the best of our knowledge, the optimized biopsy procedures are the first ones that use (macro-level) spatial cancer distributions to estimate GS and CV. More validations might be needed to reveal its generalization ability.

Method: This is a population-based study, where histological images from a population of prostatectomy specimens are first reconstructed, spatially normalized into a stereotaxic coordinate space using an elastic warping method [6] and stacked into an atlas, reflecting different spatial distributions between specimens having high and low GS/CV. The main problem is then how to select optimal biopsy locations that could effectively sample the (macro-level) spatial cancer distributions, for the purpose of estimating high or low GS/CV for a prostate cancer patient. Selecting optimal biopsy locations is formulated into a feature selection problem, where biopsy outcome (1 for cancer presence and 0 for cancer absence) at each potential biopsy location is regarded as a feature. Given those optimized biopsy locations, estimating GS/CV of a prostate cancer patient is formulated into a binary classification problem, where a supervised classifier labels high or low GS/CV by jointly considering biopsy outcomes at these locations (reflecting macro-level spatial cancer distribution of this patient). In our implementation, the feature selection problem is solved by a feature selector developed in [7], and the binary classification problem is solved by support vector machine (SVM) [8] with Gaussian kernels. Cross-validation is conducted and ROC curves are plotted to reflect the sensitivity and specificity of our optimized biopsy procedure in classifying patients having high or low CV/GS.

Results: In our study, 83 specimens have been collected, of which 46/37 having high/low GS and 45/38 having high/low CV. The atlases in Fig. 1 visually demonstrate that specimens having high and low GS/CV exhibit different spatial distribution in the prostate space. In trying to sample these distributions, optimized biopsy locations are shown in Fig. 2, in both transrectal (anterior-posterior) and transperineal (apex-base) settings. Then, the sampled pattern of the spatial cancer distribution is the factor that determines high or low GS/CV. For example, using 7 optimized needles for CV in transrectal setting (lower left, Fig. 2), a prostate with the sampled pattern [1 1 0 0 0 1 0] (corresponding to cancer status from 1st to 7th biopsy) would indicate high CV, even though the percent positive biopsies is only 3/7, while another prostate with the sampled pattern [0 0 1 1 1 0 0] would indicate low CV, even though it also has 3 out of 7 biopsies being positive. Figs. 3 & 4 show the leave-one-out cross validation results, where high classification rates (0.8193 for GS and 0.9479 for CV) and large areas under the ROC curve (AUC=0.83 for GS and 0.98 for CV) have been obtained when differentiating between specimens having high GS/CV and low GS/CV.

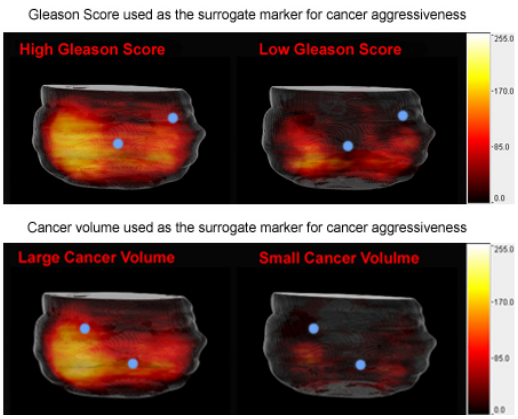

Fig. 1: Cancer distributions in two groups of prostate specimens. Blue dots are some intuitively observed biopsy locations where two groups of specimens would most likely to be differentiated.

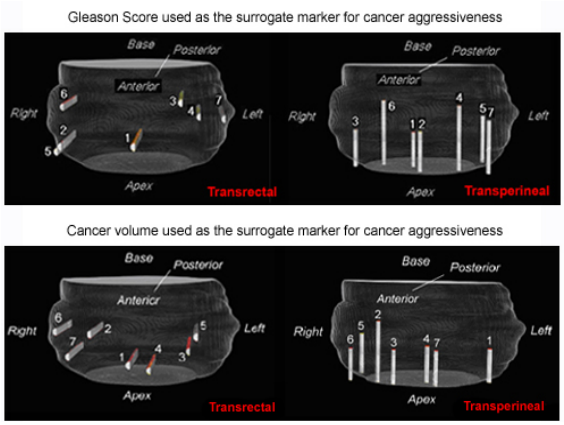

Fig. 2: Optimized biopsy procedures (7 needles) in transrectal and transperineal settings, when Gleason Score and cancer volume are used as the surrogate marker for cancer aggressiveness, respectively.

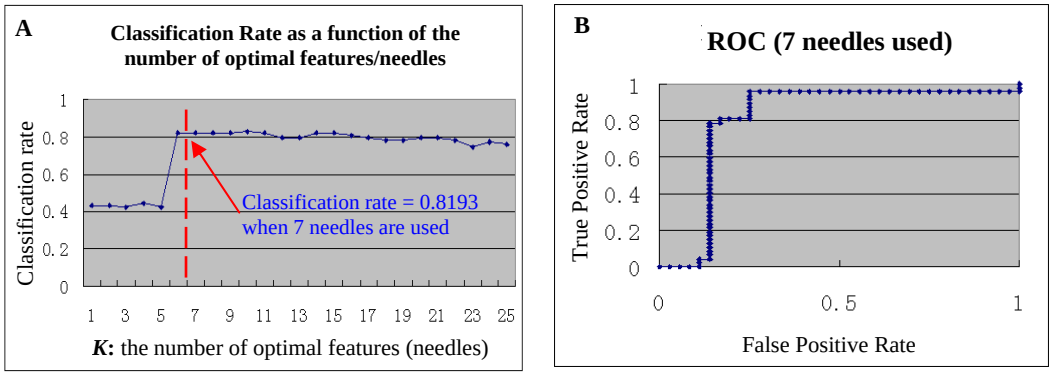

Fig. 3. Classification (differentiation) rate of the optimized transperineal biopsy (Fig. 2, upper right), when GS is used as the surrogate marker for cancer aggressiveness. (A): classification rate as a function of the number of optimal needles; when 7 needles are used, classification rate of 81.93% is achieved. (B): ROC curve when 7 needles are used, AUC=0.83.

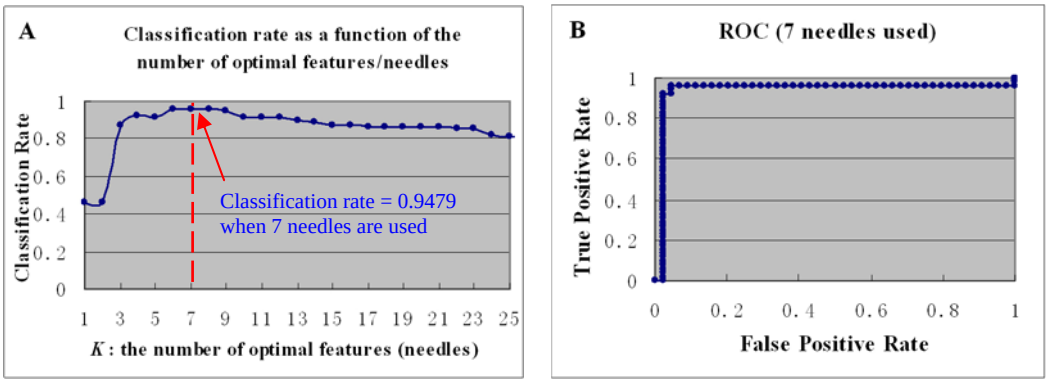

Fig. 4. Classification (differentiation) rate of the optimized transperineal biopsy (Fig. 2, lower right), when CV is used as the surrogate marker for cancer aggressiveness. (A): classification rate as a function of the number of optimal needles; when 7 needles are optimized, classification rate is 94.79%. (B): ROC curve when 7 needles are used, AUC=0.98.

Discussion: We have developed optimized biopsy procedures for estimating Gleason Score (GS) and cancer volume (CV) of prostate cancer patients. In contrast to the traditional methods, which estimate GS/CV by examining *micro*-level cancer patterns or the proportion of biopsy sites with cancer presence, our method assumed and experimentally demonstrated that prostate specimens having high and low GS/CV would exhibit different spatial cancer distributions at the *macro* level (Fig. 1), which could be sampled by our optimized biopsy locations (Fig. 2), resulting in improved estimation accuracy (Figs 3&4). Our estimation framework is binary (high or low) in accordance to clinical decisions that tend to binary (treatment or watchful waiting). Our framework is general and applicable to any population of prostatectomy specimens. Future work includes validating on a larger population and combining the optimized biopsy procedure with other pre-operative variables, such as PSA, to more accurately estimating surrogate markers for cancer aggressiveness.

Reference

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