Curvature Estimates of Point Clouds as a Tool in Quantitative Prostate Cancer Classification

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Prostate cancer is one of the most commonly diagnosed cancers. Diagnosis involves several factors, including analysis of 2D cross-sections of prostate tissue needle core biopsies. In such biopsies, glands appear as loops defined by the nuclei of cells defining the gland. As cancer progresses, glands often transform from circular to finger-like to unstructured, as molecules that keep the glands together are no longer sufficiently expressed in cancerous cells. Currently, the severity of cancer (and thus, treatment recommendations) is determined using the Gleason grading system, a visual analysis that compares biopsy features to a standard set of patterns in gland size, shape, and organization, and assigns regions of biopsies grades from 1 to 5 [4]. In particular, pathologists analyze the appearance the tubelike glands of such cross sections. Typically, a less cancerous prostate has fairly circular tubelike glands, whereas a more cancerous prostate has less uniformly circular glands; see Figure 1 for examples.

Although the Gleason grading system is certainly helpful to patients and doctors, its qualitative nature has the potential to lead to inconsistencies in scores given to biopsies [2] [5]. Such inconsistencies motivate the goal of quantifying gland curvature to aid in developing a more consistent method of classifying prostate cancer. In this paper, we propose a method to describe the shape of glands using curvature.

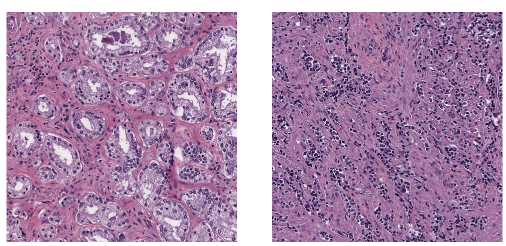

Figure 1 Example of stained cross sections of needle core biopsies of prostate tissue. The dark purple dots correspond to nuclei and outline each tubular gland. The example on the left contains fairly uniformly curved tubular glands, and would not be classified as severely cancerous. The example on the right shows a more cancerous sample; note that glands are beginning to lose their loop-like structure, and instead form sheets of cells. Our methods are particularly applicable to glands which still retain a clear loop structure.

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Methods We focus on studying the curvature of glands. To use this in practice, we would need to take the following steps: (1) extract nuclei defining a single gland; (2) order the nuclei in a counter-clockwise loop around the gland; (3) define curvature for a discretized curve. We focus on step (3). We defer step (1) to the full paper and use the CRUST algorithm [1] for step (2).

For a smooth curve C embedded in $\mathbb{R}^2$, the extrinsic curvature at a point $x \in C$ is equal to $1/r$, where r is the radius of the circle that best approximates C at x [6]; the total curvature of a piecewise linear curve can be captured by turning angles [7]. We emulate the definition of curvature given above for smooth curves to estimate the curvature of prostate gland cross sections. For each nuclei n_i, we estimate the curvature by finding the best fitting circle containing n_i along with m neighbors on each side. Note that since a circle is defined by a minimum of three points, we require $m \geq 1$. Since we used the CRUST algorithm to find an ordering of our nuclei around a gland, these are the m nuclei before n_i and m nuclei after n_i. (If the number of nuclei is less than $2m + 1$, then we have duplicates in this set). Doing this for each nucleus, we obtain a distribution of local curvature estimates.

Experimental Results To test our method, we computed curvature distributions on simulated glands [3] for three different aggression levels; see Figure 2. As expected, preliminary results on simulated glands indicate that more cancerous glands tend to have higher variation in estimated local curvature than less cancerous glands.

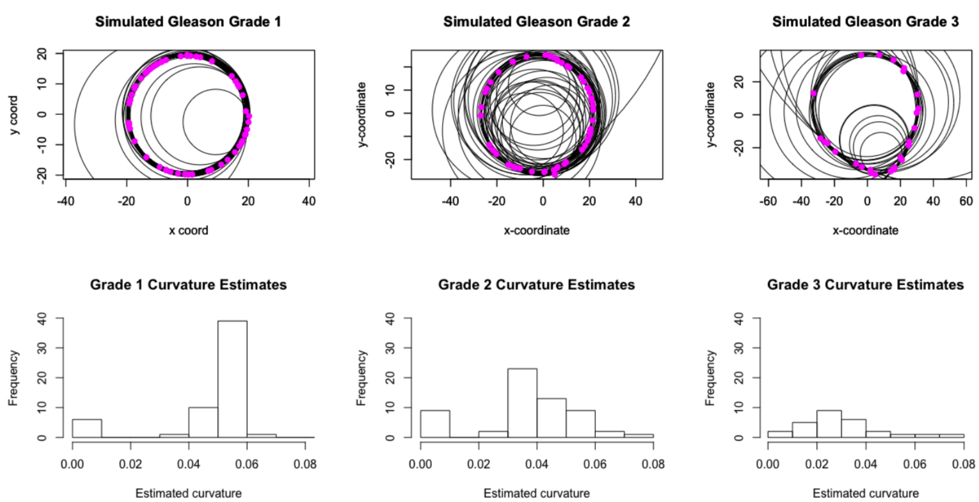

Figure 2 Curvature distributions for three simulated glands. The magenta dots in the top row are a simulation of the position of nuclei in glands. The best fitting circle for each nuclei using m neighbors on each side is shown (we used $m = 2$). Curvature at a nuclei is then estimated as the reciprocal such a circle, the corresponding histogram of which is shown on the bottom row.

Continued Research and Acknowledgements The next step is to study how the curvature distribution varies with Gleason grade and cancer severity for human biopsy data, which will ultimately be used in automated histology slide analysis.

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