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Multi-scale lacunarity as an alternative to quantify and diagnose the behavior of prostate cancer

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ABSTRACT

Prostate cancer is a serious public health problem accounting for up to 30% of clinical tumors in men. The diagnosis of this disease is made with clinical, laboratorial and radiological exams, which may indicate the need for transrectal biopsy. Prostate biopsies are discerningly evaluated by pathologists in an attempt to determine the most appropriate conduct. This paper presents a set of techniques for identifying and quantifying regions of interest in prostatic images. Analyses were performed using multi-scale lacunarity and distinct classification methods: decision tree, support vector machine and polynomial classifier. The performance evaluation measures were based on area under the receiver operating characteristic curve (AUC). The most appropriate region for distinguishing the different tissues (normal, hyperplastic and neoplasic) was defined: the corresponding lacunarity values and a rule's model were obtained considering combinations commonly explored by specialists in clinical practice. The best discriminative values (AUC) were 0.906, 0.891 and 0.859 between neoplasic versus normal, neoplasic versus hyperplastic and hyperplastic versus normal groups, respectively. The proposed protocol offers the advantage of making the findings comprehensible to pathologists.

1. Introduction

Prostate cancer is the fifth most frequent form of cancer worldwide with significant morbidity/mortality rates and loss of quality of life. It is considered a disease of the elderly, with a peak incidence and mortality around 70 years of age, accounting for up to 30% of clinical tumors recorded in men and 60% of all cancer-related deaths in the gender (de Arruda et al., 2013; Grönberg, Damber, & Damber, 1996; Schröder et al., 2009).

The diagnosis of prostate cancer is based on clinical (digital rectal exam), laboratorial (prostate-specific antigen test) and radiological (ultrasound and computed tomography) exams. However, the results of this well-defined protocol may underestimate the extent of the cancer (Cooperberg, Lubeck, Grossfeld, Mehta, & Carroll, 2002; Dangle, Shah, Kaffenberger, & Patel, 2009; Leewansangtong, Wiangsakunna, & Taweemankongsap, 2009; Lilja, Ulmert, & Vickers, 2008). In addition, the examination of histological specimens under the microscope is one of the most reliable methods to verify the glandular architecture of the prostate, such as the stroma, the epithelium and the lumen. Roughly speaking, the stroma can be defined as the gland unit consisting of smooth muscle cells, fibroblasts and endothelial cells. In normal prostate tissue, the gland units are together and surrounded by fibromuscular tissues. The epithelium is comprised of basal epithelium, secretory epithelium, neuroendocrine cells and stem cells. A gland unit is made of rows of epithelial cells located around of a lumen, which can be understood as a "hole" or gap in the tissue (Barry, 2001; Chung, Baseman, Assikis, & Zhau, 2005; Gann, Hennekens, & Stampfer, 1995; Lilja et al., 2008). The regular arrangement of the gland units is disrupted with the uncontrolled replication of the epithelial cells. The consequence is the lumen filled with epithelial cells and the stroma with an architecture showing evidence of decline. These findings indicate prostate biopsy images with hyperplasia or

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cancer. In Fig. 1 is shown samples of prostatic images illustrating normal, hyperplastic and neoplasic (cancer) regions.

Methods based on image processing or pattern recognition have been developed to examine the glandular architecture of the specimen. The approaches have considered measurements describing the color, shape or texture properties of the components cited previously (Huang & Lee, 2009a; Huisman et al., 2007; Keipes, Ries, & Dicato, 1993; Sertel et al., 2009; Tabesh et al., 2007; Taverna et al., 2009; Wong et al., 2006; Zhu, Williams, & Zwiggelaar, 2006). The fact is that there is no an universal descriptor of texture able to provide the best quantification for different types of images. However, fractal techniques appeared to be an alternative for texture analysis with properties of self-similarity, mainly when compared to Gabor filters, Wavelet transform, Markov Random Field, Multichannel filtering and Haralick descriptors (Li, Chang, Ke, & Huang, 2012; Lopes & Betrouni, 2009; Lopes et al., 2011b; Ohanian & Dubes, 1992). Furthermore, features based on fractal geometry can enhance the discriminative power and contributed to new texture characterization, mainly using multi-scale approach (Huang & Lee, 2009a; Li et al., 2012; Lopes & Betrouni, 2009; Lopes et al., 2011a; Ohanian & Dubes, 1992). The fractal literature shows that most models are still based only on the fractal dimension approach, which may to quantify many problems with a good efficiency (Atupelage, Nagahashi, Yamaguchi, Sakamoto, & Hashiguchi, 2012; Bizzarri et al., 2011; Huang & Lee, 2009b; Lopes et al., 2011a; Smith, Marks, Lange, Sheriff, & Neale, 1989; Tai, Li, Wu, Jan, & Lin, 2010; Tambasco, Costello, Kouznetsov, Yau, & Magliocco, 2009; Yu et al., 2011). However, the fractal dimension may present the same self-similarity law for distinct structures. An alternative is the lacunarity descriptor, which is based on term defined by Mandelbrot (1983). This descriptor quantifies the distribution of gaps in the fractal, being that a fractal with high lacunarity has large gaps (Plotnick, Gardner, Hargrove, Prestegaard, & Perlmutter, 1996). Beyond being an intuitive measure of gaps, lacunarity can quantify additional features of patterns such as rotational invariance and more generally, heterogeneity. This descriptor can be an effective method for discrimination of cancer cell (Borys, Krasowska, Grzywna, Djamgoz, & Mycielska, 2008; Ivanovici & Richard, 2009; Smith, Lange, & Marks, 1996). Studies on prostatic images with fractals methods have been proposed but are not yet based on lacunarity.

In this paper are presented techniques for the identification and quantification of regions of interest in prostatic images representing normal, hyperplastic and neoplasic (cancer) groups. The novelties of the proposed study are: (1) a new segmentation method; (2) the most appropriate region for distinguishing among the different groups was defined by applying the multi-scale lacunarity as descriptor of prostatic tissues stained with hematoxylin and eosin (H&E); (3) the quantifications allowed determining the tendency of the groups studied and a rule's model for the evaluation of prostatic images; (4) the proposed protocol offers the advantage of making the findings comprehensible to pathologists, considering classifications with combinations commonly explored in clinical practice and/or Computer-Aided Diagnosis. In the next sections a discussion concerning our strategy is presented.

2. Methodology

The proposed method was organized as follows: in Section 2.1 is described the employed image database; in Section 2.2 is defined the segmentation method applied to the color channels, which was useful for separating the regions of interest (stroma, epithelial cells and lumens); in Section 2.3 is described the formalization of multiscale lacunarity, which was used to quantify images from each group (normal, hyperplastic and neoplasic); and, in Section 2.4 is defined the quantitative evaluation used to validate the proposed method.

2.1. Image database

The processing was applied to histological samples produced from the prostates of thirty-four patients of different races – aged

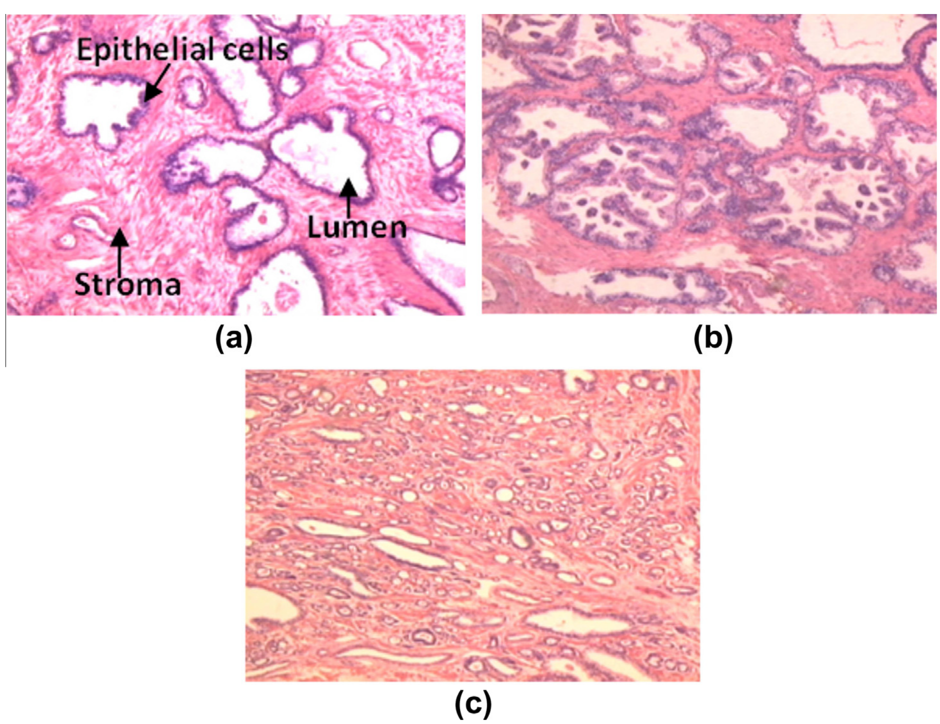

Fig. 1. Samples of H&E-stained prostatic tissues from serial sections of the same histological prostate specimen: normal is illustrated in (a), hyperplastic is shown in (b) and neoplasic is presented in (c).