ELSEVIER

Urologic Oncology: Seminars and Original Investigations ▮ (2017) ▮▮▮–▮▮▮

UROLOGIC ONCOLOGY

Original article

Computer-assisted cystoscopy diagnosis of bladder cancer

Martin E. Gosnell, Ph.D.[a,b], Dmitry M. Polikarpov, M.D., M.Res.[a,c,e,f,*], Ewa M. Goldys, Ph.D.[a], Andrei V. Zvyagin, D.Sc.[a,d,e], David A. Gillatt, M.B., Ch.B.[c]

[a] *ARC Centre of Excellence for Nanoscale BioPhotonics, MQ Photonics, Macquarie University, Sydney, Australia*
[b] *Quantitative Pty Ltd, Sydney, New South Wales, Australia*
[c] *Department of Clinical Medicine, Faculty of Medicine and Health Sciences, Macquarie University, Sydney, Australia*
[d] *Institute of Molecular Medicine, Sechenov First Moscow State Medical University, Moscow, Russia*
[e] *Laboratory of Optical Theranostics, Institute for Biology and Biomedicine, Lobachevsky State University of Nizhny Novgorod, Nizhny Novgorod, Russia*
[f] *Young Urology Researchers Organisation (YURO), Melbourne, Victoria, Australia*

Received 29 May 2017; received in revised form 16 August 2017; accepted 29 August 2017

Abstract

Objectives: One of the most reliable methods for diagnosing bladder cancer is cystoscopy. Depending on the findings, this may be followed by a referral to a more experienced urologist or a biopsy and histological analysis of suspicious lesion. In this work, we explore whether computer-assisted triage of cystoscopy findings can identify low-risk lesions and reduce the number of referrals or biopsies, associated complications, and costs, although reducing subjectivity of the procedure and indicating when the risk of a lesion being malignant is minimal.

Materials and methods: Cystoscopy images taken during routine clinical patient evaluation and supported by biopsy were interpreted by an expert clinician. They were further subjected to an automated image analysis developed to best capture cancer characteristics. The images were transformed and divided into segments, using a specialised color segmentation system. After the selection of a set of highly informative features, the segments were separated into 4 classes: healthy, veins, inflammation, and cancerous. The images were then classified as healthy and diseased, using a linear discriminant, the naïve Bayes, and the quadratic linear classifiers. Performance of the classifiers was measured by using receiver operation characteristic curves.

Results: The classification system developed here, with the quadratic classifier, yielded 50% false-positive rate and zero false-negative rate, which means, that no malignant lesions would be missed by this classifier.

Conclusions: Based on criteria used for assessment of cystoscopy images by medical specialists and features that human visual system is less sensitive to, we developed a computer program that carries out automated analysis of cystoscopy images. Our program could be used as a triage to identify patients who do not require referral or further testing.

Keywords: Urinary bladder; Urinary bladder neoplasms; Cystoscopy; Image interpretation, Computer-assisted; early detection of cancer; Endoscopy

1. Introduction

Bladder cancer is one of the most expensive cancers to treat on per patient basis. Among the reasons for that is the need for a long-term surveillance, which is caused by high rates of recurrence and progression [1,2]. The key diagnostic modality for bladder cancer detection and surveillance is cystoscopy with a follow-up histological evaluation of resected tissue [3–5]. In this approach, a cystoscope is inserted into the bladder and its inside is surveyed for suspicious lesions. The clinician makes a judgement based on their professional experience as to whether they need to take a biopsy for subsequent pathological analysis. In a clinical situation, this process may involve a triage where less experienced personnel make a negative determination in straightforward cases and

This work was supported by the Government of the Russian Federation (Megagrant) (Grant no.: 14.Z50.31.0022); and Macquarie University, Australia (Grant no.: 9201 400 205).

* Corresponding author. Tel.: +61-41-347-4975.
E-mail address: dmitry.polikarpov@hdr.mq.edu.au (D.M. Polikarpov).

http://dx.doi.org/10.1016/j.urolonc.2017.08.026
1078-1439/

refer suspicious cases to more experienced staff or perform a biopsy. The subjective character of the assessment leads to errors and positive diagnoses that could be made at earlier cancer stages, as well as unnecessary further interventions associated with negative affect on patient outcomes and cost of the treatment.

Over the past few decades, information technologies have been developing rapidly and have become widely used in medicine [6–10]. Computer-assisted detection and diagnosis systems, that can capture information and present it in an unambiguous way, tend to be increasingly valued, as they reduce subjectivity and error rates.

In this project, we introduce a computerized triage system that can automatically analyze cystoscopy images taken in standard examinations and determine whether further evaluation is required. The purpose of the system is to classify images as means of removing (or assigning low priority to) those cases, where the system indicates that clearly no malignant disease is present. Cystoscopy images are highly heterogeneous and, to accurately extract the information they contain, we first partitioned the images into tissue image segments, classified these and used these results to bin images into healthy or diseased based on a segment class voting system. As in any triage, it is important that the classifier does not miss even slightly suspicious and only potentially neoplastic changes, whereas producing a false positive is acceptable, as those images will be re-examined by a specialist urologist who makes a final decision. The software could automatically parse the cystoscopy image data as a means of prioritizing treatment. As a further extension to this, patients could be shown the result of the classifier as a probability, which they can take into account considering further testing. In general and especially in circumstances where patient prioritization is necessary, if the classifier threshold were set such that the number of false negatives is minimal (preferably zero), then any negative disease result produced by the classifier could be used to assign a low priority to this patient.

2. Materials and methods

2.1. Cystoscopy data

This study included 233 anonymised cystoscopy images with a biopsy pathology report obtained during diagnostic and surveillance cystoscopy. Out of them, 110 images demonstrated malignant tumors confirmed by pathology and 123 images were nonmalignant. Inflammation or scarring was observed in 60 benign images. These had the potential to affect the specificity of this triage system, however, none of the images were considered indeterminate after assessment by an experienced surgeon in our team. A total of 93 images (40%) were used for selection of features, whereas training and testing required 70 images (30%) each.

2.2. Graphical user interface for supervised extraction of 4 classes of tissue

To capture criteria used by experts in visual analysis, we created a graphical user interface for subjective images classification, segmentation, and supervised extraction of 4 tissue classes: healthy, cancer, inflammation, and vein. Experts were also required to indicate the reasons for their decision, such as color, surface, shape, and size of the object of interest. These reasons were further ranked according to clinical opinion regarding their importance, to enhance the expertise encapsulated in the automated system.

2.3. Specialised color segmentation system for automated tissue classification

Our next task was to develop an unsupervised segmentation system to mimic the capability of experts to see distinct segments of tissue which they would then classify. This distinction is partly based on color: inflamed tissue appears to occupy a region within color space ranging from a brighter orange red color through to a paler looking pink, therefore, we were particularly interested in good red separation. As, in general, segmentation algorithms require a contrast image to capture meaningful edges while reducing the effect of gradients in connected areas, the color image we generate should be minimally affected by nonuniformity in illumination. However, the source of illumination in cystoscopy is very nonuniform owing to proximity and angle of the probe to the tissue. In this situation, simple intensity level-based segmentation gave poor agreement with an expert segmentation ($\sim$30%), whereas our more sophisticated segmentation gave good agreement (80%). This was because the most common red-green-blue color space suffers from an intrinsic condition that a color vector cannot simply be scaled while retaining the same color. To develop appropriate segmentation, we, therefore, transformed the images to an illumination sensitive color space L*a*b, one of several color spaces engineered specifically for characterization such as skin tone, where quality of color gradient images is critical [11–13]. Here, L stands for luminance, a for red-green, and b for blue-yellow color. We also used hue, saturation, and value color space [11–13].

To optimally capture changes in tissue color, luminance, and texture, we developed 3 separate algorithms found to work well specifically on the bladder images. The first algorithm involved the use of an illumination insensitive color space (a*b of an L*a*b image) and a color morphological reconstruction to capture color information. We obtained local neighborhoods of pixels, treated each pixel color as a vector, calculated the distance between the vectors of adjoining pixels, as a measure of color gradient, and assigned each centre pixel location within the new gradient image with the maximum value of neighboring