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Polarised infrared light enables enhancement of histo-morphological diagnosis of prostate cancer

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RESEARCH

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ABSTRACT

Background
In general, histomorphologic examination of a prostate tissue is necessary after the prostatectomy.

Aims
This study was carried out to investigate a possibility of the usage of polarized light for the formation and analyse of infrared images of prostate cancer.

Methods
Experiments were carried out in isolated prostates. For the obtaining of prostate infrared images a light source in the spectral range of 840–900nm was used. Infrared light polarization measurement was performed using polarizers working in 700–2000nm. Infrared polarized light incident on a CCD camera matrix was converted into electrical signals and sent to the PC for the creating visible image.

Specially elaborated software converts the electrical signals, received from the CCD camera, from near infrared (NIR) into visible image, that allows us to discriminate infrared images of healthy tissue from the malignant ones.

Results
It is shown that the intensity of near infrared (NIR) light passing through the cancerous outgrowth is lower than the intensity of NIR light passing through the non-cancerous tissue and the cancerous formations are differentiated as the dark areas in the relatively white background.

Conclusion
It has been shown that the utilization of polarized NIR light for prostate cancer targeting and visualization is a promising imaging modality for the discrimination of malignant areas in prostatectomy specimens.

Key Words
Prostate cancer, histo-morphology, polarized infrared light

What this study adds:

1. What is known about this subject?
Near infrared transillumination technology was applied to the breast cancer diagnosis.

2. What new information is offered in this study?
Near infrared transillumination technology is applied to the prostate cancer in this study for the first time.

3. What are the implications for research, policy, or practice?
There is a need to increase effectiveness of histo-morphological investigations of prostate specimens after prostatectomy.

Background

Patients with a diagnosis of prostate cancer are suggested radical prostatectomy in many cases. After this surgical operation prostatectomy specimen usually examined with histomorphologic method.[1] The aim of this examination is a detection of cancer with a high accuracy in prostatectomy specimens and the determination of its aggressiveness correlating with the Gleason score. This examination would

have a significant impact on the prediction of outcomes for patients after surgical operation. Conventionally the entire gland and seminal vesicles are sectioned, and examined microscopically. This often means that 20–40 microscopic sections are examined. It is evident that an investigation of a histomorphologic samples and the detection of cancerous malignancy is a timely and a labour consuming task. In our previous work we have shown, that near infrared radiation could be used as a tool for cancerous outgrowth detection in prostatectomy specimens.[2] In this paper we show, that the polarized infrared radiation could be successfully used as an effective tool for the cancerous outgrowth detection in prostatectomy specimens. Thereby, positive correlation between infrared radiation and macroscopic and microscopic findings could lead to higher accuracy and efficiency of histomorphologic investigations.

Method

Experimental materials, such as prostate glands, were obtained from the radical prostatectomy. The number of prostates investigated with the use of polarized light was 32. Light emitted diodes (LEDs) (QT Brightek Company, USA), were utilized as the light sources, emitting infrared light in the 850–900 nm range of the optical spectrum. The irradiated power of LEDs was low, in the range of 0.08–0.14 Watt and therefore, they did not cause any heating and damaging of the prostate tissues. To observe the prostate glands in the near infrared spectrum a CCD camera (Dage-MTI, USA) coupled with the computer was used.

It is known that light is an electromagnetic waves, with its electric field vectors vibrating in all planes that are perpendicular with respect to the direction of propagation. This is true to visible wavelengths of the spectrum and invisible infrared waves. If the electric field vectors are restricted to a single plane by filtration of the beam with specialized materials, called polarizers, then the light is referred to as plane or linearly polarized light.[3] In Figure 1 a schematic is shown depicting the conversion of non-polarized light into polarized one.

If optical active substances are placed on the path of the polarized beam the electric vector polarization angle changes. Consequently, corresponding rotation of the second polarizer causes passing of the light through it (Figure 2).[4] For the polarizing of infrared light we used a Linear Polarizer APIR29-020 (American Polarizers, Inc). In experiments LED was placed outside the prostate gland, from the bottom side, enabling near infrared light to totally penetrate a first polarize film, prostate tissue sample, another polarize film and finally to the CCD camera. Figure 3 shows the experimental setup.

Cancerous outgrowth is observed as areas with high optical density. The optical density of healthy area is much lower. Developed software measures average densities for cancerous and healthy areas and calculates their ratio. Method for measurement of the optical density in the IR image is described elsewhere.[5]

For histomorphologic investigation, prostate tissues were fixed in formalin. After that prostate was weighted and measures in three projections. Sectional slices were made inter-perpendicularly with 4mm steps. Each slice was divided into four parts and was labelled as right, left rear, and front specimens. Then, slices were placed in cartridges. Each slice was documented photographically. After fixing in paraffin, tissues were sliced with a microtome for dyeing and processing. The Hematoxilin- eosine was used as the dye. The microscopic investigations: surgical boundaries (apex, prostate basis, right and left bounders) were investigated for detection of morphological stage. Then, the exact localization of tumour was determined. After that Gleason score was determined and a volume of tumour in the prostate was measured. Pathological stage was determined (pT NM): capsule was investigated. Vesicular invasion and number of metastatic lymph noodles were investigated. Perinervous invasion was determined.

Results

Experiments have shown that a prostate tissue behaves like above-mentioned optically active substances and causes turn of the polarization angle. By selecting an appropriate angle between polarizers, the infrared rays passing through the prostate tissue, hits a CCD camera matrix and are transformed into the electrical signals that are transferred to a computer. The software developed by us, transforms these signals into visible images. In this way the prostate infrared image is obtained. In the infrared images the cancerous formations correspond the areas with high optical density, which are enclosed with a much lower optical density. Figure 4 shows the infrared image of single cancerous prostate in the polarized and non-polarized light. In the image the cancerous outgrowths in polarized IR light are distinguished much sharper then in unpolarized IR light. In the infrared images, the cancerous formations are observed as the dark areas in the brighter background. However, the intensities of illumination of these dark areas are not homogeneous and there are differences in the intensity. It should be noted that the histomorphologic investigations followed to the examinations in the infrared

rays, have shown that the areas with different high optical density correspond to the cancer outgrowths characterized with different aggressiveness. In the case of prostate shown in Figure 4 cancerous domain with Gleason score 7 was observed as the most dark area. The relatively bright areas corresponded to the non-cancerous regions. Histomorpologic proof of this statement is shown Figure 5.

In some cases, cancerous formations in the prostate tissue are distributed in the form of bounded areas that are characterized by the same aggressiveness. One of such prostate infrared image is shown in Figure 6.

An infrared image of prostate slice in polarized light is shown in Figure 7. The thickness of slice is 10 millimetre. It is important to note that this slice is obtained after the processing of prostate in formalin. Processing of prostate in the formalin does not prevent the formation of infrared image of the prostate. As shown in the figure cancer is distributed throughout the prostate in the form of bounded areas. In this infrared image we observe two main different intensities of illumination of the areas. The dimensions of the areas are in the range of several millimetres. Further histomorphologic examinations have confirmed that these high optical density areas correspond to cancer outgrowths.

Discussion

Radical prostatectomy is conducted in patients who have diagnosed with prostate cancer. A postsurgical histomorphologic examination is necessary in order to be correctly plan and perform prediction of outcomes for patients after surgical operation. Therefore, a Histomorpologic study should examine in detail whole tissue of prostate rather than sections. Our experiments have shown that the use of polarized infrared rays to get the infrared image of the isolated prostate, gives the opportunity to differentiate the malignant areas from non-malignant ones, with high accuracy. This method allows us to visualize the cancer outgrowths the size of which is in the millimeter ranges. Thus, when IR light passes through the non-cancerous and cancerous tissues, having the same thicknesses, the light intensity passing through the cancerous tissue is much lower, than the light intensity passing through the non-cancerous tissue. To explain this phenomenon we cite the following reasons: the cancerous cells are characterized by non-controlled and chaotic division. Normal cells have one nucleus and one nucleolus. Chromatins are threadlike before the division. Cancerous cells have more than one large, irregularly shaped nucleus and nucleolus, and condensed chromatins. Due to this reason the light penetration in normal and in cancerous cells is not the same, healthy cells are nearly transparent to light, whereas cancerous cells are much less transparent to the light.[6] This judgment is also fair with respect to IR rays, when considering the healthy and cancerous cells of the prostate.

The criteria used by the pathologist for detection of cancer are architecture atypia (invasive growth, perineural infiltration, micro and cribriform glands) and cellular atypia (enlarge nuclei with prominent nulceoli. Thus, for histo-morphological investigation the entire gland and seminal vesicles are sectioned and examined microscopically.[7] This often means that 20–40 microscopic sections including several whole-organ sections from the central part of the gland are examined. Consequently, an examination of prostatectomy specimens is hard and time consuming task. Prior to histomorphologicexaminations, an investigation of prostate in the infrared polarized rays will enable us to discriminate the different aggressive areas from each other and precisely determine their location. This will allow us to significantly reduce the number of microscopic sections and as the result increase the accuracy and quality of histomorphologic investigations.

Conclusion

It has been shown that the execution of polarized NIR light for prostate cancer targeting and visualization is a promising imaging modality for the discrimination of malignant areas in prostatectomy specimens. Our experiments have shown that a passage of polarized NIR light through the cancerous and non-cancerous prostate tissues significantly differs from each other. Therefore, the infrared images of cancerous outgrowth are observed as the dark areas in the relatively bright background. However, it should be noted that the further studies are needed in order to be precisely identified and discriminated different aggressive cancer formations according to Gleason score.

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PEER REVIEW

Not commissioned. Externally peer reviewed.

CONFLICTS OF INTEREST

The authors declare that they have no competing interests.

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ETHICS COMMITTEE APPROVAL

Ethical approval for the conduct of this study was obtained from the Institutional Ethical Committee of the Clinics GIDMEDI of the Tbilisi State Medical University with the reference number 2015- 80/2.

Figure 1: Schematic representation of the light polarization

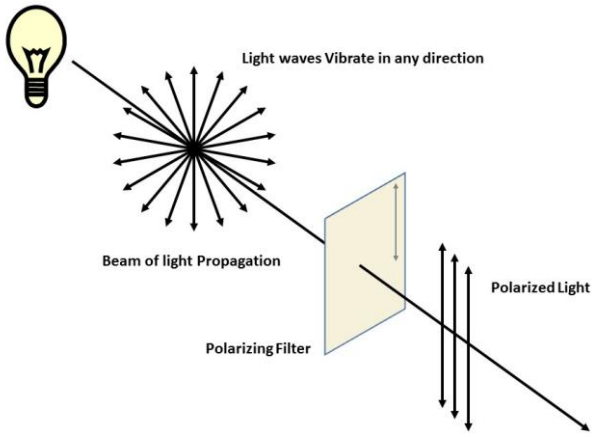

Figure 2: Blocking of polarized light by use of second polarizer film. Wave passing through the polarizer is subsequently blocked by the second polarizer, if this polarizer is oriented horizontally with respect to the electric field vector in the light wave. However, if the second polarizer is oriented parallel with respect to the electric field vector, polarized light will pass through it

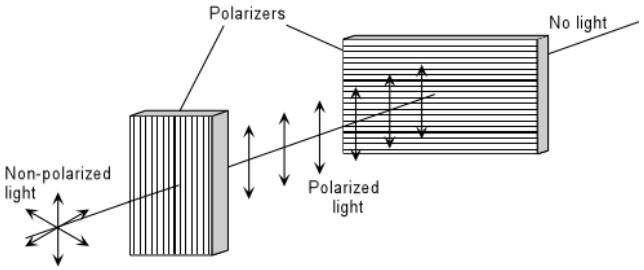

Figure 3: Experimental setup. Yellow arrow indicates a LED holder, Black arrow indicates CCD camera. Infrared light passes through the prostate and enters into the CCD camera. Polarizer films are placed under the Petri dish and in the front of CCD camera lens; thereby the polarizer films are not seemed in this figure. CCD camera is connected to a computer on which monitor we observed an infrared image of the prostate

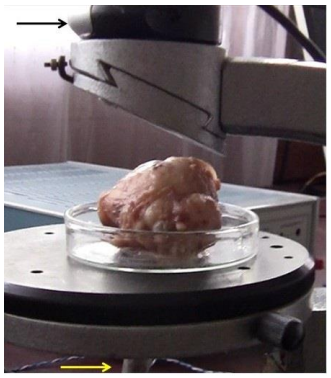

Figure 4: Infrared image of prostate cancer in unpolarized (left) and polarized light (right). Cancerous areas are shown by the arrows

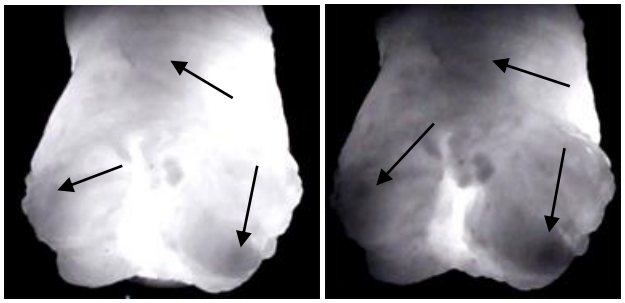

Figure 5: Histologic photomicrograph of the prostate (shown in the figure 4) carcinoma. Intraluminal mucins are observed

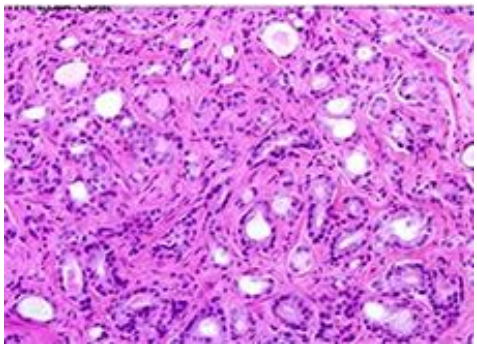

Figure 6: Infrared image of prostate. The arrow indicates one of the cancerous areas. Here are observed the cancer formations, the dimensions of which are several millimetres. Below a scale bar corresponds to a length of 1 centimetre

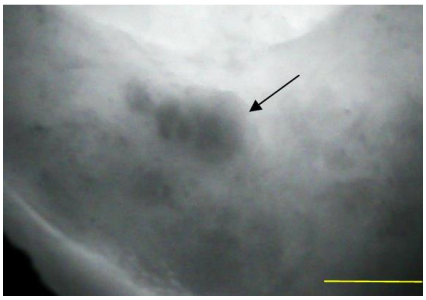

Figure 7: Infrared image of prostate slices in polarized light. The arrow indicates one of the cancerous areas. Below a scale bar corresponds to a length of 1 centimetre