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PROSTATE CANCER DIAGNOSTICS MODELING USING THE INFRARED IMAGING METHOD

Background. Imaging plays an important role in the identification of prostate cancer (PCa). However, a shortcoming of the current imaging techniques is their inability to detect PCa at an early stage of development when tumor volume is small. This led us to explore new and improved imaging methods. The phenomenon that infrared (IR) light penetrates biological tissues caused our efforts to utilize IR rays for PCa visualization. **The aim** of this study was to conduct model experiments to demonstrate how IR light could be used in the future to detect PCa *in vivo*. **Materials and Methods**. Experiments were carried out on prostates obtained after radical prostatectomy. The study was approved by the ethical commission of the Georgia-Israel Joint Clinic "Gidmedi". We developed a device that uses IR light to illuminate a prostate from the inside. In order to get IR images of the prostate, we developed a device with an IR-sensitive charge-coupled device (CCD) camera. The model experiments showed that the intensity of IR light passing through noncancerous and malignant prostate tissues is significantly different allowing their distinguishment. The visualization device can detect PCa lesions as small as several millimeters. **Conclusion.** These results suggest that our device could be useful for the detection of small PCa lesions.

Keywords: prostate cancer, non-invasive diagnosis, modeling.

Prostate cancer (PCa) is the second leading cause of cancer-related death in males globally, according to the World Health Organization [1]. PCa often does not show any symptoms unless quite advanced, and the treatment or surgery is ineffective at the later stages. An early detection of PCa allows for the successful treatment using a variety of techniques.

A key factor in identifying PCa at an early stage is screening, which is based on the detection of prostate-specific antigen (PSA) in the blood that should be not higher than 4 ng/mL. However, PSA lacks selectivity and may even rise in the case of other prostate diseases [2]. If the PSA is elevated, several techniques, such as digital rectal examination (DRE), transrectal ultrasound (TRUS), and magnetic resonance imaging (MRI), are used to diagnose cancer. In addition, positron emission tomography (PET) [3] and computed tomography can be used [4].

These instrumental methods have some shortcomings. DRE is highly subjective and is based on the skills and expertise of the doctors [5]. MRI for PCa detection is of lower specificity with the potential for false positives, and its cost is high [6—8].

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Fig. 1. Prostate illumination tool. Infrared LEDs are mounted on a flexible light guide. The length of the light guide is 50 mm, width 1.8 mm, height 1.68 mm. The light guide is placed into a catheter (shown in the Figure), which is subsequently inserted into the prostatic urethral channel

Fig. 2. The device for the visualization of prostate cancer for model experiments. The dimensions of the tool are: the length is 175 mm, and the diameter is 19 mm. The pinhole diameter is 10.8 mm

Only 60% of PCa hypoechoic on ultrasound, so TRUS should not be used as a first-line screening study as it lacks acceptable specificity [9]. CT scans are utilized in PCa cases where a diagnosis has been established to assess the spread of the tumor to nearby tissues and identify metastases [10]. The shortcomings of PET methods for PCa detection include their limited sensitivity compared to other screening methods like PSA assessment [11]. The last step in any diagnostic process involving instruments is usually a biopsy.

Radical prostatectomy is typically performed in the PCa cases where the cancer spread is limited to the prostate gland. Men younger than 75 years with limited PCa spread and a life expectancy of at least 10 more years are often candidates for radical prostatectomy.

The shortcomings of imaging methods for detecting PCa have led to the search for alternative techniques, such as the IR imaging method. Although near-infrared (NIR) technology has been used in several works for intraoperative image-guided prostate surgery [12, 13], it has not been used for PCa diagnosis.

Our previous research [14, 15] has shown the potential of NIR technology for the detection of some tissue inhomogeneity. In this study, we present model experiments for the detection and imaging of PCa using IR, which helps us better detect real processes.

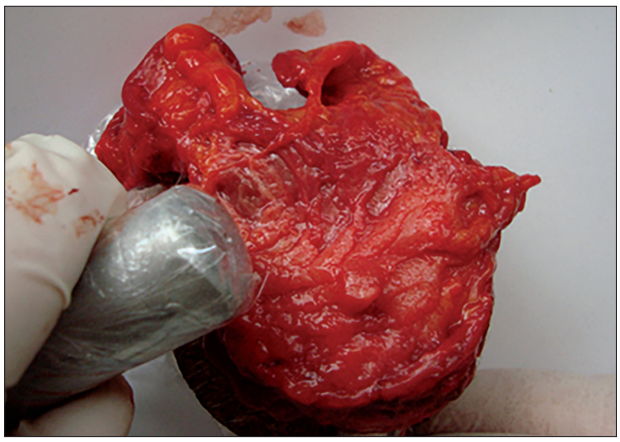


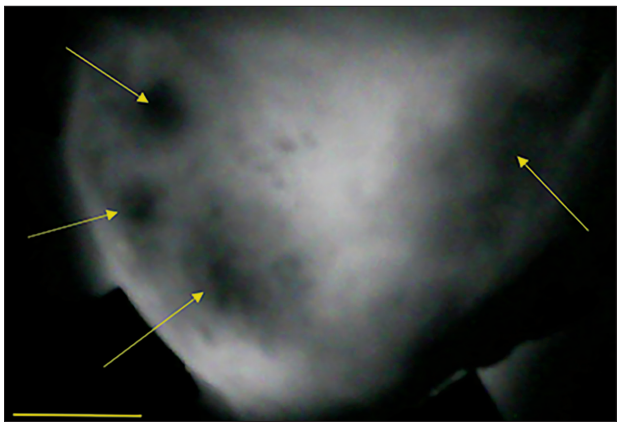
Fig. 3. Isolated prostate and the device

Materials and Methods

For the experiments, prostates obtained after radical prostatectomy in patients aged 65—75 were used. All patients were informed and gave their written consent. The study protocol was approved by the Independent Local Ethical Commission of the Georgia-Israel Joint Clinic "Gidmedi" (ILEC ID NO: 35). We conducted 30 experiments.

We have developed an IR light tool for illuminating the prostate from within (Fig. 1). The tool is a flexible IR light strip that could be placed in a catheter. The dimensions of the light strip and catheter allow for easy location inside the urethral channel of the prostate and provide illumination of the whole prostate tissue. The light-emitting diodes (LEDs) (QT Brightek Company, USA) emitting IR light in the 850—900 nm range were mounted on the strip. The consumption power of LEDs is low, in the range of 0.08—0.14 W, and therefore, they do not cause any heating or damage to the prostate tissues. The light strip can be turned 360 degrees in the catheter and illuminate any desired zone of the investigated prostate gland.

It should be noted that since IR rays are invisible to the human eye, they need to be converted into visible ones to be used for visualization. To obtain IR images of the prostate, we created and assembled an original device. The device (shown in Fig. 2) consists of a charge-coupled device (CCD) camera sensitive to NIR light. The device is equipped with a lens system and allows an observa-



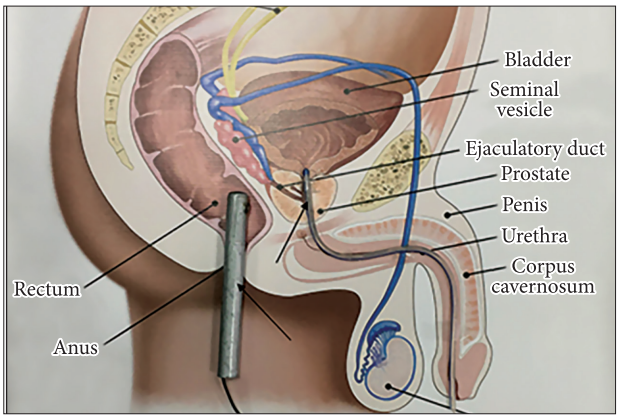


Fig. 4. Infrared image of cancerous prostate. The tumor lesions, which have dimensions of several mm, are shown with arrows. The image below contains a 1 cm scale

Fig. 5. A model of IR imaging of the prostate. It shows the prostate and other male organs. Black arrows indicate the device used to obtain the prostate IR image and the IR illumination strip. The dimensions correspond to an average-sized man. This figure represents a scenario where the device is inserted into the rectum, and a catheter with a light guide inside the urethral channel is used to illuminate the prostate internally

tion of the prostate. Fig. 3 shows the device with an isolated prostate.

IR light emitted from LEDs passes through the tissue providing data on the prostate tissue heterogeneity after its conversion into the electrical signals by the CCD camera. The device output is connected to a laptop. Here, the signals from the CCD camera are processed to create a visible image. This is a two-dimensional (2D) IR image of the prostate. We developed the software that produces the image [14]. The essence of the program is that it compares the illumination intensities of the areas corresponding to malignant tissue to the illumination intensities of areas corresponding to noncancerous tissue on the IR image and calculates their ratio. Based on the calculated meaning of this ratio, the malignancy of the prostate tissue is determined with a probability of 95%.

The following method is used by the software to calculate the ratio of illumination intensities at the areas on the IR image that correspond to malignant and healthy tissues: The software assigns a number between 0 and 255 to each dot of the IR image depending on the illumination (brightness) of that point. Number 0 is assigned to a completely black dot, while number 255 is assigned to a point with the highest brightness. The program measures the light intensities at each point on the IR image corresponding to tumorous as well as noncancerous tissues. The program then calculates the mean illumination intensity of the areas corresponding to both noncancerous and malignant tissues. The mean illumination intensity of the malignant area was designated as X, and the mean illumination intensity of the noncancerous area — as Y on the IR image. After that, the program calculates a ratio of X to Y.

After the IR examination, the prostate was always investigated by the standard histomorphological method. This study, in all cases, revealed PCa lesions and precisely indicated their locations. As a result, we were aware of the existence of the tumor sites determined by histomorphological analyses as well as the areas determined to be malignant based on IR imaging.

Results and Discussion

The investigation has revealed that the IR illumination intensity corresponding to cancerous tissue was significantly lower than that of areas identified as noncancerous tissue. Consequently, the areas corresponding to malignant tissue appeared much darker on the IR image compared to the areas corresponding to noncancerous tissue (Fig. 4). This new IR imaging method enables the detection of cancerous areas as small as a few millimeters (Fig. 4).

The 95% confidence interval calculated for 30 X to Y ratios was 0.46—0.57. Thus, the IR signal intensity of cancerous tissue was approximately twice lower than that for noncancerous tissue due to the higher optical density of the former.

We can use the program to examine any prostate gland, and if the computed aforementioned falls within the range of 0.46—0.57, one can conclude the presence of PCa with a 95% probability.

The purpose of conducting model experiments was to simulate real-life scenarios using an isolated prostate. Fig. 5 illustrates such a scenario for the generation of an IR image of the prostate of a patient undergoing examination.

Model experiments on resected prostate glands have demonstrated that our device may be effective in detecting and visualizing PCa lesions in patients. The evident benefit of the NIR method is its ability to detect small cancerous areas. The absence of photodamage, deep tissue penetration, and simplicity of the NIR LED-based technique provide distinct advantages for PCa diagnostics. However, it is important to emphasize that additional research is necessary to distinguish and identify IR images of PCa with different aggressiveness.

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Conflict of interests

The authors declare no conflict of interest.

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МОДЕЛЮВАННЯ ДІАГНОСТИКИ РАКУ ПЕРЕДМІХУРОВОЇ ЗАЛОЗИ
ЗА ДОПОМОГОЮ ВІЗУАЛІЗАЦІЇ В ІНФРАЧЕРВОНОМУ СВІТЛІ

Стан питання. Методи візуалізації відіграють важливу роль в ідентифікації раку передміхурової залози (РПЗ). Однак. недоліком існуючих методів візуалізації є нездатність виявити РПЗ на ранніх стадіях, коли розміри пухлини невеликі. Тому постає завдання розробити нові та вдосконалити існуючи методи візуалізації. Оскільки інфрачервоне випромінювання проникає крізь біологічні тканини, це дає змогу застосувати його для візуалізації РПЗ. **Мета** дослідження полягала у проведенні модельних експериментів, які б продемонстрували можливість застосування інфрачервоного випромінювання в майбутньому для виявлення РПЗ. **Матеріали та методи**. Для експериментів використовували зразки передміхурової залози, одержані при радикальній простатектомії. Ми розробили пристрій, який дозволяв візуалізувати тканини передміхурової залози за допомогою інфрачервоного випромінювання. Для одержання зображень тканин передміхурової залози використовували камеру на базі пристрою із зарядовим зв'язком. **Результати**. У модельному експерименті було доведено, що інтенсивність інфрачервоного випромінювання, що проходить крізь злоякісну та неушкоджену тканини передміхурової залози, суттєво різниться, що дозволяє їх диференціювати. Наш пристрій дозволяє виявити осередки РПЗ розміром у кілька міліметрів. **Висновок**. Розроблений пристрій може бути корисним для виявлення осередків РПЗ малих розмірів.

Ключові слова: рак передміхурової залози, неінвазивна діагностика, моделювання.