Multi-Channel LED Light Source for Fluorescent Agent Aided Minimally Invasive Surgery

Jiacheng Ren, *Student Member, IEEE*, Janani Venugopalan, *Student Member, IEEE*, Jian Xu, Ph.D., *Member, IEEE*, Brad Kairdolf, Ph.D., Robert Durfee, and May D. Wang, Ph.D., *Senior Member, IEEE*

***Abstract*— Cancer is one of the most common and deadly diseases around the world. Amongst all the different treatments of cancer such as surgery, chemotherapy and radiation therapy, surgical resection is the most effective. Successful surgeries greatly rely on the detection of the accurate tumor size and location, which can be enhanced by contrast agents. Commercial endoscope light sources, however, offer only white light illumination. In this paper, we present the development of a LED endoscope light source that provides 2 light channels plus white light to help surgeons to detect a clear tumor margin during minimally invasive surgeries. By exciting indocyanine green (ICG) and 5-Aminolaevulinic acid (ALA)-induced protoporphyrin IX (PPIX), the light source is intended to give the user a visible image of the tumor margin. This light source is also portable, easy to use and costs less than $300 to build.**

I. Introduction

Cancer figures among the leading causes of death worldwide, accounting for 8.2 million deaths in 2012 [1]. It is the second most common cause of death in the US, after heart disease, accounting for nearly 1 of every 4 deaths [2]. Common types of cancer treatments include surgery, radiation therapy, and many others. Surgeries, when used for treatment, offer the greatest chances of cure for most type of cancers [3].

The academic field has made great progress on cancer treatment by surgical excision, but much work remains to be done to further increase the effectiveness of cancer surgeries. Today, minimally invasive surgery is favored over open surgery because it is less painful and allows shorter recovery time for the patients, with similar effectiveness [4]. However, during cancer excision, it's difficult for the surgeon to see the tumor margin under the endoscope. Detection of tumor margin and clean cut of tumor is vital for long-term patient survival because it lowers the recurrence rate [5]. Fluorescent labels have been widely adopted in many surgical instances to improve the effectiveness of the cancer surgery. There is evidence that the use of tumor-specific fluorescence imaging techniques increases the rate of detecting and quantifying tumor growth [6].There is also evidence that the use of ICG and 5-ALA-induced PPIX helps the surgeons to visualize the tumor during standard surgical resections [7,13]. However, the current use cases of fluorescent dyes are all during open surgeries, which cause more difficulties and longer times to recover.

Portable spectroscopic device (termed SpectroPen) have been used to observe fluorescent labeled cancer tumor margins [8]. The SpectroPen allows convenient tumor margin detection during an open surgery and ex vivo tissue study. However, there are currently no commercial or academic light sources to assist a contrast-enhanced minimally invasive surgery. Jian Xu et al. at Emory University are using optic fibers to guide laser during minimally invasive surgeries [9]. The problem, though, with fiber optics laser assisted endoscopy is that the surgeon cannot see the tissue in visible colors unless another white light source is provided. The optical fiber also needs to be placed in an independent channel of the endoscope. Therefore, one of the ports of the endoscope is always engaged and cannot be used for other purposes such as biopsy and suction. To solve this issue, we proposed a single endoscope light source with colored and white LEDs, which offers both fluorescent excitation and general lighting.

In addition, we decided to include the idea of multiplexed spectroscopy in the design, which uses multiple fluorescent labels at the same time to compare different images, revealing more information about the cancer site [10]. With a wide selection of wavelengths and narrow peaks, LED becomes one of the best light source choices for this kind of study.

In order to achieve the aforementioned goals, in this paper we present the development and testing of a LED light source for minimally invasive surgery which can be used for contrast-enhanced endoscopy and multiplexed spectroscopy. The light source provides two peak wavelengths (750nm and 405nm) and white light for general purpose, as well. LED lights can be coupled to an Olympus OSF-3 endoscope for surgery and an SMA905 fiber bundle for multiplexed spectroscopy. The two-peak wavelengths are chosen to work with two fluorescent agents (ICG and PPIX). The device provides two convenient use cases in a portable and cost efficient manner.

This research has been supported by grants from The Health Systems Institute (HSI) of Georgia Tech and Emory University, National Institutes of Health (NIH) (U54CA119338, 1RC2CA148265), Georgia Cancer Coalition (Distinguished Cancer Scholar Award to Professor MDW), Georgia Research Alliance, Hewlett-Packard (HP) and Microsoft Research.

J. Ren is with the School of Electrical and Computer Engineering, Georgia Institute of Technology and Emory University, Atlanta, GA 30332 USA (e-mail: jc.ren@gatech.edu)

J. Venugopalan is with the Wallace H. Coulter Department of Biomedical Engineering Department, Georgia Institute of Technology and Emory University, Atlanta, GA 30332 USA (e-mail: jvenugopalan3@gatech.edu)

J. Xu is with the Department of Biomedical Engineering, Emory University School of Medicine, Atlanta, GA 30322, USA (e-mail: jian.xu@emory.edu)

B. Kairdolf is with the Department of Biomedical Engineering, Emory University School of Medicine, Atlanta, GA 30322, USA (e-mail: bkairdo@emory.edu)

MD Wang is the corresponding author with the Biomedical Engineering Department, Electrical and Computer Engineering, Winship Cancer Institute, Parker H. Petit Institute of Bioengineering and Biosciences, Institute of People and Technology, Georgia Institute of Technology and Emory University, Atlanta, GA, USA (email: maywang@bme.gatech.edu)

978-1-4244-7929-0/14/$26.00 ©2014 IEEE

II. Design and Development

The LED light source was designed to offer excitation light for ICG and PPIX, while being portable, cost efficient and easy to use. The two fluorescent dyes were chosen because they are both FDA approved, and they can help surgeons to visualize tumor margin better during a surgery. By knowing exactly the location of the tumor margin, the surgeon is more likely to cut the tumor completely.

A. Fluorescent Dyes

1) Indocyanine green (ICG)

Indocyanine green (ICG) is an FDA proved fluorescent dye that has been used in medical domain for over 30 years [11]. ICG has a peak absorption spectrum at 785nm and a peak emission spectrum at ~810nm in water solution. The selection of LED wavelength is influenced by the limited separation between the excitation and emission spectrum of ICG. Therefore, a 750nm IR LED was chosen to excite the ICG and avoid the ~810nm emission band.

2) 5-ALA-induced protoporphyrin IX (PPIX)

5-Aminolaevulinic acid is a precursor of protoporphyrin IX in the biosynthetic pathway for heme [12]. The fluorescent characteristics of PPIX make it useful for cancer detection. PPIX has a strong absorption band in the violet spectral range (380-420nm) and an emission spectrum at ~634nm [13]. In the tissue, the red fluorescence bands emitted by PPIX at 635 and 704 nm are superimposed by a broad band of autofluorescence, peaking at approximately 520nm.

B. Design of the Light Source

The multi-channel LED light source was designed for detecting ICG and PPIX, while offering white ambient light for vision. Figure 1 shows the block diagram of the light source. The light source is powered using an external power supply. The green and red dashed boxes are circuit sections, indicating the main circuit board that consists of LED drivers and Pulse Width Modulation (PWM) generator circuits, respectively. Three independent knobs allow the user to adjust light intensity of the LEDs. The red box indicates a circuit board which only contains the three LEDs and heat sinks on the back. This LED board will be vertically placed so that the light path is horizontal. The LED lights travel through the optics and land on the light output hole which adapts to SMA 905 fiber standard. The endoscope light guide adaptor is an install option that can be substituted fast and easily. The key features of the device are: (i) 330mW maximum 750nm output; (ii) 2W 405 nm output; (iii) high power white light output that does not overlap with the emission band of ICG (814-851 nm); (iv) all LEDs are dimmable and controlled independently; and (v) output adapts to SMA 905 fiber standard and the light guide of the Olympus OSF-3 endoscope.

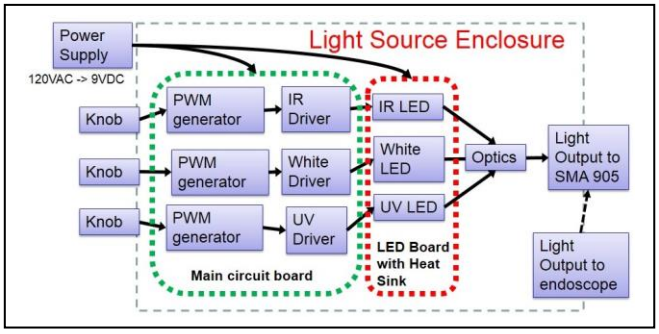

Figure 1: The block diagram of the LED light source.

1) Circuits

The LED circuit was designed to drive the LEDs with fixed currents and to control the light intensity with PWM. PWM controls the LED by switching it on and off at a preset frequency and duty cycle, so that the LED appears dimmer while the crossing current does not change. For example, with a 50% duty cycle and 100Hz the LED is ON half of the time and switched every 5ms. In lighting applications, PWM dimming is always a better way of dimming than changing current, because it is easier to control, energy efficient and prolongs the LED's life time. The PWM signal in our application has a frequency of 100Hz, which is higher than common 50Hz or 60Hz bulb. Therefore, the high frequency allows no blinking effect being seen by the user.

A sample circuit schematic is shown in Figure 2. It mainly consists of two parts: the LED driver and the PWM generator. The LED driver uses the LM3401 chip from Texas Instruments, which has a PWM dimming control pin. Connected to the PWM pin is the PWM generator circuit, which is based on a common 555 timer chip and a potentiometer. There are three sets of such circuit each controlling one LED, so that each LED has an independent switch and dimmer. The circuits drains a maximum current of 1.5A (white) + 0.8A (IR) + 0.8A (UV) =3.1A, so a 9VDC/3.5A wall adaptor was chosen as the power supply.

2) Optics

The circuit powers up the LEDs and controls the light intensity, but one more step is needed to collect the light into the output adaptor. Therefore, a lens set was designed to gather as much light as possible before the light goes to the output.

The optical system of the light source should focus the lights coming from the LEDs to a small spot, so that the maximum intensity can be collected by the output. The number of lenses should be kept low to reduce complexity and increase light efficiency. The distance between the LEDs and the output should be minimized to reduce light loss and the size of the whole device.

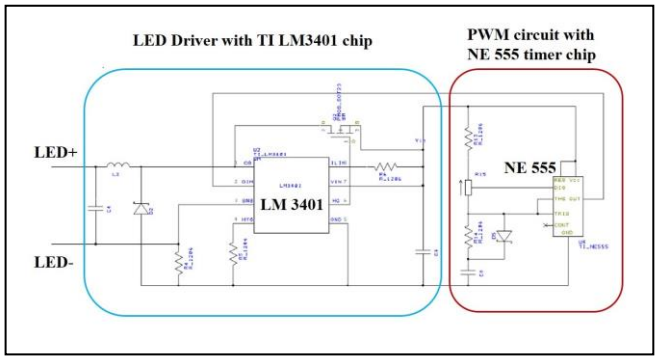

Figure 2: Single LED circuit schematic (shown in DesignSpark PCB). Blue box: LED driver circuit with a Texas Instrument LM3401 chip; Red box: PWM circuit with an NE 555 timer chip.

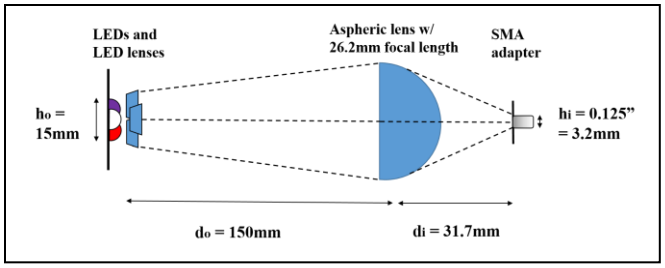

Figure 3: Method of focusing LED light to a 0.125" SMA output.

$$\frac{1}{f} = \frac{1}{do} + \frac{1}{di} \quad (1)$$

$$\frac{do}{di} = \frac{ho}{hi} = M \quad (2)$$

Figure 3 shows the detailed lens setup. The values were calculated by using two fundamental physics equations: equation (1) and equation (2) [14]. Equation (1) shows the relationship between the object distance (do), the image distance (di) and the focal length (f). Equation (2) shows the equality relationship between the ratio of the object distance and the image distance, and the ratio of the object height (ho) and the image height (hi). The ratio is also called magnification (M). Three LEDs were designed to be mounted to a small circuit board with a heat sink (2.88 °C/W). The LEDs were arranged close to each other so that less distance is needed to focus the light. The three LEDs are Roithner LaserTechnik SMB1W-750 LED (750 nm peak, 330mW max power), Lumex TitanBrite UV LED (405 nm peak, 2W max power) and Cree XLamp XML2 white LED (153lm/W, 4.5 W @ 1500mA). Each LED will have a 10mm individual Lens to reduce the view angle. Then the light will go through an aspheric lens (lens detail), which focus the light on to a 0.125" spot. An SMA fiber adaptor (Thorlabs SM1SMA) will be installed at the end of the light path. An additional coupler can be attached to the SMA adaptor to allow connection to the endoscope light guide.

C. Demo Testing

A demo board was built on a perforated circuit board as shown in Figure 4. It contains all the circuit components and is powered by a 9V battery. The demo board was then evaluated on spectrum and light intensity. Each LED was measured with a spectrometer to show its spectrum. Then a 10uM ICG solution sample (excited by the IR LED) and a 2uM PPIX solution sample (excited by the UV LED) were measured with a spectrometer to see if there is any response. The light intensity was measured by a power meter (Newport 1815-C with 818-SL detector) placed 10mm in front of the LED without lenses. The dimming knob was switched from maximum to minimum so that the dimming range was tested.

III. Results & Discussion

A. Spectrum and Light Intensity

The spectrum test results of the LEDs are shown in Figure 5. The three spectra were individually tested and then shown in one graph. The UV LED has a peak of 408nm with full width half maximum (FWHM) of 20nm. The IR LED has a peak of 743nm with an FWHM of 30nm. The white LED has a peak of 440nm and another combined peak at 570nm. It is important to see that the white LED spectrum has nearly no signal above 800nm, so that it does not influence the collection of the ICG responding signal (~810nm).

For the power test, we used the power meter readings of the 90% duty cycle and 10% duty cycle. The maximum light intensity of the white and IR LED exceed the limitation of the power meter, so the measurements of the UV LED were accepted. For the UV LED, the power meter reads 0.13 at 90% duty cycle and 0.052 at the 10% duty cycle. Therefore, the light intensity can be reduced to 40% of its maximum by adjusting the potentiometer. Since all three PWM circuits are identical, the other two LED should have the same dimming range as the UV LED. The optical power of the LEDs on the demo board is lower than expected, meaning that the LEDs are not running under optimum current rating. This should mainly be caused by the added resistance from wires and through-hole circuit components.

B. Fluorescent Dyes Excitation and Visualization

Solution samples containing ICG and PPIX was exposed to the LED light source to measure its effectiveness in exciting the fluorescent agent. Figure 6 and 7 show the collected response collected from fluorescent dye labeled sample when exposed to the LED light source.

It is clear from the graphs that there are significant emission signals when the samples were excited by the corresponding wavelengths. Therefore, this device meets for detecting fluorescent labeled cancer margin.

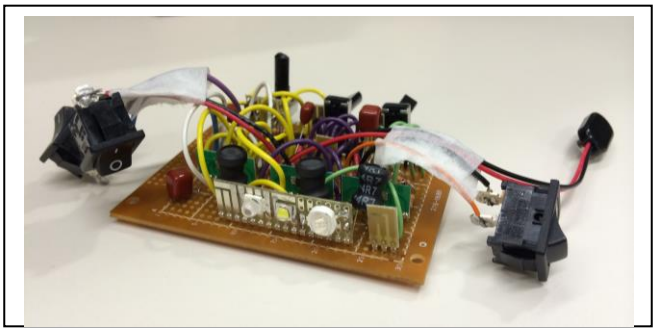

Figure 4: The Demo board. LEDs from left to right: IR, white and UV. Each LED can be individually controlled by a switch and a dimmer.

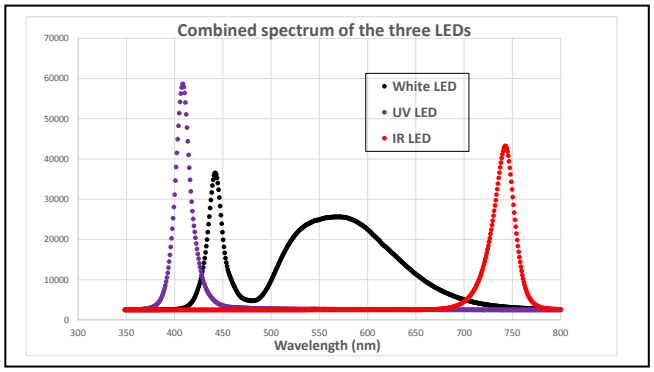

Figure 5: Spectrum of the white, UV and IR LED. The x-axis is wavelength in nm and y-axis is spectrum intensity.

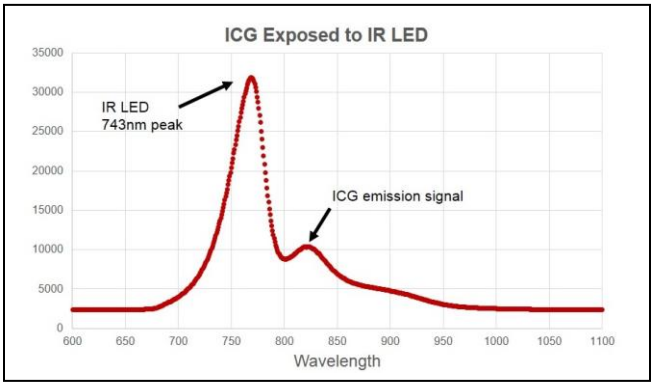

Figure 6: The spectrum result of ICG when exposed to the IR LED. The left peak is the IR LED spectrum and the signal on the right is the ICG emission spectrum.

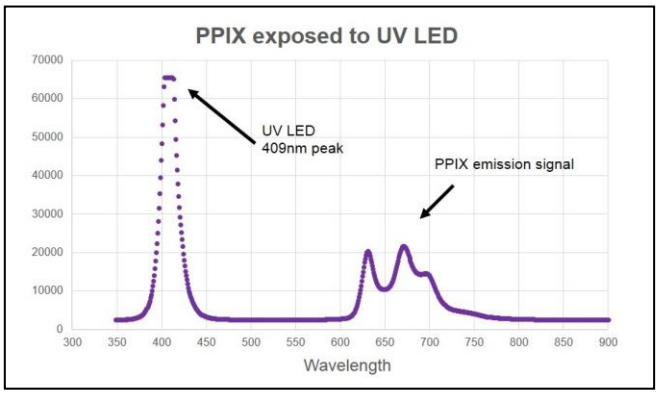

Figure 7: The spectrum result of PPIX when exposed to the UV LED. The left peak is the UV LED spectrum and the signal on the right is the PPIX emission spectrum.

In the near future, we will build a complete prototype with surface mount circuit components, lenses, 9VDC wall adaptor, heat sink and enclosure. By using surface mount resistors, capacitors and inductors, wire resistances can be reduced. A heat sink is also required to cool the LEDs because LEDs are very sensitive to temperature change. Therefore for the future prototype, the LEDs will be mounted on another circuit board with heat sink to simplify the physical structure and heat management. After the prototype has been built, we can then test the device during minimally invasive surgeries performed on cancer treated animals.

IV. Conclusion and Future Work

Surgical resection offers cancer patients better chances of cure for most types of cancer. The effectiveness of the surgery heavily depends on the accurate detection of the tumor margin. In this paper, we propose the design and development of a multi-channeled LED light source. It helps the surgeon with contrast-enhanced agent excitation during minimally invasive cancer surgery and comparing different fluorescent images in multiplexed spectroscopy. The light source was designed to have three LEDs each controlled by an individual circuit, and an optical system to guide the light into a small output port. The circuit features the use of PWM signals to control the light intensity of the LEDs, resulting stable operation, reliable dimming, conservation of energy, and longer LED lifetime. The device provides excitation source for both ICG and PPIX, and white light for general purposes. The testing results showed functional effectiveness of the demo board, by successfully exciting the fluorescent samples and measuring light intensity change when dimming. More LEDs can be added to the existing design to enable multiplexing of more dyes. This can be done by attaching identical LED circuit in parallel as long as the total current draw does not exceed the rating of the 9VDC wall adaptor.

We are planning to use the complete prototype in animal studies (about 10~20 animals). We plan to develop cancers (breast cancers, pancreatic cancers, head and neck cancers) on mice and dogs, and use the light source to perform surgeries on the test animals. We will then evaluate the improvement of the surgery results in comparison with other existing devices such as the fiber optic assisted cancer endoscopy. LEDs with different wavelength can be added to the design as needed to conduct more comprehensive multiplexed spectroscopy with more fluorescent dyes. Ultimately, we can combine more use cases (such as biopsy) to this device and make it a good multifunctional substitute minimally invasive light source for labs and operation rooms.

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