System for Image-Guided Cancer Surgery

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Abstract

Due to development of two fluorescent compounds intended for identification of suspected tumors, there is a need for an endoscope that is capable of exciting both compounds and capturing images of the emissions from the fluorophores. In addition to that, the endoscope will also need to provide a white light image. Several initial concept designs have been created; however, a final design still needs to be created. Once created, the design will need to be analyzed to check its feasibility before it can be put into production. The following is report of the progress made through the design process, including background information, potential designs, and future work.

Introduction

Early detection of cancer cells in patients is one of the primary goals in imaging technology. Identifying tumors at an early stage greatly increases the probability for successful treatment and removal. Dr. Jamey Weichart's lab has developed two fluorescent phospholipid ether small molecules, CLR 1501 and CLR 1502, that are intended for fluorescent image guidance for detection and removal of cancerous tissue. The use of tumor-specific fluorescent molecules allows for a higher level of visual aid in determining location and size of tumors. These fluorophores were developed from CLR 1404, which is a radioiodinated alkyl phosphocholine analog that has shown significant tumor selectivity and prolonged retention. Due to CLR 1404 not localizing in inflammatory lesions and the prolonged retention, CLR 1404 has the potential to be a superior alternative to fludeoxyglucose (FDG), which is a current radiopharmaceutical used in medical imaging modality positron emission tomography (PET). CLR 1404 is currently going through clinical trials. CLR 1501 and CLR 1502 are created by incorporating fluorophores into the hydrophobic alkyl chain of CLR 1404 (Pinchuk, AN et al., 2006). CLR 1501 is excited at 500 nm of light and emits at 520 nm, and CLR 1502 is excited at 772 nm and emits at 790 nm.

With the potential for these fluorescent alkyl phospholipid analogs to be used widely in cancer detection and elimination, it is imperative to have medical devices that can be used with these compounds. The creation of an endoscope that can both excite and capture images of the fluorophores is essential for these compounds to be used most effectively in minimally invasive procedures. The goal of this project is to design an endoscope that is capable of exciting the fluorophores, as well as capturing images that can effectively aid the surgeon during medical operations. In addition to light assembly needing to emit light at 500 nm and 772 nm for excitation, it must also emit white light and capture a white light image.

Design

Design 1 - Switch

Design 1 would use two laser light sources for the excitation wavelengths of 500 nm and 772 nm. This would provide better imaging due to more intense excitation of the fluorophores; however, lasers are about five times the cost of LED lighting. These light sources will be filtered by bandpass filters, which filter out higher and lower wavelengths allowing for a tight excitation band. A beam combining dichroic will reflect one wavelength while allowing the other to pass through (See **Figure 1**). The light sources are located in a cooled tower with the cameras, fiber optic cables transmit the light sources and produce images back and forth. Note that light traveling in different directions in fiber optic cables does not interfere with each other. For this design the fluorescent images are taken during one frame and the visible light image is taken on the following frame. The light paths are switched by placing a mirror in and out of the light paths (See **Figure 2**). This allows for the lighting to be sent down the endoscope through the same optic fibers as the image comes back through, which is beneficial due to it allowing optimal use of all fibers for lighting and receiving instead of having to split them into two groups, one for receiving and one for lighting. A collimated LED light source would be used for the visible light image. No filters are needed, and the images would be recorded by a 30 fps CCD camera designed for visible light. The fluorescent images are taken simultaneously. A beam splitting dichroic splits the returning light into visible and IR. The IR light goes to an IR camera with a bandpass filter, while the 520 nm visible light goes through a bandpass filter to a CCD camera. This design allows for optimal HD imaging, because all images can be taken at 30 fps. The highest quality image is produced by this design, but it is also the highest in cost due to the use of lasers and multiple cameras.

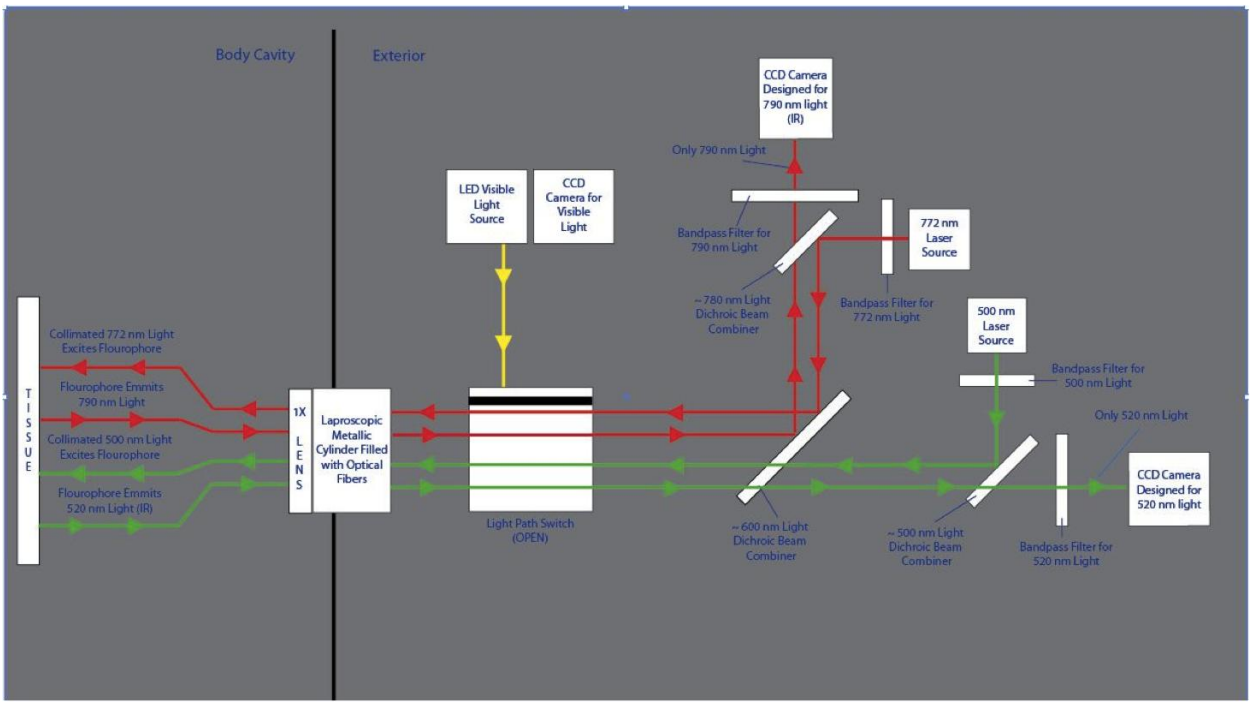

Figure 1. Design 1 with switch open, allowing for excitation and capture of fluorescent images.

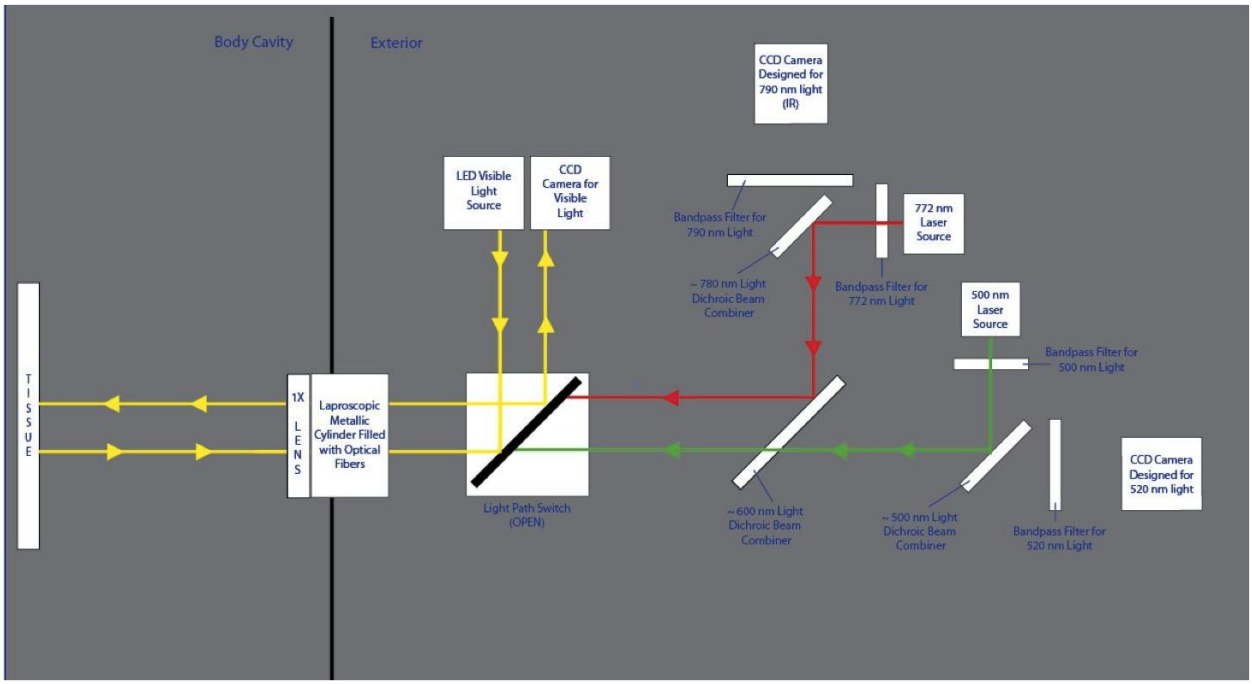

Figure 2. Design 1 with switch closed, allowing for excitation and capture of visible light image.

Design 2 - No Moving Parts

Design 2 would have no switch like in design 1. This design uses two LED light sources, one white and the other in the IR range. The visible light image, IR image and 520 nm image are all captured simultaneously. The laparoscope barrel is split into two bundles of fibers, one connected to the light source and one connected to the cameras. The LEDs are collimated then coupled before being sent down the bundle of the laparoscope. The visible light contains the 500 nm excitation wavelength. The images travel up the other bundle of fibers, where a dichroic pulls out the IR and sends the light through a bandpass filter to an IR camera. The visible spectrum is then split into two optical fibers, one is sent through a 520 nm bandpass filter and then to a camera and the other is sent to a visible camera (See **Figure 3**). By not using a switch, this design allows for the highest fps; however, the green spectrum (520 nm) must be cut out of the visible image which is not ideal. Therefore, even if lasers were used with this design, opposed to LEDs, the image would be of lesser quality than design 1.

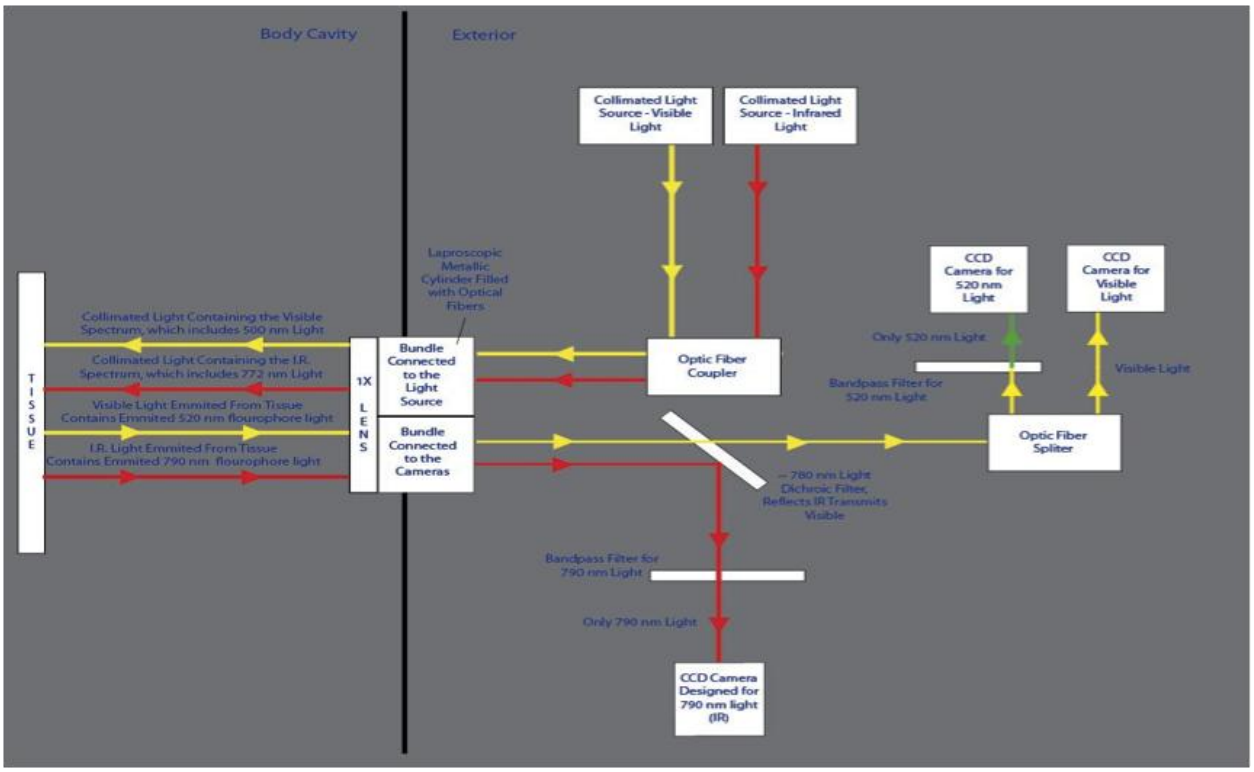

Figure 3. Design 2 with no moving parts (no switch). The 520 nm green is cut out of the visible light image.

Design 3 - Filter Wheels

Design 3 uses two LED light sources, one white and the other in the IR range. IR is captured every frame, while visible and 520 nm light alternate being captured, giving a fps of 40 for IR and 20 for visible and 520 nm light. A high speed filter wheel block is used to put a 500 nm bandpass filter in front of the visible light source to create the excitation wavelength of 500 nm (See **Figure 4**), and then removes the filter for the next frame allowing for the visible light image (See **Figure 5**). The IR and visible light sources are coupled and sent down one bundle of the laparoscope. The return image is split into IR and visible. IR is sent through a 790 nm bandpass filter and then imaged with an IR camera. There is another filter block in front of the visible range camera, allowing for the capture of the 520 nm image and the capture of the visible light image. The light sources are not as powerful with this setup, which produces a lower quality image. Also, the filter block has a match switch speed of 23 milliseconds which limits the fps. This design provides the lowest quality image of the three designs, but it is the least expensive.

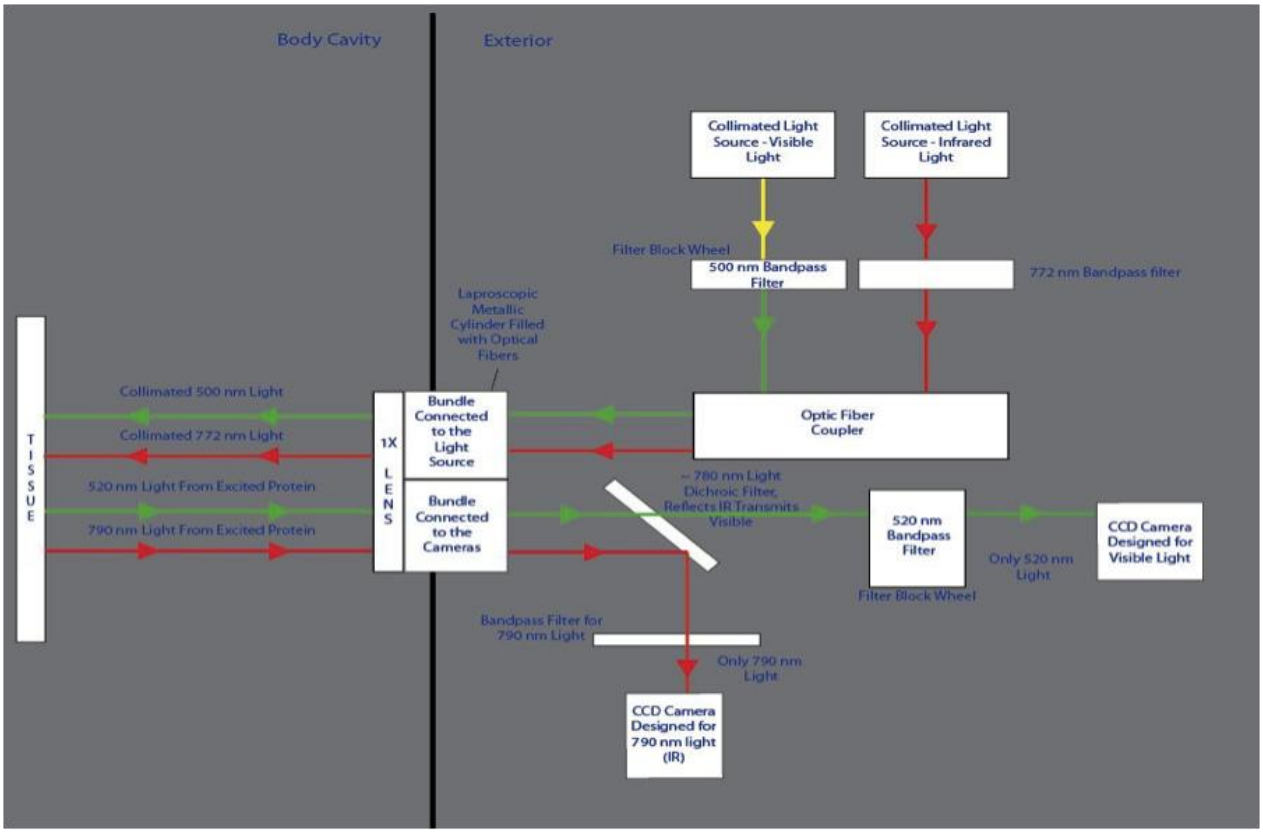

Figure 4. Design 3 with filter wheels. Bandpass filters are present allowing for the excitation and capture of the 520 nm fluorescent image.

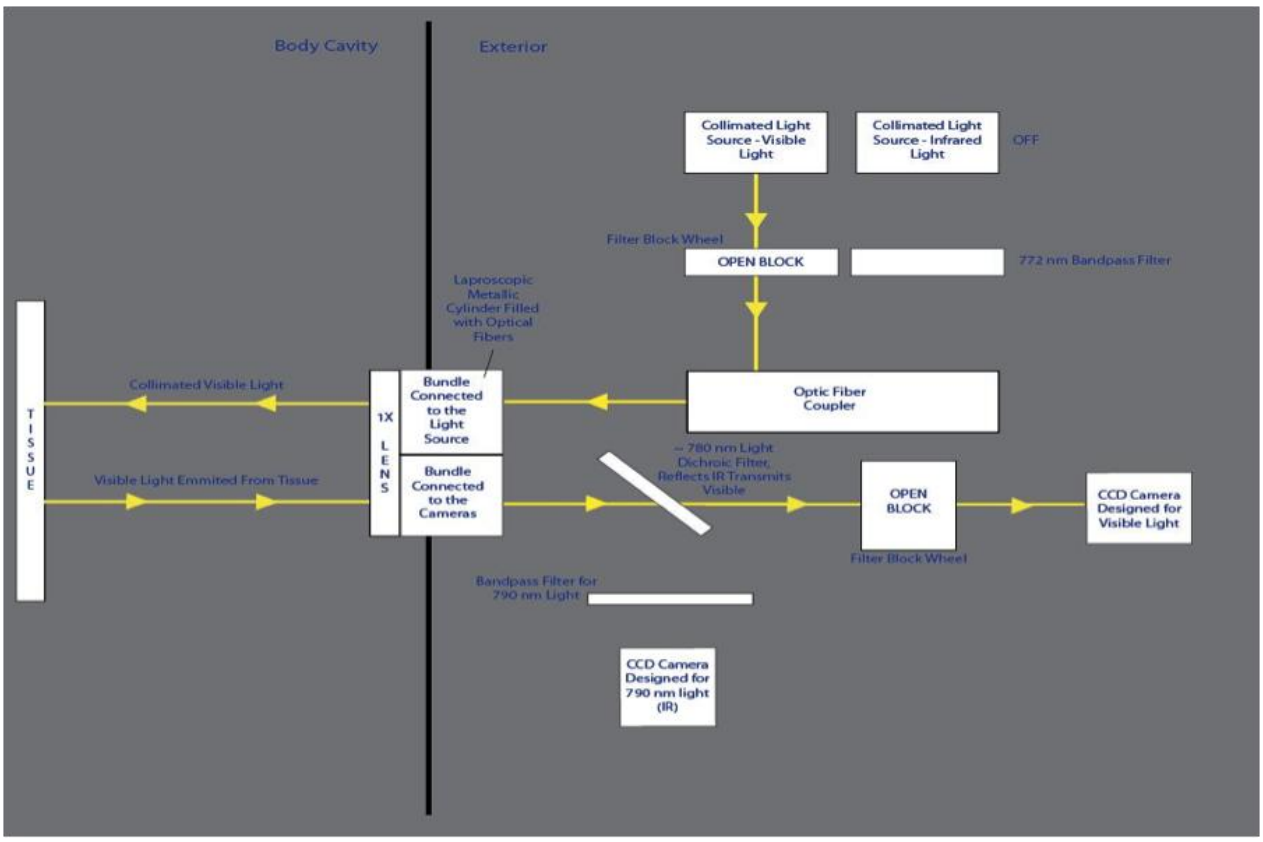

Figure 5. Design 3 with filter blocks open, allowing for capture of visible light image.

Design Matrix

The three designs are evaluated in the design matrix (See **Figure 6**). The number one priority when choosing the final design is the image quality. The purpose of our project is to design a system that will allow a surgeon to have a clear image of the incision area. Other important factors include ease of use for the surgeon and cost to produce. The surgeon needs to be able to easily maneuver the device. The device also needs to be within a reasonable price range; otherwise, manufacturing it will be unrealistic. Durability, ease of production, and image processing were also considered. Design 2 came out on top upon evaluation of the design matrix. This is largely due to it having no moving parts, making it the most basic design. Using LEDs instead of lasers cuts down on manufacturing costs. At this point, the design is not completely finalized; therefore, changes and improvements will be made to the design.

Criteria	**Weight**	**Design 1**	**Design 2**	**Design 3**
Ease of Use	20	15	18	16
Ease of Fabrication	10	7	8	9
Cost	20	12	15	18
Durability	15	13	14	12
Image Processing	5	2	3	4
Image Quality	30	27	25	23
Total	100	76	83	82

Figure 6. Design matrix

Discussion

The switch in design 1 is unrealistic in its current state. However, the design can be tweaked to realistically deflect the light as needed, if that design is further pursued. Upon further evaluation, it was decided the initial design should use a beam splitter instead; therefore, the switch concept will be put aside for the time being. The problem with the beam splitter is light being lost. Currently, the beam splitter appears feasible, but further calculations will need to be done.

Design 3 is currently the least appealing. With the current state of the design, the filter wheels make it too inefficient. However, a filter wheel may be considered for design 2, in order to reduce the number of cameras needed. From these designs, a new design will need to be created for further work. With this improved design, a light budget analysis will need to be done to check the feasibility of the designs.

Each laser and camera would cost about $5000-10,000, and each glass piece or LED would cost about $1000. The budget for project is undetermined at the moment, but as seen from the estimated costs of materials, the cost of manufacturing could be fairly expensive. Future work will include determining a budget and brainstorming ways to most cost effectively create this product.

Future Work

The next step is to finalize a design. This design should not be too fancy with the optics, as the main goal is to begin checking the feasibility of the light sources in exciting the fluorophores and checking whether or not enough light is being emitted back to the cameras for the necessary high quality images. It is expected that the design will be continually improved upon throughout further evaluation.

A light budget analysis will need to be done to check the viability of the design. The light budget analysis will be fairly straightforward for the optical parts, but estimations will need to be made for the fluorophores. Ideally data directly from CLR 1501 and 1502 would be used to make the estimations for the fluorophores but may not be possible. For estimations of the fluorophores, it may possible to use widely accessible data for fluorescein, a common fluorescent tracer. This however will most likely give some degree of error.

Once there is reasonable proof that the design will be able to achieve the goals established, manufacturing will come into play. Due to the high cost of the project and the uncertainty in budget, manufacturing from new parts may not be an option. In order to work around this, it may be necessary to reach out to LOCI or other organizations at the university to see if spare or old cameras and optic parts are available for use. It is also possible that demo cameras may be obtained.

References

1. Pinchuk AN; Rampy MA; Longino MA; Skinner RWS; Gross MD; Weichert JP; Counsell RE. *Fluorescent Alkyl Phospholipid Analogs for Fluorescent Imaging of Tumors*, *J Med Chem*, **2006**, *49*, 2155-2165.

Acknowledgements

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Appendix

Project Design Specification

Our client, Professor Thomas “Rock” Mackie is in need of an endoscopic camera that will be used during the surgical removal of cancerous tumor cells. Recent work in Jamey Weichert’s UW lab has provided two fluorescent phospholipid ether small molecules, CLR-1501 and CLR-1502. These compounds are fluorescent versions of CLR-1404, a current radiolabeled cancer drug under clinical trial. A typical cancer patient would be injected with CLR-1501 and CLR-1502 two or more days before surgery. These compounds build up in tumor cells allowing the surgeon to efficiently and wholly remove any cancerous material. The surgeon must be able to view these cells during their excision, to accomplish this they must be excited with a specific wavelengths of light so that they fluoresce. Our team will be creating an endoscopic camera with an LED assembly and self-cleaning mechanism to allow the surgeon to effectively view these cells.

The LED light assembly will sequentially emit light at 500 nm (excitation wavelength for CLR-1501), 772 nm (excitation wavelength for CLR-1502), and a visible white light. The switching of the LED assembly will be timed to the frame rate of the camera, allowing the camera to capture three different images every three frames, one at 520 nm (emission spectrum for CLR-1501), 790 nm (emission spectrum for CLR-1502), and the third capturing all visible light. These three frames will then be separated into three different live video feeds, with each feed having a frame rate one third that of the camera and displaying its corresponding light spectrum image. The images will be displayed on a hands free monitor system. The endoscopic camera must also be able to clean the camera lens well within the patient’s body. Finally the camera and its lighting/cleaning assembly must all fit through a two cm incision in the patient.

Equipment and funding will be provided to us by Thomas Mackie. Our team will also have access to the rapid prototyping equipment at MIR. Finally Jamey Weichert will supply fluorescent compounds and existing minimally invasive surgical cameras and lighting systems that are currently available.