Intraoral NIR Device for Radiation Induced Oral Mucositis – Design and Development

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ABSTRACT: Radiation induced oral mucositis is a common side effect of radiation therapy in cancer patients. Many oral imaging techniques are available to assess the severity of oral mucositis and complement the subjective visual assessment. Non-contact commercial near-infrared (NIR) devices to evaluate oral mucositis currently are not available. NIR fluorescence imaging has been used, but it is an invasive technique involving injection of a contrast agent prior to imaging. Our objective was to develop and evaluate a non-invasive intraoral NIR probe, that can be used with minimal contact to the mouth during imaging. The probe was designed, and 3D printed as a hand-held device consisting of inter-changeable NIR light emitting diodes (LEDs) (680, 810, 830 nm) and an NIR-sensitive camera, both connected to a raspberry pi (a mini programmable computer) for remote operation of the device. The ability of the probe to perform non-contact imaging, detect NIR signals and penetrate beyond the scattering tissue surface was tested via phantom studies. The hand-held NIR probe could image the mouth without contacting the inside of the mouth 87% of the times it was used. It can detect NIR light and from beneath the surface of the oral tissue, demonstrating its potential for future assessment of oral mucositis.

KEYWORDS: Radiation included oral mucositis; near-infrared imaging; intraoral probe; NIR device; oral mucositis; head and neck cancer; radiation therapy.

Introduction

Radiation Induced Oral Mucositis:

Radiation induced oral mucositis (RIOM) is the medical term used for painful sores and ulcerations in the mouth, tongue, and gums. It is a tissue injury that leads to the development of sores and ulcerations because of damage received from radiation therapy (RT) on epithelial cells. Epithelial cells are rapidly dividing cells that make up the lining of the mouth. During RT for head and neck cancers, RT damages rapidly alimentation dividing cells such as epithelial cells, which leads to the development of ulceration and sores that are the hallmark of RIOM. RIOM is a major dose-limiting toxicity that has negative impacts on treatment and a patient's quality of life.[1] Dose limitation is harmful for treatment as it can lead to poor local tumor control. It can develop into a major life-threatening condition due to obstruction of food, as patients are unable to swallow solids due to pain and swelling.

Statistics of Radiation Mucositis:

In the United States, it is estimated that there are 1.9 million new cancer cases in the year 2021.[2] Around 650,000 patients (36% of patients) receive chemotherapy ever year in the United States alone.[3] Approximately 50% of cancer patients receive RT for treatment against cancer.[4] Over 40% of all cancer patients receiving chemotherapy or RT develop oral mucositis. Of these cancer patients, those receiving RT in the head and neck area or undergoing bone marrow or stem cell transplant are at a higher risk of RIOM. Head and neck cancer patients comprise around 4% of all cancer cases and an estimated number of 66,630 people were expected to develop it in 2021.[5] Up to 80% of patients with head and neck cancer develop RIOM, making RIOM a critical issue for many cancer patients.[1]

Clinical Determination/Diagnosis:

Current clinical diagnosis for RIOM patients is subjectively assessed visually by a doctor based on the World Health Organization (WHO) mucositis scale (Table 1). The WHO mucositis scale categorizes severity of mucositis into four grades, based on soreness, ulceration, and oral functioning such as the ability to swallow food (as given in Table 1).

Table 1: The WHO mucositis scale used for medical diagnosis.[6]

WHO Mucositis Scale	
Grade	**Clinical Features**
1	Soreness/erythema
2	Erythema, ulcers, but able to eat solids
3	Ulcers, requires liquid diet
4	Oral alimentation not possible

The Oral Mucositis Assessment Scale (OMAS) is another grading technique. It is used mainly in research protocols due to the criteria considering ulcerations and erythema separately as well as specific to mouth locations (Table 2). The different mouth locations are further divided into more specific areas such as the palate being divided into the separate soft and hard areas. Therefore, OMAS is informative to researchers since it is capable of separating severity of symptoms from oral functioning. It helps researchers record and analyze results, which are usually acquired to test imaging hardware or potential treatments for RIOM. Apart from the visual clinical diagnosis using WHO mucositis scale or OMAS, researchers implement optical tools and techniques to diagnose and/or assess the severity of oral mucositis. A limitation of both measures is that they require subjective assessment by the assessors.

Table 2: Oral Mucositis Assessment Scale, with grading severity of symptoms from 0 (least severe) to 3 (most severe).[6]

Oral Mucositis Assessment Scale (OMAS)		
Location	**Ulceration**	**Erythema**
Lip - Upper, Lower	0, 1, 2, 3	0, 1, 2, 3
Buccal Mucosa - Right, Left		
Floor of Mouth		
Palate - Soft, Hard		

Optical tools/methods for oral imaging:

There are multiple optical tools and methods used for oral imaging, which includes oral mucosa, teeth, and throat. Optical tools and methods are important for medical imaging because they are more reliable and accurate than visual assessment.[7] Some of these various imaging methods and techniques include near-infrared (NIR) imaging, fluorescence imaging (NIR, autofluorescence, and red light), optical coherence tomography (OCT), and endoscopy (with visible light). Based on the imaged location in the mouth, the above techniques are categorized below in Table 3.

NIR imaging is a noninvasive imaging technique that has a deeper tissue penetration than visible light. NIR light emits light waves between 650-1450 nm.[8] Based on how the tissue scatters or absorbs the NIR light, the imaging technique can detect functional (physiological) changes in the tissue before oral mucositis symptoms, like sores and ulcers, become visible. NIR Imaging is predominantly used for the imaging of the teeth in the mouth (Table 3). For example, NIR Imaging is used to monitor prosthetic implants in the mouth[9] and detect teeth decay and enamel caries.[10]

Fluorescence imaging is a noninvasive imaging technique which uses a wavelength specific dye to help visualize biological processes.[11] Fluorescence imaging is performed using NIR light (700-1700 nm)[12] or red light (400 nm).[13] Fluorescence can detect differences in the tissue when a dye is injected into the tissue and light with different excitation wavelengths are illuminated onto it. The tissue emits a higher wavelength than the excitation wavelength, which is used to detect functional (or physiological) changes. NIR fluorescence has been used to detect oral cancer and tumors in mice.[14] Red fluorescence has been used to detect dental plaque.[13] On the contrary, autofluorescence techniques occur naturally without injecting a dye. Autofluorescence emits visible wavelengths between 375-460 nm.[15] The VELscope is a commercial device that uses autofluorescence techniques to image oral cavities.[11] Clinicians predominantly use fluorescence and autofluorescence techniques to image the oral mucosa and teeth in the mouth (Table 3).

Optical coherence tomography (OCT) is a noninvasive imaging technique to detect structural changes of collagen. OCT techniques typically uses NIR light between 650-1450 nm for oral imaging. OCT is predominantly used to image the oral mucosa and teeth in the mouth (Table 3). OCT has been utilized to analyze the structure of the tooth to detect cavities, fractures, and interfacial gaps, as well as detecting oral lesions.[16,17]

Endoscopic imaging is a minimally invasive technique that uses an endoscope, or a long, slender, flexible instrument, to image inside the body. It usually emits visible light between 400-700 nm.[18] The endoscope is inserted through the esophagus to view the gastrointestinal tract. Endoscopic imaging using visible light is predominantly used to image the throat. Endoscopes are mostly utilized to image esophageal cancer and caustic injuries.[19] Endoscopy has also been used to image oral mucositis when the mucositis extends to the small intestine.[20]

Table 3: Optical tools/methods for imaging of oral mucosa, teeth, and throat.

TOOL/METHOD	MOUTH PART	APPLICATION(S)
Near-Infrared Imaging	Teeth	Prosthetic implants [9], teeth decay, enamel caries[10]
Fluorescence	Oral mucosa (NIR Fluorescence)	Oral squamous cell carcinoma/tumors [14]
	Teeth (red and autofluorescence)	Dental plaque[13], Oral cavities - VELscope [11]
Optical Coherence Tomography	Oral mucosa	Oral Lesions [17]
	Teeth	Enamel caries, tooth fractures, interfacial gaps [16]
Endoscopy (visible light)	Throat	Esophageal cancer, caustic injury [19], small intestinal mucositis [20]

Imaging techniques for oral mucositis:

The above imaging techniques (in Table 3) were used in general to image the oral mucosa, teeth, and/or throat. More specific to RIOM, four studies were found that specifically imaged oral mucositis in cancer patients receiving RT or chemotherapy (Table 4), using OCT, NIR fluorescence, or thermal imaging techniques.

Studies using OCT: One of the studies used OCT and performed contact-based imaging of the mucosa.[21] It imaged and monitored blood vessel density in the mouth region. Since doctors had noticed that patients with oral mucositis tended to have higher blood vessel density, this study aimed to detect early development of oral mucositis before symptoms become severe enough to be visible. They concluded that longitudinal OCT angiographic monitoring can shed light on early-stage symptoms of oral mucositis development.

Unlike the above study, a second study using OCT was performed via non-contact imaging of the mucosa.[22] It imaged the skin for minute ulcerations and sores that would not yet be visible to the naked eye, but those ulcerations and sores if not cared for could develop into oral mucositis. They concluded that with further research more diagnostic points can be identified to provide a more comprehensive evaluation and statistical analysis for this method.

Studies using NIR fluorescence imaging: One study used NIR fluorescence imaging to distinguish between healthy and unhealthy cells.[23] Indocyanine green (ICG), a fluorescence dye used in medical diagnosis, was injected into the mouths of the subjects. After a 30–45-minute interval the Artemis camera system and Quest Imaging Software was used to image for fluorescence intensity distribution of ICG in the mouth. Different intensities of the fluorescence dye in different areas helped identify healthy cells from unhealthy cells.

Studies using thermal imaging: One study used thermal imaging and monitored skin temperature in the mouth region.[24] Since temperature is a reflection of how much blood an area

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is receiving, this study aimed to monitor temperature to detect blood flow since higher blood density is an early symptom of oral mucositis.

In summary, there is no NIR based imaging probe (without the injection of fluorescence contrast agent) to assess the onset or progression of oral mucositis. NIR imaging has been used to image teeth, prosthetic implants in the mouth, enamel carriers, and teeth decay. However there exists no NIR based probe or related imaging studies that specifically image for oral mucositi s. Herein, the focus of our study is to design and develop an NIR probe for RIOM.

Table 4: Compiling of studies discussing imaging oral mucositis specifically caused by radiation therapy or chemotherapy in cancer patients.

Imaging Technique	Optical Coherence Tomography		NIR Fluorescence	Thermal Imaging
Reference	Maslennikova,2017[21]	Calantog, 2013[22]	Cortese 2020[23]	Cohen 2013[24]
Population	Oral, Oropharyngeal and Nasopharyngeal	Primary Breast Cancer Patients	Head and neck squamous cell carcinoma	Head & neck cancer patients
Method	Contact	Non-Contact	Non-Contact	Non-Contact
Measured parameters	Monitors blood vessel density	Images minute ulcerations	Uses Indocyanine green (ICG) to distinguish between healthy and unhealthy cells	Monitors skin temperature changes

Objective of this work:

The objective of this project was to design a noncontact, intraoral near-infrared (NIR) probe to efficiently image RIOM with minimal discomfort. NIR light is useful for imaging the mouth sores produced by oral mucositis due to the light's ability to penetrate deeper into the tissue. Based on the previous studies mentioned above, there is currently no NIR imaging device (without injecting fluorescence contrast agents) for imaging the oral mucosa. A probe, with a size determined by a mucositis patient's ability to open their mouth, was designed. The efficacy of the probe's ability to not touch the inside of the patient's mouth was determined by testing the probe on simulated mouths of different sizes. The camera and NIR light were tested through a variety of studies, including a field of view test, the camera's ability to detect NIR light, and the penetration ability of the NIR light beyond the surface.

■ Methodology

Design and prototyping of the NIR probe:

Various design requirements and their solutions were identified before a prototype could be designed and 3D printed. These are listed below in Table 5. The height, width, and length of the probe had to be accommodative for the patient's needs. This is because, most RIOM patients cannot open their mouth beyond 3 cm[25] with the onset of oral mucositis. Hence, the dimensions of the probe must be smaller than 3 cm in width and height to accommodate for the patient's limited mouth opening. The height and width of the probe were set at 1.5 cm while the length was set at 24 cm so the probe would have less chances of touching the inside of the patient's mouth. The length was set at the above dimension to image the mouth without the clinician's hand being too close to the mouth. The probe should also be able to image all six parts of the mouth where mucositis occurs (gums, gum line, palate, buccal mucosa, tongue, and lips) (Figure 1). Therefore, the neck of the probe should either have a gooseneck or a narrow neck that can easily be moved inside the mouth with minimum contact. The edges were filleted to not poke the patient's mouth. To accommodate the electronics, the probe includes snap fits, a hole for the wires to connect to the raspberry pi (a mini programmable computer), and holes to ease the fitting of the optical components. All the design requirements and solutions are listed below in Table 5.

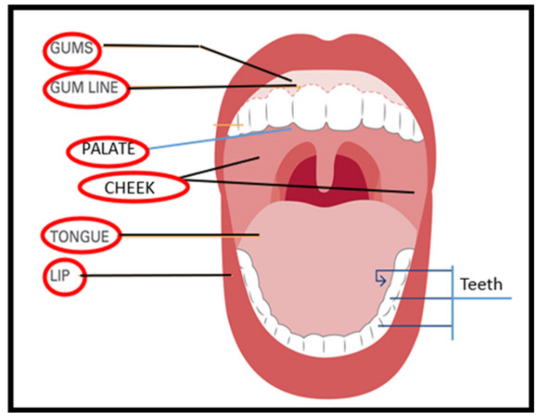

Figure 1: The six areas of the mouth where mucositis typically occurs (gums, gum line, palate, buccal mucosa, tongue, and lip).

Table 5: Design requirements of the NIR imaging probe and their solutions

Design Requirements	Solution
The size of the head of the probe must not be too big to fit inside the mouth of a radiation mucositis patient.	The height and width of the head of the probe was set to 1.5 cm, which is not too big to fit inside the mouth and also not too small to fit the optical components.
The length of the probe should be long enough to image inside the mouth without the hand getting too close to the mouth.	The length of the probe was set to 24 cm.
The probe should be able to image all 6 parts of the mouth where mucositis occurs (gums, gum line, palate, buccal mucosa, tongue, lips).	The neck of the final design is set in a way that all six mouth parts at visible (either through a flexible gooseneck or through a narrow neck).
The edges of the probe should not poke the inside of the patient's mouth.	The edges of the probe were filleted or rounded.
The electronics must be accommodated into the probe.	There are 4 snap fits located along the sides of the probe to open and close it. There is also a hole on the bottom of the prototype for the sensor and LED wires to exit and connect to the raspberry pi.
The sensor and LED must fit inside the probe without moving from its position.	There are two holes inside the probe to hold the sensor and LED. Since the LED is made of glass, there is also a small LED holder to prevent it from cracking.

To create a non-contact, intraoral NIR probe for RIOM imaging, two designs of a probe were created, as given in Figure 2 and design specification provided in Table 6. These prototypes were created based on the design requirements of the probe and their solutions (Table 5). Both designs use an NIR LED and an NIR sensitive camera. The main difference between the first and second design is the location of the LED and sensor, as can be seen in Figure 2. Design 1 has the LED and sensor placed on the side of the probe. This design is similar to that of an intraoral camera, where the sensor and light source are on the flat side of the device (mimicking a toothbrush). Design 2 has the LED and sensor placed on the top side of the probe. This design is similar to that of an endoscope, where the sensor and light source on the circular surface of the flexible cylindrical tube (mimicking a flexible straw).

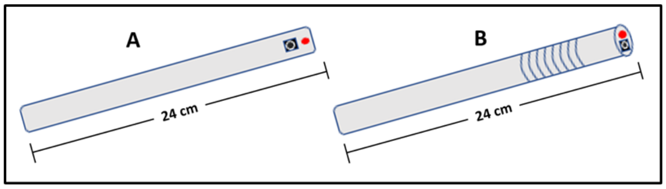

Figure 2: A) Design 1, the first design model (based on intraoral camera). B) Design 2, the second design model (based on endoscope). Both designs have a length of 24 cm.

Table 6: Comparison of Two Mechanical Designs of an Intraoral NIR Probe

	Design 1 (intraoral camera)	Design 2 (endoscope)
Optical components	NIR LED/NIR sensitive camera	NIR LED/NIR sensitive camera
Dimensions	1.5 cm x 24 cm x 1.5 cm (cuboid)	1.5 dia. x 24 cm (cylindrical)
Sensor/LED placement	On side (like intraoral camera) – easier to view cheek	On top (like endoscope) – easier to view throat
Flexible or rigid neck	-Rigid neck	-Gooseneck design – flexibility
Easy imageable areas of the mouth	Gums, gum line, palate, cheeks, tongue, lips (can image 6/6 areas where mucositis occurs).[26]	Gums, gum line, lips (limited only image 3/6 areas where mucositis occurs)

The first design, due to its 'toothbrush' based sensor and light source placement, can be rotated inside the mouth to view the all the areas where mucositis occurs (except the throat). The second design, due to its 'straw' based sensor and light source placement, (as shown in Figure 2), cannot easily image the palate, cheeks, and tongue (three out of six regions where mucositis occurs). The second design is more practical for imaging the throat (which mucositis rarely occurs) because the sensor and LED are placed on the top of the probe. Even though design 1 is not flexible, this design 1 can image all six areas of the mouth where mucositis occurs. For this reason, design 1 was chosen as the final design. The final prototype, which was designed on Fusion 360, had a rectangular shape with overall dimensions of 1.5 cm × 24 cm × 1.5 cm. It was printed on the Creality Ender 3, a 3D printer, with PLA (polylactic acid) plastic. All the components of the final prototype of the intraoral NIR probe are given in Figure 3.

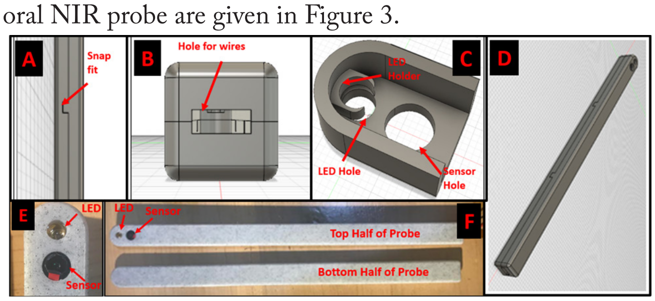

Figure 3: A) The snap fit on the probe to accommodate electronics. B) The hole for the connecting wires to exit the probe. C) The LED and sensor hole, along with the LED holder. D) A full view of the final prototype on Fusion 360. E) The head of the 3D printed probe with the LED and sensor attached. F) The top and bottom halves of the entire 3D printed probe with the LED and sensor attached.

Optical component assembly of the NIR probe:

The prototype of the device is composed of several components as listed in Table 7. The detector had to be able to fit inside a person's mouth, and hence the size restraints were used in the camera and LED selection of the NIR probe. The NIR camera chosen was 8.5 × 11.3 mm to fit inside the probe casing. The LEDs were interchangeable between wavelengths of 680, 810, and 830 nm. The probe uses raspberry pi as the processor. The raspberry pi is lightweight and portable, and thus can be used for handheld based devices and applications. It used an external monitor for viewing and power the LED light source. A variable resistor was implemented to control the amount of current sent to the LED light source. The circuit design of the optical components of the NIR probe is given in Figure 4.

Table 7: The design specifications of the components utilized for the prototype of the intraoral NIR probe.

Component	Specifications
Camera	NIR sensitive, 8.5 mm × 11.3mm cable Resolution: 2592p × 1944p, 5 megapixels Sensor: Sensor: OV5647
LED	680nm, 810nm, 830nm (interchangeable) 6.4mm × 4.7mm × 19.9mm
Potentiometer	6mm
Raspberry Pi	4GB of ram, 85mm × 56mm
Flex Board	Need to measure

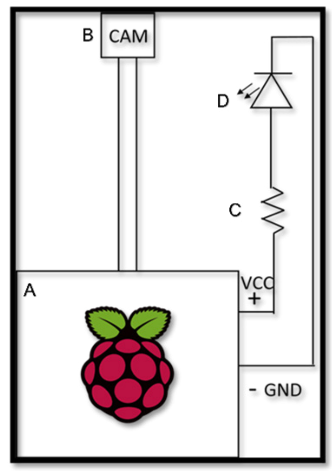

Figure 4: Circuit design of NIR optical probe. The Raspberry Pi (A) is utilized as an all-in-one controller. The Raspberry Pi controls a single LED (D) that shines NIR light onto the cheek of the patient's mouth. The diffused reflected signal is captured by the NIR-sensitive camera (B) that sends the image back to the Raspberry Pi where it is stored. The potentiometer (C) or a variable resistor controls the amount of current to the LED (D).

Study 1: How frequently does the probe contact the inside of a (simulated) mouth?:

The intraoral NIR probe is built to serve as a non-contact imaging device during oral imaging. The focus of this study was to see how frequently the probe contacts the inside of a mouth for a person with radiation mucositis and trismus. Trismus, a medical condition which affects oral mucositis patients, prevents patients from opening their mouth more than 3 cm.[25] Different open mouth sizes were simulated using paper cones (as can be seen in Figure 5) to test how frequently the probe contacts the inside of the mouth. Paper cones were created to simulate open mouth sizes with the cone diameter being 2, 3, 4, and 5 cm (2 cm being extreme trismus cases, and 5 cm being the average person). Ten trials per mouth part were completed on the cone (palate, left cheek, right cheek, and tongue) to see how many times the probe would not touch the inside of the mouth. The number of times the probe touched the cone was determined visually. Three operators performed the experiment to get more realistic results. Forty trials were conducted on each paper cone per operator, for a total of 120 trials per cone. The average of the 10 trials per location was calculated as a percentage based on the number of times the device did not touch the inside of the cone. A formula to calculate the percentage of no-contact at each location on the mouth part by each operator is given in equation (1).

$$No\ contact\ \% = \frac{n}{10} * 100 \tag{1}$$

where *n* is the number of times the probe did not contact the specific part of the mouth (palate, tongue, left cheek and right cheek). The no-contact % is also termed as the avoidance of mouth %, stating the percentage of times that the mouth was not touched when using the probe by the operator.

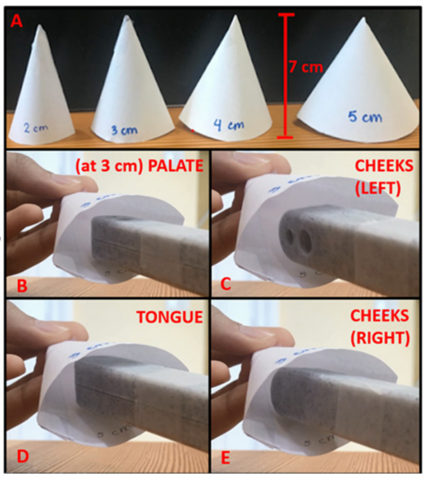

Figure 5: A) The different paper cone sizes representing the severity of trismus in radiation mucositis patients. B) Probe imaging the palate of the 3 cm cone. C) Probe imaging the left cheek of the cone. D) Probe imaging the tongue of the cone. E) Probe imaging the right cheek of the cone.

Study 2: What's the field of view of the NIR probe's camera?:

The focus of this test was to determine the camera's field of view (FOV) and identify the imaging area it can capture at different distances from the imaging surface. Using a grid paper consisting of 5 × 5 mm squares, we placed the probe from 5-15 mm at incremental distances of 5 mm. In Figure 6, a schematic of the FOV tests is shown.

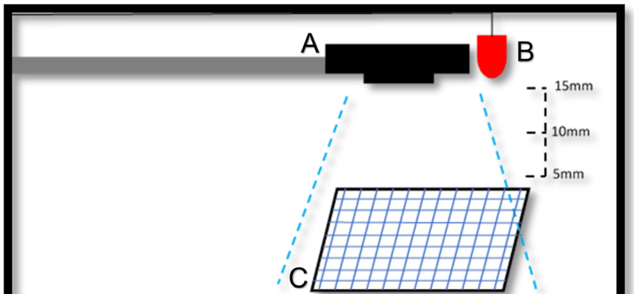

Figure 6: The optical probe (A/B) is secured horizontally above the grid target (C). Starting at 5mm, NIR images were acquired, and the setup adjusted to the next level.

Study 3: Can the custom intraoral probe detect NIR light?

The focus of this test was to determine if the probe could detect diffused reflected NIR signals from a highly absorbing media, in this case wine. It is known that wine absorbs NIR light and visible light differently as it has different properties for both optical regions. It is known that under NIR lighting, wine minimally absorbs light and will appear clear. Hence, the NIR images should be able to capture whatever is in the bottom of the jar. As seen in Figure 7, a target card was placed under a small jar filled with two inches of wine with the probe placed ~15 cm above the card.

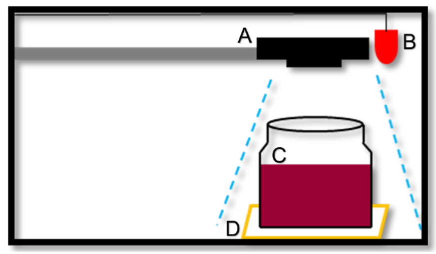

Figure 7: Schematic of the experimental set-up with the NIR probe (A/B) secured horizontally ~15 cm above the target card (D) under the wine jar (C) to assess its ability to detect NIR signals

Study 4: Can the NIR light from the probe penetrate beyond the surface?:

The focus of the final test is to determine if the probe could detect NIR light that can penetrate through a scattering media such as the tissue surface to image beneath the superficial surface. For this study, a white paper (highly scattering or diffusing) is used to mimic the tissue. To test this, a target card was placed between two sheets of this white diffusing paper with the NIR probe placed ~12 cm above the target (as shown in Figure 8). Typically, visible light illuminating the paper, which is highly reflective, will scatter. However, NIR light can penetrate deeper than the visible light through a scattering medium and has to ability to image the target car beneath the white paper. This hypothesis was tested via imaging studies to demonstrate that NIR light penetrates beyond the surface unlike the visible white light.

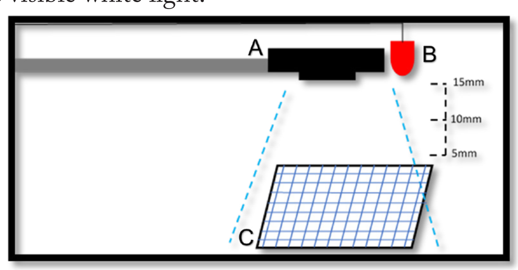

Figure 8: Schematic of the experimental set-up with the NIR probe (A/B) secured horizontally above the target card (C). pleased beneath the while sheet of paper.

Results and Discussion

Study 1: How frequently does the probe contact the inside of a (simulated) mouth?:

The results from Study 1, which tested the percentage of no-contact imaging in the mouth with a simulation of paper cones, is plotted in Figure 9. The data was taken as an average of the three operators who took part in this study and the avoidance percentage (i.e., the percentage of times that the operator avoided touching the mouth, i.e. No-contact% in equation (1)) was based off the average of ten trials. At an open mouth diameter of 3 cm, which is the typical diameter of mouth opening in radiation mucositis patient[25], the probe did not touch the inside of the mouth 87% of the times. The standard error of each mouth part was taken to obtain the error bars in Figure 9. From this study it can be concluded that the probe is able to image the inside of the mouth with minimal contact for typical mouth diameter of 3 cm or greater. Thus, the custom developed intraoral NIR probe is beneficial to clinicians because it can image the mouth with minimal contact in RIOM patients.

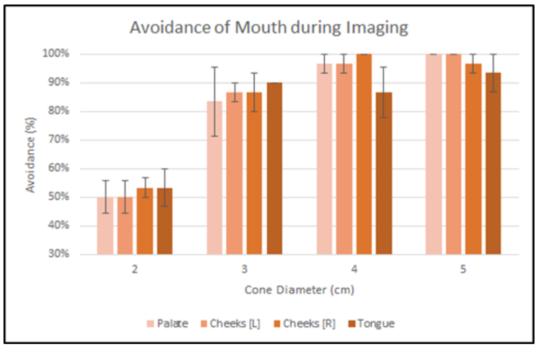

Figure 9: The figure shows the percentage of avoidance of the inside of the cone across four cone sizes (2, 3, 4, and 5 cm in diameter) at each mouth part (palate, left cheek, right cheek, and tongue). As the cone diameter increases, the percentage of avoidance of the mouth increases.

Study 2: What's the field of view of the NIR probe's camera?:

The results from Study 2, testing the camera's field of view, is shown in Figure 10. The area was measured by counting the number of squares from the grid paper measuring 5 × 5 mm, in each image captured. When the probe was at a height of 5 mm, the camera's FOV was 25 mm^2 area (Figure 10A). The next height was at 10 mm, where the camera's FOV was 50 mm^2 (Figure 10B). The last height tested was at 15 mm, and the camera's FOV was 77.5 mm^2 (Figure 10C). Thus, the NIR probe's camera had a FOV ranging from 25-77mm^2, which was sufficiently large for intraoral imaging studies. Hence the probe is appropriate for imaging different areas of the mouth, and not just a point location.

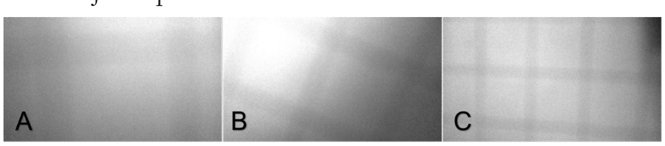

Figure 10: The NIR images acquired when the camera was (A) 5 mm, (B) 10 mm, and (C) 15 mm away from the grid.

Study 3: Can the custom intraoral probe detect NIR light?:

The result from Study 3, assessing the probe's ability to detect the diffused reflected NIR signals from an absorbing media, is shown in Figure 11. When visible light illuminates the wine sample. The card below is blurred. On the contrary, when NIR light was used to illuminate the wine sample. the card (with text written on it) was clearer and the contrast in the shapes are much more visible. The wine absorbs the white light significantly and hence in the presence of white light (or visible light) it appears dark, and we can barely see through the wine medium. However, NIR light is not absorbed by wine, and hence in the presence of NIR light, the detected image of the wine appears as clear as water and the target card below is visible. This implies that the probe can detect NIR light, and thus validated as an NIR probe that can be used for RIOM imaging.

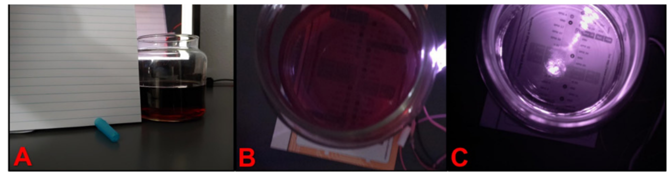

Figure 11: (A) Materials used for the experiment. (B) The card beneath the wine sample is not visible in when illuminated with white light (or visible light). (D) The card beneath the wine sample is distinctly visible when illuminated with NIR light and the wine sample also appears clear (since NIR light was not absorbed by wine).

Study 4: Can the NIR light from the probe penetrate beyond the surface?:

The result from Study 4, determines if the NIR light from the probe can penetrate through a scattering media (such as the white paper). When illuminated using white light, the details of the card are faint, However, when illuminated using NIR light the card's details are clearer, giving a better outline of the card. The NIR light was able to penetrate more deeply into the paper, a scattering media, than visible light (as shown in Figure 12). This demonstrates the capability of our NIR probe to be used towards imaging RIOM, where sub-surface physiological changes in response to radiation therapy could possibly be detect.

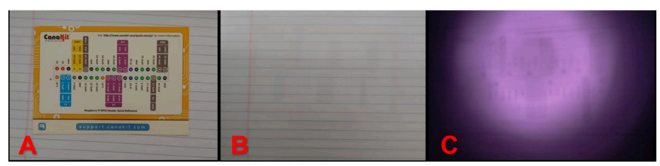

Figure 12: (A) The target card before being covered by the paper. (B) The white light image of the target card when covered by a white ruled paper. (C) The detected NIR diffuse reflected signal of the target card when covered by a white ruled paper. This demonstrates that NIR light penetrates beyond the surface.

Conclusions

In this study, we designed and 3D printed a handheld NIR probe (1.5 cm x 24 cm x 1.5 cm) towards imaging of oral mucositis. The hand-held NIR probe was equipped with an NIR LED (inter-changeable between 680, 810, and 830 nm) and an NIR-sensitive camera, connected to a raspberry pi outside the probe. From preliminary phantom tests, it was observed that the probe does not contact the mouth most of the times (>87% of times) when the mouth diameter is 3cm or greater. The field of view of the probe was sufficiently large to allow area imaging of the mouth. The probe's camera was sensitive to NIR light and also could image beneath a scattering surface. Therefore, it can be concluded that the first custom-developed handheld, NIR probe has been developed and preliminary testing has demonstrated its ability to image large areas without

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panding the features of the probe to allow multi-wavelength imaging such that hemoglobin concentration maps can be obtained during oral imaging to assess the severity of mucositis from a physiological perspective. Clinical scoring systems for oral mucositis are subjective across clinicians and are applicable only after visual clinical manifestation of the condition. The use of an NIR imaging technique can potentially assess onset or severity of RIOM sooner and objectively, thus complementing the subjective clinical evaluation using clinical scoring systems.

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