

Interstitial Optical Probe Device

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Background

Radiation Therapy and Cancer

Radiation therapy (RT) has long been an efficient and powerful treatment for cancer in the medical fields [1]. Currently, RT boasts the ability to precisely destroy tissue regardless of its location within the body while remaining non-invasive and causing minimal damage to surrounding areas [2]. A treatment given to nearly two-thirds of all cancer patients, radiation therapy can be considered one of the most diverse and capable drugs of modern medicine [3]. The inception of radiation use, however, was neither as graceful nor accurate as it is today. Discovered empirically by Wilhelm Rontgen in 1895, radiation application as a medical treatment began almost immediately thereafter. Before long, the unsightly and dangerous side-effects were quickly realized and accounted for. Developments like medical linear accelerators in the 1940s, computed tomography (CT) in 1971, and most recently tomotherapy at UW-Madison, field advancements quickly turned a raw dose into a precisely manufactured treatment plan [4].

Headed by advancements in Intensity Modulated Radiotherapy (IMRT) in the 1980s, today's therapies focus on applying more controlled and uniform dose treatment plans. As will be discussed in the next section, this goal is not necessarily the most effective. Behind this methodology are extremely precise machines such as the CyberKnife combined with increasingly rigid calibration standards. Additionally, radiation treatments have become more and more fractionated, splitting large scale doses

into multiple sessions. These methods all result in radiotherapy treatments today being accurate to less than 1% error [5].

Hypoxia as a Dominant Factor

As standards and instruments become more powerful, the question of what makes the most biologically meaningful dose application has re-emerged. In our new understanding of tumor growth and development, the “ideal model” of using uniform dose treatment plans has become outdated [6].

The answer to the question posed above seems to be in the oxygen dynamics of cancerous tissue and tumors. Because a large majority of the tissue damage that occurs from radiation is as a result of secondary free radicals, the presence of oxygen has been demonstrated to largely dictate the effectiveness of dose treatment plans. This results in implementation of treatment that takes advantage of oxygen levels to create more biologically meaningful applications of dose.

Hypoxia, or the deprivation of oxygen and oxygen supply, is now understood to be to the dominant factor in how cancer reacts to radiation treatment [7]. This important factor realized was first hypothesized by one of the fathers of radiobiology, Louis Gray who said “the concentration of oxygen dissolved in tissues at the time of irradiation is a factor in radiotherapy” [8]. Despite this early warning, researchers and doctors are only now realizing that the mechanism of free radical therapy can be used to dictate the effectiveness of radiation therapy.

The Current State of Radiotherapy: Non-Uniform Doses

Though not yet largely implemented, the current methods of improving radiotherapy seem to be adapting dose platforms to match (or resemble) the dynamics of oxygen distribution within the tumor itself. This statement is reinforced by the increasingly strong argument for treatment hypofractionation to avoid potential dangerous dosing to healthy tissue. As treatment plans become more fractionated, they too must become more dynamic [9].

An easy and time-efficient way to track and respond to tumor reoxygenation will yield the answer for how to adjust treatment throughout its course. A simple way to provide insight as to the reoxygenation of a tumor is by taking advantage of well-defined diffuse optical techniques. Other methods, such as PET scanning have the ability to track tumor growth, but lack the precision that optical techniques could bring. Using and measuring optical diffusion properties could result in even less damage to healthy tissue in addition to faster lesioning of cancerous tissue.

Design Motivation

Economic and Social Motivation

Each year, over one million patients are treated with radiation therapy. Populated largely with breast, prostate, and lung cancer, over 60% of patients with cancer will experience radiotherapy. With prices of therapy sessions ranging from \$1,700 to \$4,000

per session, radiation therapy is economically stressful both on the patients and the country [10]. While the economic motivation is not the most influential factor, more efficient treatment plans could save the United States population billions of dollars per year.

As mentioned, the yearly patient number for radiation therapy continues to raise over one million people per year. While treatment plans have benefited largely from recent advancements such as CT and tomotherapy, the next advancement in providing more successful dose treatment could save even more lives. Radiation therapy is a treatment method built with the intent to cure the tumor over 75% of the time. Unlike other methods, radiation therapy is employed not to relieve symptoms or control growth, but to save the life of a person who can still lead a successful life.

Client Motivation

Dr. Michael Kissick is an assistant professor of Medical Physics at the University of Wisconsin-Madison and is currently developing a novel approach towards analyzing oxygen saturation in cancerous tissues [11]. The ability to measure oxygen saturation levels in tumors can potentially lead to more detailed classifications of cancerous tumors and more accurate treatment plans. The overall goal of Dr. Kissick's research is to create a bedside device to measure oxygen saturation dynamics of cancerous tumors in humans. Currently, he is conducting trials of his device on tumors of mice xenografts. The device used in this research consists of two probes that connect to a full spectrum light emitter. The two probes are identical and consist of optical fiber that is thread through 28 gauge

(0.362mm outer diameter) needles. One probe emits light and the second probe collects the light that has diffused throughout the tissue. To take measurements on the mice, the probes are set at a 3mm distance, side-to-side, and puncture the skin as they are placed inside the tumor. Dr. Kissick currently uses a Styrofoam block and tape to hold the probes at the 3mm distance. Styrofoam is a weak material and the needles may move when they enter the tumor, therefore, Dr. Kissick has requested the design of an easy-to-use device that holds the needles steady at a fixed distance and aids in the penetration of the skin. The device should be reusable and easily built.

As Dr. Kissick's research progresses, he would like to create a bedside device that holds the optical probes at a set distance to be entered into a human tumor. The design of this device would seek to minimize invasiveness without sacrificing the efficacy of the probes. We will be considering how our design can evolve into a medical device for human use because that is the overall goal of Dr. Kissick's research.

Problem Statement

Oxygen saturation in cancerous tissue can be analyzed to indicate possible transformations and adaptations to the development of future cancer tissue. By observing optical diffusion under the epidermis, doctors can very closely track possible changes or instigations in tumor development. Currently, clinical trials are being run solely on mice and with a probe that, as a result of a poor-quality design structure, may give potentially inconsistent results. Our goal is to rebuild the probe in a fashion that provides both

consistent results and applicability for human use. Additionally, long term goals include making the probe convenient and reusable for the doctor and patient.

Existing Devices

Dr. Kissick's design is novel and addresses drawbacks of current probes that are used to measure oxygen saturation invasively. There are currently two devices that are similar in function and theory: the Eppendorf probe the Oxylite probe. Both of these devices use interactions between light and tissue to analyze oxygen saturation. The aspect of Dr. Kissick's design that



Figure 1: Oxylite probe needle and connector

differentiates it from these two probes is the functional scale of operation. The large area sensor Oxylite probe [Fig. 1] is advertised to have a sampling area/volume of 8mm^2 , which is much smaller than Dr. Kissick's probe. The problem with having a small sampling area is that the probe may hit deoxygenated pools of blood where the oxygen saturation reading is nonexistent.

Design Alternatives

Modified Parallel Clip

The modified parallel clip [Fig. 2] is the closest design to Dr. Kissick's existing foam needle clip. This design would consist of a rubber coated hook latch to support the needles parallel at a $>3\text{mm}$ separation. The clip would also have a static rubber support at

the rear of it in order to organize and support the optic fibers attached. The design could be made from inexpensive materials, and has the potential for fabrication by rapid prototyping. The benefit of this design is its simplicity and size, which would reduce its cost of manufacture and increase its relative durability and user friendliness.

These aspects resulted in a high score in the longevity, cost, and size areas of the design matrix. However, the

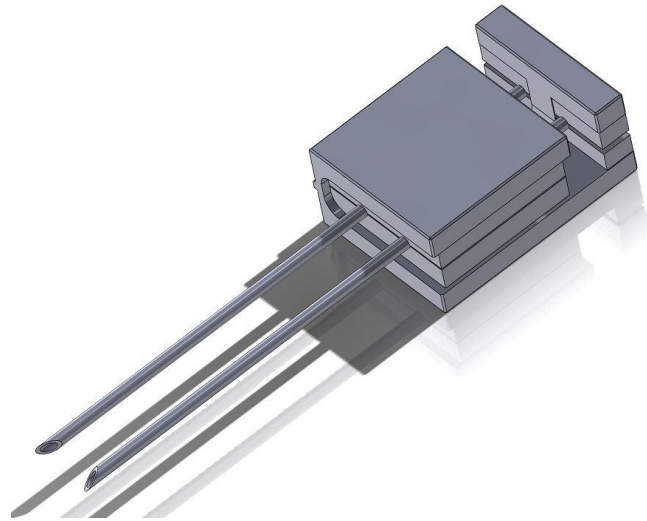


Figure 2: A SolidWorks model of our Modified Clip Design

parallel arrangement of the needles in the clip would make for a less than ideal insertion scenario. Since the needles are separated by 3 mm, the accuracy of the needle insertion ultimately relies on the skill of the doctor/nurse applying it. Its wide span also means that possible tugging or pulling on the clip would cause painful torsion on the needles. As a result the needle scored lower on both the safety and ease of use criteria.

Staggered Clip

The staggered clip design [Fig. 3] is based on one of the fundamental concepts of diffuse light transport theory, which states that in a diffuse medium a directional light source, radiates in all directions and can be considered a point source at any distance

greater or equal to the mean free path of the tissue. In other words, even if a light source

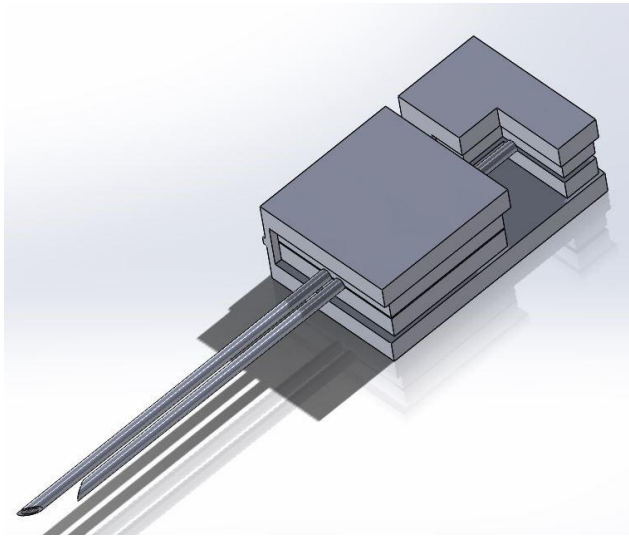


Figure 3: A SolidWorks drawing of our Staggered Clip Design

is directional, if it is placed in a diffuse medium the light will be refracted in a way in which the directional light source appears multidirectional. As a result, rather than needing to position the needles parallel and facing each other, the needles may be staggered and facing any direction, as long as the distance between needle points is sufficient.

Similar to the modified parallel clip, this design would consist of a rubber coated clip to hold the needles, but at a much smaller separation ($<1.5\text{mm}$). The clip would also have a static rubber pad at the rear to organize the wires, and also act as a measurement bumper to set the fiber optic needles at their appropriate depths. This design shares the strengths of the modified parallel clip; however, it excels in being inserted into tumors that happen to be narrower than 3mm. Having the needles located close together also means that orientating and inserting the needles would be both safer and more accurate. The disadvantages of this design are in its complexity and cost. The uneven orientation of the needles when they are so close together would make this clip significantly harder to load by hand, and the organizer/bumper at the rear of the clip would be more difficult to fabricate. It's more complicated holding arrangement may also result in wear over time, reducing its longevity. In conclusion, the staggered needle design scored high in ease of

use, precision, size, and safety; however, it suffered in the cost and longevity components of the design matrix.

Two Unit Clasp

The third and final design alternative was the two unit needle clasp [Fig. 4]. This design is composed of two primary identical components, which when combined form a needle clasp which holds two optical needles parallel again at a separation of 3mm. By expanding the design into two components, the moving clasp component of the previous designs can be removed. This eliminates the need for more durable

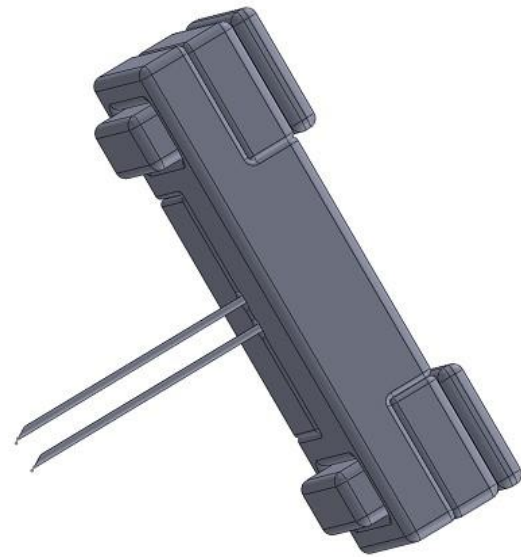


Figure 4: A SolidWorks drawing of our Two-Unit Clasp Design

materials, due to the removal of repeatedly bending components. This design also allows for a greater degree of versatility with a wide range of needle sizes and shapes. However, the breakdown of the needled clamp into multiple components also brings a variety of disadvantages. A greater amount of material would be needed to execute this design, increasing the cost of fabrication as well as the relative size of the design. Its larger size and 3mm parallel needle arrangement would cause the device to be both cumbersome and difficult to use, resulting in a lower degree of precision and safety. Overall, this design

excelled in its ease of use and longevity, however, it lacks in the areas of precision, size, cost, and ease of use.

Design Matrix

Our design matrix, which can be seen in Fig 5., has six different categories with which we scored each design. These categories were developed after reviewing our client’s requirements and recommendations.. Once all of our categories were selected, we weighed them based on what Dr. Kissick felt was essential and what we felt we could sacrifice in order to make a better design.

With the design matrix made, we began to score each one of our devices. The first

Interstitial Optical Probe Design Matrix	Design 1		Design 2		Design 3	
	Criteria (weight)	Modified Clip	Staggered	Two Unit Clasp	Two Unit Clasp	Two Unit Clasp
Ease of use (30)	4	24	5	30	3	18
Precision (25)	5	25	4	20	3	15
Longevity (25)	4	20	3	15	5	25
Size (10)	5	10	4	8	2	4
Safety (5)	4	4	5	5	4	4
Cost (5)	5	5	4	4	3	3
Total (100)		88		82		69

Figure 5: A comprehensive matrix quantifying important qualities of our three designs.

category we scored, the ease of use of the product, was the highest weighted category at 30% of the total score. This received the highest weight because our client is performing his tests on mice that are not a part of his lab. Since he is borrowing another researchers lab to test, it is paramount that our device can be handled easily and allow for quick data collection.

With a weight of 25% each, precision and longevity are the next highest weighted categories. This device will be used for data collection, so to ensure that the data collected when using this device is valid and as accurate as possible, it must be able to hold the needles in exactly the same way every time. Similarly, our client does not want to replace this device often. This means the more durable it is; the better it will be suited for our client's use.

Size is the fourth ranked category at 10% of the total score. There was no real size requirement from Dr. Kissick; however, a device that is too large or too small might affect how easy it is to use. Along these same lines, if the device is too small it will be easier to lose pieces which would in turn decrease the longevity to the product.

Finally cost and safety are the lowest ranked categories at 5% of the score each. This device will be 3D-printed and will therefore have a relatively low cost. Dr. Kissick also has a contact with access to a 3D-printer, which means cost is not a real factor to be worried about. Finally safety was tied with cost for the least weighted category. This is due to the fact that the current needle holder is a block of Styrofoam. The devices that have been designed will hold the needles much more securely than they currently are

being held. This means that the safety aspect of the device was of less importance than the other categories.

Design One: The Modified Clip

The modified clip design received the highest score in three of the categories of our design matrix, including precision, size, and cost. We felt that this would be the most precise device due to the fact that it would replicate Dr. Kissick's set up allowing for seamless integration of the device. It took first in size for the exact same reason. It would be very similar in size to the foam block currently being used. Finally it received first in cost simply because it will have the least number of parts. Although design one did not win every category; it took second in all of the categories that it did not take first in. This, combined with the fact that it had the highest score of 88, made us select to pursue design one.

Design Two: The Staggered Needle Design

When referring to the design matrix, one can see that design two took first in ease of use and safety. This is due to the fact that the needles act as one needle and it will therefore be easier, quicker, and safer to insert the needles into the tumor. Design two had an overall score of 82, which is very respectable. This design, however, would lack in longevity. We felt that having the needles this close together would lead to a device with some very small parts. These small parts are more likely to break.

Design Three: The Two Unit Clasp

The only category that design three scored the highest in was longevity. This is due to the fact that there was no moving parts and can pinned together. With no moving parts, the wear on this device will be minimal. Even though this device took first in longevity, it was severely lacking in ease of use and precision, and had an overall score of only 69. We felt that this device would be a little harder to put together and therefore would affect how easy it is to use. Also, with it being harder to put together, there is a greater chance that the needles are not aligned properly, and this would affect the precision.

Future Work

With the design selected, we have several goals for the rest of the semester. First and foremost, we would like to stay in close contact with our client to continue improving our device before prototyping. There are currently two additions we are looking to add to our device. First, Dr. Kissick has asked us to look into a way to stabilize the device so that it doesn't shift in use. Also, we are working on a way to clip the needle into place and then use our device to thread them with the optical fibers.

Once a prototype device to use with the mice is made, we will begin looking into making a device that is more suited towards human use. We hope to be able to make something that will allow for long term study of the tumor as well as data collection during treatment. To do this, we will need to design a device that is capable of staying on

the body while remaining comfortable and usable. Similarly we will want to look into ways to leave the device implanted while minimizing infection. One way that we have already brainstormed is making a device that can implant the optical fibers and then have the needles be removed. The main struggle with this design is determining a way to ensure the ends of the fibers remain three mm away from each other.

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