**THE ELECTRICAL PROPERTIES OF HUMAN TISSUE FOR THE DIAGNOSIS
AND TREATMENT OF MELANOMA SKIN CANCER**

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ABSTRACT

THE ELECTRICAL PROPERTIES OF HUMAN TISSUE FOR THE DIAGNOSIS AND TREATMENT OF MELANOMA SKIN CANCER

By

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This thesis discusses the research, experimental methods, and data gathered for the investigation of a novel method for the diagnosis of melanoma skin cancer. First, a background about human skin tissue is presented. Then, a detailed description of melanoma along with current diagnosis techniques and treatment options are presented. In the experimental methods, the electrical properties of several types of tissue were analyzed, the purpose of which was to discover if a tissue type can be distinguished by its electrical properties alone. This would allow for the diagnosis of melanoma to be done by examining the electrical properties of the suspected tumor and comparing the results to known values of healthy and cancerous skin. After analyzing the data, it was concluded that tissue types can be identified by their electrical properties and it may be possible to diagnose melanoma through this method. Finally, the possibility of using a similar technology and radiofrequency tissue ablation to treat melanoma is presented.

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Introduction

Thesis Objective

The objective of this thesis is to create, test, and evaluate a new method for the diagnosis of skin cancer. This new diagnosis method utilizes bipolar electrodes and an analysis of the electrical properties of the skin to differentiate between healthy and cancerous tissue. This thesis includes the initial steps in developing this new diagnostic method. In order to complete the objective of examining the electrical properties of skin, a fixture was designed and fabricated and the electrical properties of skin analogues were measured. The purpose of this data is to determine if there is a statistical difference between healthy and cancerous tissue.

The objective of this thesis is also to discuss future steps that can be taken to extend this technology to include a method of skin cancer treatment using radio frequency tissue ablation. The technology to ablate cancerous tissue is similar to the diagnosis technology discussed in this thesis. To accomplish this objective, previous uses of tissue ablation to treat cancer were researched and are discussed.

Purpose of Thesis

The purposes of this thesis are to: 1) present information on skin cancer, 2) identify a new method of diagnosing skin cancer, 3) collect preliminary data on such a method of skin cancer diagnosis, 4) review previous research in the area of radio frequency tissue ablation to treat cancer, and 5) make conclusions on these new methods of diagnosing and treating skin cancer. This thesis also outlines the next steps that need to be taken to further develop this technology.

Background

The Skin

In order to understand skin cancer, it will be helpful first to have an understanding of skin and the different layers of tissue that comprise it. The skin is the largest organ in the human body [1]. The surface area of skin is approximately 22 square feet and weighs between 10 and 11 pounds, depending on body size [2]. The primary functions of skin are to [3]:

- protect the body from damage and infection
- excrete salts, wastes, and water to help the body maintain homeostasis
- sense touch, pain, pressure, and temperature
- regulate body temperature
- store fat
- synthesize vitamin D which allows the small intestines to absorb calcium and phosphorus into the bloodstream

The skin consists of three main layers of tissue (see Figure 1 [4]). From the most external to internal, these layers are the: epidermis, dermis, and subcutis. The epidermis is approximately one hundredths of an inch thick. The thickness of the dermis varies between 0.012 inches to 0.12 inches, depending on the area of the body. The thickness of the subcutis varies greatly from person to person depending on the amount of body fat. The epidermis will be the main concern of the experiments discussed later in this thesis, so the structure of the epidermis will be focused on.

Figure 1 – Skin Cross Section

A cross section showing the different layers of skin

The purpose of the epidermis is to protect the deeper layers of skin [5]. The main type of cells in the epidermis is keratinocytes. Nine out of ten cells in the epidermis are keratinocytes [3]. Keratinocytes produce a protein called keratin, which contributes to the skin's ability to protect the body by making the skin hydrophobic [5]. The epidermis is separated into 5 layers of cells. These layers, from the most external to internal, are the: stratum corneum, stratum lucidum, stratum granulosum, stratum spinosum, and stratum basale [3]. The stratum corneum is composed of dead keratinocytes that originated in the stratum basale and have migrated outwards. The stratum basale is the deepest layer of the epidermis. This layer contains cells that continuously divide to produce new keratinocytes. When a cell in the stratum basale layer divides, one cell stays in the basal layer and retains the ability to divide. The other cell loses the ability to

divide and moves into a higher layer of the epidermis (see Figure 2 [6]). The rate of division at the stratum basale is the same as the rate at which dead cells are shed off of the body in the stratum corneum. This allows the number of cells in each layer to stay constant [6]. The other layers of the epidermis do not perform specific functions but are simply a progression of skin cells from internal to outer layers.

Figure 2 – Normal Skin Growth

The migration of skin cells from the basal layer

The stratum basale layer also contains melanocytes. Melanocytes produce a protein called melanin [7]. The purpose of melanin is to protect the cells of the epidermis from ultraviolet light [3]. The importance of protecting skin cells from UV light is discussed in the “What Causes Melanoma” section. Melanin is also the source of pigmentation of the skin [2]. When skin is exposed to ultraviolet light, the melanocytes produce more melanin, which causes the skin to darken [1].

The next layer of tissue in skin is the dermis. The dermis is thicker than the epidermis. The purpose of the dermis is to contain hair follicles, sweat glands, nerves, and blood vessels. The dermis is held together by a layer of collagen [5].

The deepest layer of the skin is the subcutis. The subcutis consists of a network of fat cells and collagen. The purpose of the subcutis is to conserve heat and act as a shock absorber to prevent injury to the deeper structures of the body [5].

Now that a basic understanding of the anatomy of skin has been established, a discussion about cancer and skin cancer specifically, may take place.

Cancer

This section will discuss a generalized definition of cancer, the cause of cancer, and the types of cancer. A specific discussion about skin cancer will take place in the next section, “Skin Cancer.”

Cancer is a term used to describe a disease in which abnormal cells divide and multiply without control and are able to invade other parts of the body [8]. Instead of dying after a normal life cycle, cancer cells outlive normal cells and continue to form other abnormal cells. Cancer develops due to damage to the DNA of the cell that controls normal growth and division [5]. A change to a cell's DNA is called a mutation. Mutations occur for a variety of reasons that will be discussed later. The extra cells that form due to the mutation form a mass called a tumor. A tumor can be either benign or malignant. Benign tumors are not cancerous, meaning the cells do not spread to other parts of the body. Tumors that are malignant are cancerous and can invade other parts of the body. When cancer cells from a tumor invade other areas of the body, it is called metastasis [6]. If the spread of cancer cells are not controlled, death can result from the cancer cells interfering with the normal functions of the tissues of the body [9].

There are five types of cancer: carcinoma, sarcoma, leukemia, lymphoma, and central nervous system cancers. Carcinomas begin in the skin or in the epithelial cells

that cover internal organs. Sarcomas begin in the bone, cartilage, fat, muscle, blood vessels, or other connective or supportive tissue. Leukemia begins in the bone marrow. Lymphoma cancers begin in the cells that make up the immune system. Central nervous system cancers begin in the brain or spinal cord [4].

Tumors are structurally different from normal tissue. Because the cells that compose tumors are caused by an over proliferation of cells, the cell density of tumors is higher than normal tissue [10]. This causes tumors to have different electrical properties than normal tissue, which is discussed further in the “Electrical Properties of Skin” section and will become important when trying to diagnose cancerous tissues using electrical properties.

Skin Cancer

Now that the structure and functions of skin have been discussed and a basic understanding of cancer has been established, the different cancers that are associated with the skin can be discussed. The three most common types of skin cancer are: basal cell carcinoma, squamous cell carcinoma, and melanoma. Because melanoma is the deadliest type of skin cancer, it will be discussed in depth. For the remainder of this thesis, when the term “skin cancer” is mentioned, it is assumed that this term is referring to melanoma, unless otherwise specified. The following sections will discuss the physiology, causes, risk factors, and prognosis of melanoma skin cancer.

Melanoma

Introduction to Melanoma

Melanoma is a carcinoma of the skin and is the most deadly type of skin cancer. Melanoma is more likely than other types of skin cancer to become malignant and spread to other areas of the body [9], often to the lungs and liver [11]. Each year, approximately 53,600 people are diagnosed with melanoma. In Western countries, the number of people diagnosed with melanoma is increasing each year. In the United States for example, the percentage to people diagnosed with melanoma has doubled in the last 30 years [12].

What is Melanoma?

Melanoma is a type of cancer that originates in the melanocytes of the epidermis [12]. Melanoma often begins as non-cancerous benign tumors [7]. These non-cancerous tumors are called, “nevi,” or their common name, “moles.” Nevi are clusters of melanocytes and surrounding connective tissue [12]. Most nevi are harmless but some can develop into cancerous melanoma through mutations in the DNA of the melanocytes [7]. Once the melanocytes become malignant, melanoma has developed.

Melanoma is characterized by unchecked growth and replication of melanocytes (see Figure 3 [6]) [12]. Melanoma tumors are often brown or black in color because the extra melanocytes continue to produce melanin, darkening the area around the melanoma [7]. The most common area for melanoma to develop is on the skin. This type of melanoma is called cutaneous melanoma. Melanoma can also develop in other tissues where melanocytes are present, such as in the eye, the meninges, the digestive tract, or the lymph nodes [12]. These less common types of melanoma will not be discussed

further in this thesis. When the term “melanoma” is used, it is referring to cutaneous melanoma.

Figure 3 - Beginning of Cancerous Growth

The progression of Melanoma

As melanoma progresses from a cancerous nevus to later stages, it invades the deeper layers of tissue below the epidermis (see the “Staging Melanoma” section). However, it does not do so in a uniform manner. Melanoma invades the dermis and subcutis and dermis with finger-like projections (see figure 4 [12]). This non-uniformity will become important later on when discussing the possibility of the diagnosis of melanoma via electrical properties, which is the main purpose of this thesis.

Figure 4 - Cancer Histology

4 slides showing the progression of melanoma

What Causes Melanoma?

Melanoma is caused by DNA mutation in the melanocytes. These mutations are usually caused by exposure to ultraviolet light, which create an error in the DNA sequence but may also be caused by inherited genetic mutations or exposure to dangerous chemicals.

When genes that control the normal growth and replication of melanocytes are damaged, melanoma can result. Some of the specific gene mutations that result in melanoma have been identified. One non-inherited gene mutation that is found in melanoma is to the BRAF gene. The BRAF gene is responsible for making a protein called BRA-F, which is involved in cell replication. When the gene becomes damaged, the cell may no longer replicate correctly. A mutation to the BRAF gene has been found in 70% of all melanoma cancers [7].

One type of inherited gene mutation (meaning it is not caused by exposure to ultraviolet light) that may cause melanoma is the CDKN2A (also known as p16) gene and the CDK4 gene. These genes are responsible for controlling the growth of melanocytes.

Mutations to these genes cause cell overgrowth which can lead to cancer [7]. Since these gene mutations can be inherited, they may be the reason why people with a family history of melanoma are more likely to develop melanoma themselves.

Where on the Body does Melanoma Occur?

Melanoma can occur anywhere on the skin. However, there are areas that are more likely than others to develop melanoma [12]. Males are more likely to develop melanoma on the trunk (the area between the shoulders and the hips). Women are most likely to develop melanoma on the legs. The neck and face are other common areas for the development of melanoma [7].

Who is at Risk for Developing Melanoma?

There are certain risk factors that can increase a person's chance of developing melanoma. People that have been exposed to more risk factors are at a higher risk for developing melanoma than others. A risk factor is anything that raises a person's chance of developing a disease, such as cancer. Some risk factors are characteristics that can be inherited; others are due to the environment the person has been exposed to during his or her lifetime. Examples of risk factors include: exposure to ultraviolet light, a large number of moles on the skin, fair skin, and a family history of melanoma.

High exposure to ultraviolet light is the most significant risk factor for the development of melanoma. Exposure to ultraviolet light can damage the DNA in melanocytes, which can cause mutations that lead to cancer [7]. High ultraviolet exposure also increases the production of melanin by the melanocytes. If the melanocytes become fatigued, it is possible that they will be more likely to develop into

melanoma [7]. Areas of previous severe sunburns are also more likely to develop melanoma due to ultraviolet damage.

Another risk factor in the development of melanoma is a large number of nevi on the body. Most people have nevi, and usually these nevi will not become cancerous. But anyone with over 50 nevi on their body is at a higher risk of at least one nevus becoming cancerous [12]. Another risk factor associated with nevi is the presence of dysplastic nevi, which are abnormal nevi. It has been shown that nevi that are abnormal in size and shape, or have the appearance of melanoma, are more likely to develop into melanoma. A dysplastic nevus has a 6% to 10% chance of becoming cancerous during the lifetime of the person. The development of dysplastic nevi and their correlation with melanoma is hereditary. A person with a family history of melanoma is 50% more likely to develop melanoma themselves [7].

A family history of melanoma is a risk factor for the development of the disease. Ten percent of people who have been diagnosed with melanoma already have had a close family member (parent, sibling, or child) diagnosed with the disease. The increased risk for people with family members already diagnosed with melanoma may be due to inherited traits or similar lifestyles [12].

Fair skin, light eyes, and light colored hair are other risk factors in the development of melanoma [9]. People with light skin have less melanin in their skin to protect the DNA in their skin from ultraviolet light. The protective effects of high amounts of melanin can be best seen when comparing the diagnosis rates of melanoma between Caucasians, who have low amount of melanin, with African Americans, who

have comparatively high amounts of melanin. Caucasians are more than 10 times more likely to develop melanoma than African Americans [7].

Diagnosing Melanoma

For all cancers, the early diagnosis of the disease can greatly improve the prognosis. It is important to correctly diagnose cancer early in order to start treatment and stop the disease from spreading to other tissues. If the cancer is allowed to spread to other areas of the body, it becomes harder to treat and the chance of death increases. The initial diagnosis of melanoma is done visually, and then confirmed pathologically. A diagnosis is made by a doctor. If a doctor suspects melanoma after a visual inspection, they can perform an excisional or incisional biopsy to confirm the diagnosis.

The first sign of melanoma is the change in appearance of an existing nevus or the appearance of a new nevus. Doctors use the ABCD method as a rule for visually diagnosing melanoma. Each letter stands for a warning sign of melanoma (see Figure 5 [4]). They are as follows [12]:

- A-asymmetry. The shape of one half of the mole does not match the other.
- B-border. The edges of the mole are ragged, blurred, or irregular.
- C-color. The color of the mole is uneven, or contains multiple colors.
- D-diameter. The mole increases in diameter.

If after using this method the doctor suspect's melanoma, they will make a biopsy to send to a pathologist, who will then make a more definitive diagnosis. The pathologist will look at the tissue sample under a microscope to determine if it contains cancerous cells.

A *symmetry*—The shape of one half does not match the other.

B *order*—The edges are often ragged, notched, blurred, or irregular in outline; the pigment may spread into the surrounding skin.

C *olor*—The color is uneven. Shades of black, brown, and tan may be present. Areas of white, grey, red, pink, or blue also may be seen.

D *iameter*—There is a change in size, usually an increase. Melanomas are usually larger than the eraser of a pencil (1/4 inch or 5 millimeters).

Figure 5 – Melanoma ABCDs

The 4 signs of melanoma used to make a visual diagnosis

There are two types of biopsies used to diagnose melanoma: excisional and incisional biopsies. In an excisional biopsy, the doctor will remove the entire suspected tumor. A downside to an excisional biopsy is that since a large amount of tissue is

removed, healing times can be long and a scar where the tissue was removed may result [7]. In an incisional biopsy, the doctor only removes a portion of the tumor. There are two types of incisional biopsies: a shave biopsy and punch biopsy. In a shave biopsy, the doctor shaves off the top layer of skin with a scalpel. Shave biopsies are not often used when melanoma is suspected because the tissue sample may not be thick enough to determine how deep the melanoma has progressed through the skin [7]. In a punch biopsy, the doctor uses a tool that resembles a small cookie cutter to remove a core sample of the tumor. This sample includes deeper tissue such as the dermis and upper subcutis.

All melanoma diagnosis techniques currently used are invasive to the patient and can lead to scarring of the skin. A diagnosis method that does not cause damage to the skin is desired by patients and physicians. The purpose of the experiments performed later in this thesis is to develop a non-invasive diagnosis method for melanoma.

Staging Melanoma

Once a positive diagnosis of melanoma has been made, the extent to which the disease has grown and spread through the body must be determined. Cancer can spread through the body in three ways. The first is by growing and invading the surrounding tissue. Another way cancer can spread is through the lymph vessels and nodes. In this method, cancer cells break off from the original tumor and enter the lymph system and travel to other parts of the body where they can then become established in other tissues. This form of spreading through the body is called metastasis (see Figure 6 [6]). The final way cancer can spread through the body is entering the bloodstream and traveling to other areas of the body via the blood vessels, which is another form of metastasis [1].

Figure 6 – Melanoma Metastasis

The invasion and metastasis of melanoma

The process of determining how large the tumor has grown and how far the cancer has spread is called staging. To stage cancer, more tests must be performed. The stage of the cancer greatly effects the treatment and prognosis, as cancers that have progressed further will be harder to treat.

To stage melanoma, additional tests are performed by a doctor. After the initial biopsy to diagnose the cancer, a sentinel lymph node biopsy may be performed. In this procedure, radioactive dye is injected into the skin near the site of the tumor. The doctor watches the flow of the dye through a fluoroscope as it travels through the lymph system to the nearest lymph node (the sentinel lymph node). The doctor will then remove this lymph node and send it to a pathologist to determine if cancer cells have traveled to it [1]. Other tests include a chest x-ray, CT scan, MRI, and blood tests. All these tests are used to determine if the cancer has spread from the original site to other tissues in the body. Once the doctor knows how far the cancer has spread, if at all, a stage can be assigned to the cancer.

The purpose of staging cancer is to give the doctor an easy and fast way of communicating information to other doctors about how far a case of cancer has progressed in a patient. By having standard criteria for describing the state of cancer in different patients, treatment options can also be standardized.

Staging of cancer includes three different categories: T, N, and M. Each letter stands for a certain characteristic of the cancer and contains important information about the stage of the cancer. The following descriptions of the T, N, and M categories are taken from American Cancer Society's Guide to Understanding Melanoma [7].

- The **T** category stands for tumor. The T category is assigned a number (from 0 to 4) based on the tumor's thickness (how far into the skin it has grown). It is also assigned the letter "a" if it is not ulcerated or a "b" if it is ulcerated. Ulceration means a layer of skin covering the melanoma is absent. Ulceration is determined under a microscope after a biopsy.
 - To assign a T value to a case of melanoma, a physician uses a micrometer to measure how deep the cancer has spread on a tissue sample from a biopsy. The possible values of T are as follows:
 - **TX:** Primary tumor cannot be assessed.
 - **T0:** No evidence of primary tumor.
 - **Tis:** Melanoma in situ (the cancer has not moved from the original site).
 - **T1a:** The melanoma is less than or equal to 1.0 mm thick, without ulceration.
 - **T1b:** The melanoma is less than or equal to 1.0 mm thick, with ulceration.
 - **T2a:** The melanoma is between 1.01 and 2.0 mm thick without ulceration.
 - **T2b:** The melanoma is between 1.01 and 2.0 mm thick with ulceration.
 - **T3a:** The melanoma is between 2.01 and 4.0 mm thick without ulceration.
 - **T3b:** The melanoma is between 2.01 and 4.0 mm thick with ulceration.
 - **T4a:** The melanoma is thicker than 4.0 mm without ulceration.
 - **T4b:** The melanoma is thicker than 4.0 mm with ulceration.
- The **N** category stands for spread to nearby lymph nodes (see Figure 7 [11] on how a sentinel lymph node biopsy is preformed). The N category is assigned a number (from 0 to 3) based on whether the melanoma cells have spread to lymph nodes or are found in the lymphatic channels connecting the lymph nodes. The N category is also assigned the letter "a" if melanoma cells can only be seen under a microscope or the letter "b" if they can be seen with the naked eye. The letter "c"

is assigned if there are very small amounts of melanoma in the nearby skin or if the melanoma is in skin lymphatic channels around the tumor.

Figure 7 – Sentinel Node Biopsy

How a sentinel lymph node biopsy is performed

- To assign an N value to a case of melanoma, the results of a sentinel lymph node biopsy are used. The possible values of N are as follows:
 - **NX:** Nearby lymph nodes cannot be assessed.
 - **N0:** No spread to nearby lymph nodes.
 - **N1a:** The melanoma has spread to 1 nearby lymph node and the melanoma in the lymph node is only seen under the microscope.
 - **N1b:** The melanoma has spread to 1 nearby lymph node and the melanoma in the lymph node is visible to the naked eye.
 - **N2a:** The melanoma has spread to 2 or 3 nearby lymph nodes and the melanoma in the lymph node is only seen under the microscope.
 - **N2b:** The melanoma has spread to 2 or 3 nearby lymph nodes and the melanoma in the lymph node is visible to the naked eye.
 - **N2c:** The melanoma has spread to 2 or 3 nearby lymph nodes, or the melanoma has spread to very small areas of nearby skin, or has spread to skin lymphatic channels around the tumor.
 - **N3:** The melanoma has spread to 4 or more lymph nodes, or spread to lymph nodes that are clumped together, or spread to nearby.
- The **M** category is based on whether the melanoma has metastasized to distant organs.
 - To assign an M value to a case of melanoma, the results of the chest x-ray, MRI, CT scan, and/or blood tests are assessed by a doctor. The possible M values are as follows:
 - **MX:** Presence of distant metastasis cannot be assessed.
 - **M0:** No distant metastasis.

- **M1a:** Distant metastases to skin or subcutaneous (below the skin) tissue or distant lymph nodes.
- **M1b:** Cancer cells have metastasized to the lung.
- **M1c:** Cancer cells have metastasized to other organs

To make staging information even more accessible, a technique called stage grouping is also used. Stage grouping is a process where common combinations of the T, N, and M stages are combined into even simpler groups, and are labeled: I, II, III, or IV. In general, patients with a lower stage grouping will have a better chance of surviving their cancer. The following are the stage groupings for melanoma as stated by the American Cancer Society's Guide to Understanding Melanoma [7]:

- **Stage 0**
Tis, N0, M0: The melanoma is in situ, meaning that it involves the epidermis but has not spread to the dermis (see Figure 8 [1]).

Figure 8 – Stage 0 Melanoma

The appearance of stage 0 melanoma

- **Stage IA**
T1a, N0, M0: The melanoma is less than 1.0 mm in thickness. It is not ulcerated, appears to be localized in the skin, and has not been found in lymph nodes or distant organs (see Figure 9 [1]).
- **Stage IB**
T1b or T2a, N0, M0: The melanoma is less than 1.0 mm in thickness and is ulcerated or, or it is between 1.01 and 2.0 mm and is not ulcerated. It appears to be localized in the skin and has not been found in lymph nodes or distant organs (see Figure 9 [1]).

Figure 9 – Stage I Melanoma

The appearance of stage I melanoma

- Stage IIA**
T2b or T3a, N0, M0: The melanoma is between 1.01 mm and 2.0 mm in thickness and is ulcerated, or it is between 2.01 and 4.0 mm and is not ulcerated. It appears to be localized in the skin and has not been found in lymph nodes or distant organs (see Figure 10 [1]).

Figure 10 – Stage II Melanoma

The appearance of stage II melanoma

- Stage IIB**
T3b or T4a, N0, M0: The melanoma is between 2.01 mm and 4.0 mm in thickness and is ulcerated, or it is thicker than 4.0 mm and is not ulcerated. It appears to be localized in the skin and has not been found in lymph nodes or distant organs (see Figure 10).

- **Stage IIC**
T4b, N0, M0: The melanoma is thicker than 4.0 mm and is ulcerated. It appears to be localized in the skin and has not been found in lymph nodes or distant organs (see Figure 10).
- **Stage IIIA**
T1a-4a, N1a or N2a, M0: The melanoma is not ulcerated. It has spread to 1-3 lymph nodes near the affected skin area, but the nodes are not enlarged and the melanoma is found only when they are viewed under the microscope. There is no distant metastasis. The thickness of the melanoma is not a factor (see Figure 11 [1]).

Stage III nonmelanoma skin cancer

Figure 11 – Stage III Melanoma

The appearance of stage III melanoma

- **Stage IIIB**
T1b-4b, N1a or N2a, M0: The melanoma is ulcerated. It has spread to 1-3 lymph nodes near the affected skin area, but the nodes are not enlarged and the melanoma is found only when they are viewed under the microscope. There is no distant metastasis.
- T1a-4a, N1b or N2b, M0:** The melanoma is not ulcerated. It has spread to 1-3 lymph nodes near the affected skin area. The nodes are enlarged because of the melanoma. There is no distant metastasis.
- T1a/b-4a/b, N2c, M0:** The melanoma can be ulcerated or not. It has spread to small areas of nearby skin or lymphatic channels around the original tumor, but the nodes do not contain melanoma. There is no distant metastasis.

- **Stage IIIC**

T1b-4b, N1b or N2b, M0: The melanoma is ulcerated. It has spread to 1 to 3 lymph nodes near the affected skin area. The nodes are enlarged because of the melanoma. There is no distant spread.

Any T, N3, M0: The melanoma can be ulcerated or not ulcerated. It has spread to 4 or more nearby lymph nodes, or to nearby lymph nodes that are clumped together, or it has spread to nearby skin or lymphatic channels around the original tumor and to nearby lymph nodes. The nodes are enlarged because of the melanoma. There is no distant metastasis.

- **Stage IV**

Any T, Any N, M1: The melanoma has spread beyond the original area of skin and nearby lymph nodes to other organs such as the lung, liver, or brain, or to distant areas of the skin or lymph nodes. Neither the lymph node status nor thickness is considered, but typically the melanoma is thick and has also spread to lymph nodes (see Figure 12 [11]).

Figure 12 – Stage IV Melanoma

The appearance of stage IV melanoma

Other factors that affect the prognosis and treatment decisions for melanoma are the location of the tumor on the body, the mitotic index of the cancer cells, the presence

of tumor infiltrating lymphocytes, and the number of regional lymph nodes involved [11]. After all these factors have been considered, a course of treatment can be chosen.

Current Treatment Options for Melanoma

The current treatment methods for melanoma will now be discussed. Knowledge of these methods will become important when discussing the possibility of using radiofrequency tissue ablation to treat melanoma in the “Next Steps: Diagnose and Treat Melanoma” section.

The cure rate for melanoma is directly related to the stage of the cancer and the treatment used [13]. Once melanoma has been properly diagnosed and staged by a physician, a course of treatment can be chosen. The type of treatment that is used to treat the cancer depends on the stage of the melanoma. The most common method of treatment for melanoma is surgery to physically remove the cancer cell, chemotherapy, immunotherapy, or radiation therapy. A combination of multiple methods may also be used.

Surgery to remove the tumor is the most common method of treatment for melanoma [12]. Surgery is also the popular method of treatment when the melanoma is still in the early stages of growth. A surgeon may use a variety of techniques to physically remove the tumor from the body or to kill the cancer cells to stop them from spreading. These techniques include: simple excision, electrodesiccation and curettage, Mohs surgery, and cryosurgery.

Simple excision is similar to a biopsy. A doctor cuts out the tumor using a scalpel, along with some surrounding healthy skin tissue [5]. Healthy tissue is also removed as a way to help assure that all the cancerous cells are removed. If all the cancerous cells are

not removed, the melanoma may reappear. The margin of how much healthy tissue is removed depends on how large the melanoma tumor is. Table 1 shows the margin of healthy tissue removed in relation to how thick the original tumor is [7]:

Table 1 – Tumor Excision Margins

Tumor Thickness	Margin of Healthy Skin Removed
In situ	.5 cm
<1 mm	1 cm
1 to 2 mm	1 to 2 cm
2 to 4 mm	2 cm
>4 mm	At least 2 cm

After the doctor removes the tumor, the skin is stitched back together at the surgery site. A scar will often form in the place of the incision. If a large amount of skin had to be removed, sometimes the doctor will perform a skin graft to cover the wound [7].

Another type of surgery to remove melanoma is called electrodesiccation and curettage. With this technique, the doctor first cuts out the melanoma tumor using a tool called a curette; a small, sharp, spoon shaped tool. The doctor then treats the area with electricity from a monopolar electrode to stop any bleeding and to kill any remaining cancer cells (see the “Monopolar versus Bipolar Electrodes” section for a discussion on how a monopolar tissue ablation system functions). This process may then be repeated as necessary. Like simple excision, electrodesiccation and curettage may leave a scar.

Mohs surgery is another type of surgery to remove melanoma. It is a technique that can only be performed by specially trained physicians. For this treatment method, the doctor first removes the visible tumor, while also only removing a very small margin of healthy skin (typically only 1 mm). The removed skin is then sectioned, stained, and

examined under a microscope. If cancer cells are detected in the sample, the doctor removes another thin slice of tissue in the area of where the cancer cells were seen. The process is repeated until no cancer cells can be identified under the microscope. This technique is useful in that very little healthy tissue is removed, which leads to smaller scars (see Figure 13 for an example of a scar caused by Mohs surgery [photo courtesy of Marlene Stante]). However, not all doctors can perform Mohs surgery [5].

Figure 13 – Mohs Surgery Scar

The scar left on a patient as a result of Mohs surgery

Another technique used to treat skin cancer surgically is cryosurgery. Cryosurgery uses liquid nitrogen applied to the tumor to freeze the cancer cells (see Figure 14 [1]). When the cells freeze, the water in the cytoplasm of the cells expands until the cell bursts, killing the cell. After the treated tissue thaws, blisters may form on the area of treatment. Healing may take 1 to 2 months and a scar will likely form. The treated area will also have less pigmentation once the skin heals [5].

Figure 14 – Cryosurgery

An example of using cryosurgery to treat skin cancer

Chemotherapy is a type of treatment used to treat melanoma that has progressed further than the early stages and to other areas of the body. Chemotherapy uses anti-cancer drugs to kill the cancer cells. There are three ways that the anti-cancer drugs can be administered to the patient: orally, intravenously, or through a technique called isolated limb perfusion. In isolated limb perfusion, blood flow to the arm or leg that has the melanoma is stopped using a tourniquet. The cancer drug is then injected into the limb. This technique allows the drug to be given in higher doses, reach the tumor site more directly, and to stay in the area for a longer period of time. No matter what delivery method is used, the anti-cancer drug travels through the blood stream and reaches all parts of the body. This means that chemotherapy can affect the entire body, not just the tumor site. The most common anti-cancer drugs used in chemotherapy are Dacarbazine,

Cisplatin, Vinblastine, DTIC, Temozolomide, and Paclitaxel [12]. These drugs may be administered by themselves or in combination with the other drugs. The drugs function by attacking cells that divide quickly, such as cancer cells. The drugs interfere with the cancer cells' abilities to replicate, thus stopping growth and killing the tumor.

Chemotherapy drugs cause side effects, such as: loss of appetite, nausea and vomiting, lowered resistance to infection (due to low white blood cell counts), easy bruising or bleeding (due to low blood platelets counts), fatigue (due to low red blood cells counts). Since the drugs effect cells in the body that divide quickly, hair loss can also occur because hair follicles contain cells that divide quickly [7].

Immunotherapy is a type of cancer treatment that is often used alongside chemotherapy. Like chemotherapy, immunotherapy is used for cases of melanoma that have progressed beyond the early stages. Immunotherapy works to fight cancer by increasing the body's own immune response to kill cancer cells. Two immunotherapy drugs that are used to treat melanoma are interferon-alpha and interleukin-2. Both of these are a classification of drugs called cytokines, which are manmade versions of substances naturally found in the body. The drugs function by activating the body's natural immune response to fight off a pathogen. Because the drugs are released into the blood stream, they can be used to fight cancer cells throughout the body that may have spread from the original tumor. Some side effects of immunotherapy drugs include: fever, chills, aches, severe tiredness, drowsiness, and low blood cell counts [7].

Radiation therapy is the final method of treatment for melanoma. Radiation therapy is usually reserved for cases of melanoma that have progressed to later stages and have metastasized to other tissues in the body. Radiation might also be used alongside

surgery at the treatment site, in order to destroy any remaining cancer cells. Radiation therapy uses high levels of ionizing radiation to kill cancer cells [7]. The side effects of radiation therapy to treat melanoma includes: red or dry skin and fatigue [12].

These treatment options can often be effective in treating skin cancer, as long as the treatment starts at an early stage. However, many of the treatment methods have undesirable side effects including: scarring of the skin, fatigue, loss of appetite, nausea and vomiting, lowered resistance to infection, easy bruising or bleeding, fever, chills, aches, severe tiredness, drowsiness, and low blood cell counts. A new method of cancer treatment that can effectively treat skin cancer yet not cause these harmful side effects is desired by doctors and patients. It may be possible that radiofrequency tissue ablation could be this treatment method. For a further discussion about the future possibility of radiofrequency tissue ablation to treat skin cancer, please see the “Radiofrequency Tissue Ablation” section.

Melanoma Statistics

This section will provide statistical data about the incidence, morbidity, and mortality of melanoma. This section will also present incidence and mortality statistics for all types of cancer, in order to make a qualitative comparison with melanoma.

Cancer is the second leading cause of death in the United States (heart disease is the leading cause of death). Cancer is the cause of 1 in every 4 deaths in the United States [9]. It is estimated that 565,650 people died from cancer in the United States in 2008, which is approximately 1500 deaths from cancer per day [14]. Cancer was the cause of death for 7.6 million people throughout the world in 2007 [7]. The incident rate, which is the number of new diagnoses during a specific time frame, for all types of

cancer in 2008 was 745,180 for men and 692,000 for women [14]. The age adjusted incident rate, which is a method of standardizing the age of a population so populations of different average ages can be compared (since the patient's age greatly effects the chance of diagnosis, populations with different average ages will have different incident rates), for all types of cancer based on data from 2001 to 2005 was 467.4 per 100,000 men and women per year. The median age at diagnosis is 67, while the median age at death from cancer is 73 [14]. Based on data from 2003 to 2005, 40.35% of men and women born today will be diagnosed with cancer during their lifetime. The lifetime risk of an individual in the United States for developing and dying from cancer is approximately 50% for men and approximately 33% for women [9].

Cancer of the skin is the most common type of cancer. Skin cancer (including basal and squamous cell cancer) accounts for approximately half of all cancers [5]. Melanoma, as has been previously stated, is the most deadly type of skin cancer. 34,950 men and 27,530 women were diagnosed with melanoma in the United States in 2008 [14]. The percentage of people that develop melanoma has doubled in the last 30 years [12]. Melanoma is the 6th most common type of cancer for men, with melanoma accounting for 5% of all new cancer cases. Melanoma is the 7th most common type of cancer for women, with melanoma accounting for 4% of all new cancer cases [9]. The age adjusted incident rate for melanoma based on data from 2001 to 2005 was 19.4 per 100,000 men and women. White males are the most likely group to be diagnosed with melanoma, with an incident rate of 28.5 per 100,000. 1.81% of people born today will be diagnosed with melanoma sometime during their lifetime [14]. Males have a 2.42% chance of developing melanoma during their lifetime, while females have a 1.63%

chance of developing melanoma during their lifetime. In the United States, California has the greatest number of new cases. It is estimated that in California there were 7,620 new diagnoses of melanoma in 2008 [9]. The median age at diagnosis for melanoma is 59. The prevalence of melanoma, which is the number of people who are alive today and have a history of the disease, is 723,416 [14].

Once melanoma has been diagnosed, the most important factor that affects the patient's chance of survival is the thickness of the tumor. Melanoma tumors that are less than 1mm in thickness have a 10 year survival rate of 95%, which is the patient's chance of surviving 10 years after diagnosis. If the melanoma is diagnosed later, the tumor will have had time to grow and spread, and the 10 year survival rate decreases. A tumor that is 1 mm to 2 mm thick has a 10 year survival rate of 80%. Tumors with a thickness of 2 mm to 4 mm have a 10 year survival rate of 55%. If that tumor is larger than 4 mm, the 10 year survival rate drops to 30% [15]. Similar to tumor thickness, melanoma survival rates are also affected by what stage the cancer is in when it is diagnosed. Table 2 shows the survival rates for melanoma by stage [7]:

Table 2 – Melanoma Survival Rates by Stage

	5 year (%)	10 year (%)
IA	99	97
IB	92	86
IIA	78	66
IIB	68	59
IIC	56	48
IIIA	Not Available	Not Available
IIIB	50-68	44-60
IIIC	27-52	22-37
IV	18	14

As the table shows, as melanoma spreads and progresses, it becomes more difficult to treat, and the chance of survival is reduced. Eighty percent of melanoma is diagnosed in the localized stage, which helps to keep deaths from melanoma low compared to the number of diagnoses and to other cancers [9]. The mortality of melanoma, which is the number of deaths during a specific time frame, in 2008 was 8,420 men and women. Melanoma accounts for less than half of all new skin cancer cases but causes the majority of deaths [7].

Melanoma not only takes lives, but also puts a very large burden on the economy. It is estimated that the cost of cancer was \$219.2 billion in 2007 [9]. This includes direct medical costs toward fighting cancer, lost productivity costs due to illness from cancer, and lost productivity costs due to premature death from cancer. Eighty-nine billion dollars was spent in 2007 toward diagnosing and treating cancer. It is very important to diagnose melanoma early since the stage of the cancer at the time of diagnosis greatly affects the patient's chance of survival. Since all of the current melanoma diagnosis techniques involve invasive procedures, doctors may be unwilling to perform biopsies on nevi that only have a slight chance of being cancerous. This may allow for some melanoma to "slip through the cracks" and progress to later stages when they could have been diagnosed earlier. A non-invasive diagnosis technique is needed. Diagnosing melanoma by comparing the electrical properties of the suspected tumor to known values of healthy and cancerous skin may be able to fill this need, and is the main objective of this thesis.

Electrical Properties of Skin

Introduction to Electrical Properties

This section will give an overview of the electrical properties of skin tissue. Since the new technology for the diagnosis of skin cancer investigated in this thesis and the future research into radiofrequency tissue ablation will use electricity, it will be important to understand how the skin conducts electricity. It will also be important to have an understanding of the electrical properties of cancer. Using information on the differences between the electrical properties of healthy skin tissue and cancer will allow a device to detect skin cancer and also assist in treating the cancer with radiofrequency tissue ablation.

It will be helpful to have an understanding on the electrical properties terms that are discussed in this thesis. Resistance is a measure of the amount of resistance to current flow through a material when a given voltage gradient is applied. Resistance of a material is determined by the number of free electrons and ions available to flow through the material and act as charge carriers. Capacitance is the ability of a material to hold a charge when a voltage gradient is applied. When the voltage source is removed, the voltage difference between the two areas remains and begins to decay at a rate determined by the material properties and structure. Impedance is a measure of a material's resistance to an applied alternating current. It is a combination of resistance and reactance (which is a method of measuring capacitance at certain frequencies, see Equation 3).

Physical Makeup and Electrical Properties

The electrical properties of biological tissues result from the interaction of the applied electromagnetic radiation and the constituents of the tissue at the cellular and molecular level [16]. The relative amounts and positions of the tissues on the micro scale and their specific resistances to high frequency current control the current distribution of the tissue on the macro scale [17]. Three other factors that greatly affect the electrical properties of tissue include: the polarization of water molecules, the polarization of cell membranes which act as barriers to the flow of ions in and out of the cell, and ionic diffusion through the cellular membrane [16].

Electrical Properties of Skin

Human skin tends to have high electrical impedance compared to other biologic tissues due to the properties of the stratum corneum [18]. It has been shown that skin has a statistically higher impedance than the other tissues of the body [19]. These higher impedances are caused by lower water content and the physical structure of the stratum corneum compared to other tissues.

The stratum corneum is believed to have high impedance because of the low water content of the tissue compared to other tissues in the body. Tissues with a similar amount of water content have been shown to have similar resistivities [19]. Water and the ions that are suspended in it, act as a medium that allows for current to flow. When water content goes down in a tissue, the ability for that tissue to transport an electrical current diminishes. As a result, the resistance of that tissue increases.

In addition to effecting the resistive properties of skin, water also affects the capacitive properties. Capacitance of skin also increases with increasing water content [20]. Previous research has shown that the capacitor properties of the stratum corneum are completely dependent on the amount of contained water. When the stacked structure of skin cells becomes hydrated, the tissue acts like a capacitor because of the presence of layers of phospholipid membranes.

Research has also found that the impedance of skin decreases as deeper layers of the stratum corneum are exposed. This is because the water content of the skin increases with an increasing depth from the surface. However, even at the same depth, not all skin has uniform impedance properties. Skin lesions, along with the limbs of the body, have lower water content, and thus higher impedances [18]. The water content of skin can vary with the seasons, time of day, and temperature [21].

Along with the amount of water in the tissue, the physical structure of the tissue can have an impact on the ability of current to flow, and thus influence the electrical properties of the tissue. An example of the physical structure of a tissue affecting the electrical properties of that tissue is muscle fibers. Muscle cells have an elongated shape, filled with cytoplasm. They are bundled into larger structures called fibers. The cytoplasm acts as an electrolyte and makes the fibers analogous to bundles of conducting wire. Because of this structure, muscle fibers have a much lower resistance in the direction of the fibers relative to the resistance across the fiber [22]. This suggests that biologic tissues can have different electrical properties depending on the direction of the measurement relative to physical structures. The physical structure of tissues also account for the high impedances observed. Each cell in a biologic tissue has a radius of

approximately 10 nanometers, and each has its own intrinsic resistance and capacitive properties. When a measurement of a 1 centimeter long sample is taken, approximately 1,000 cells are connected in series. The resistance of the entire sample increases by a factor of 1,000 while the capacitance is reduced by a factor of 1,000 (since capacitor elements add up inversely), compared to the original cell [10].

The electrical properties of skin can be modeled as an equivalent circuit of a parallel resistor and capacitor. Although, since the skin is non-uniform, when a voltage is applied the current flow is also non-uniform. The resistor of the equivalent circuit can be seen as an ionic conductor with a resistance that falls as the number of charge carriers increase [23].

Electrical Properties of Cancer

Along with an understanding of the electrical properties of normal, healthy skin, it is also important to have an understanding of the electrical properties of cancerous tumors. Knowing how the electrical properties of cancer differ, if at all, from healthy tissue, will allow one to be more confident in the data and conclusions that are presented later in this thesis.

The average cell radius of a cancerous tumor is lower than that of a healthy cell. This means that the cellular volume fraction of a tumor is higher than normal tissue. Tumors also have an increased amount of epithelial cells. The increase of cellular density and epithelial cells means that the amount of cytoplasm in a given amount of cancerous tissue increases. Since cytoplasm is a good conductor because it allows the free flow of ions, the resistance of tumors decreases compared to normal tissue. Tumors

also have an increased amount of extracellular fluid, which functions in a similar way to lower the resistance of the tumor [10].

Practical Observations

From previous research into the electrical properties of biologic tissues, there are some interesting attributes of tissues that are good to keep in mind when taking measurements of the electrical properties of skin tissue. The first is that the resistance of biological tissue is dependent on the frequency of which the measurement is taken at. Biologic tissue resistance has an inverse relationship with frequency [24]. As the frequency of the measurement signal increases, the resistance of the tissue decreases. This is due to the fact that at low frequencies, the ion densities around the area of the measurement probe increases, impeding the travel of current through the tissue. The amount of the effect the frequency has on resistance has been quantified in previous research. Resistivity decreases by 10-20% in an increase from 1 kHz to 10 kHz and 50% from 1 kHz to 100 kHz measurement frequency. Conversely, resistivity rises 5% in a decrease in frequency from 1 kHz to 100 Hz and 20% in a change from 1 kHz to 10Hz [25].

Another interesting attribute of the electrical properties of biologic tissue is that the resistance of biologic tissue increases with tissue necrosis. This is caused by the fact that when a cell dies, the cell membrane loses its' ability to maintain its' insulating properties and ionic gradients [22]. Other research has confirmed this observation, noting that tissue undergoes large changes upon death of the cell, especially in low frequency ranges. This is important to note because an electrical current will follow a path that offers the least resistance. This holds true for when the current is passing through

biologic tissues, as a current that transverses a tissue sample will follow the path of least electrical resistance and will avoid tissues of higher resistance [17]. The fact that tissue impedance increases as cell necrosis progresses will be important to keep in mind in the “Radiofrequency Tissue Ablation,” as many radiofrequency ablation generators use this phenomenon to monitor the progress of treatment.

Previously Recorded Values

When reporting values for the resistance of biologic tissues, researchers convert resistance values into units of resistivity, or specific resistance. This converts the values from units of Ohms to units of Ohms*cm. To make this conversion, Equation 1 is used [17]:

Equation 1-Specific Resistance:

$$R_S = R_M * S_A / D_E$$

Where:

R_S = Specific resistance

R_M = Measured resistance

S_A = Electrode surface area

D_E = Distance between electrodes

The purpose of making this conversion is to control for different-sized electrodes and electrode spacing that are used by different groups of researchers. By reporting specific resistance instead of measured resistance, researchers are able to compare values, even though those values were recorded using different experimental setups. There are two electrode setups that are used most commonly to determine the impedance of biologic tissues. One system uses two electrodes, known as a Schwan electrode to drive a current through tissue and obtains measurements using the same two electrodes (see figure 15 [25]).

Figure 15 - Schwan Electrode

An example of a Schwan electrode

The other system uses four electrodes. In the four electrode setup, the two outer electrodes drive a current through the tissue, while the two inner electrodes are the measurement electrodes (see Figure 16, where electrodes S_1 and S_2 drive the electrical current and electrodes m_1 and m_2 measure the electrical properties [25]). Some believe that the 4 electrode system prevents polarization (or the buildup of ions) at the measurement electrodes which can lead to artificially higher values for the resistance. Other research has suggested that there is no significant difference between the two setups [24]. Other research has also found that the four electrode system does not eliminate polarization [25]. The electrode setup that was used by the author of this thesis most closely resembles the Schwan electrode.

Figure 16 – 4 Electrode Tissue Probe

A schematic of a 4 electrode 3 tissue probe

Below are the summarized tissue resistance values found in the literature. The values for muscle and fat are also included because they may be important to quantifying the electrical properties of a tumor that have advanced into deeper tissue. The purpose of listing these previous measurements of the electrical properties of biologic tissues is to show that since there is little agreement among experts on the methods used and results obtained, it does not make sense to compare these measurements with data found during experiments performed for this thesis. It is important to note that no previous research into the area of measuring the electrical properties of melanoma or comparing the electrical properties of normal and cancerous tissue was found in the literature.

Hemingway and McClendon found skin to have a specific resistance of 289 Ohms*cm, fat to have a specific resistance of 2,180 Ohms*cm, and Muscle tissue to have a specific resistance of 110 Ohms using the 2 electrode setup and a frequency of 1MHz [17].

Geddes and Baker found that human muscle has a specific resistance of 110 Ohms*cm at 1MHz (2-pp284). They measured dog fat as having a specific resistance of 1500-3000 Ohms*cm at 10-100 kHz. They also used a 2 electrode setup [22].

Burger and VanDonger found that the specific resistance of muscle fibers varies by 3% between the longitudinal and transverse directions. They found that on average, muscle fibers have a specific resistance of 675 Ohms*cm [24].

Gabriel and Corthout found that when measured at 10,000 Hz, human skin has a permittivity of $1\text{E}5$ to $1\text{E}3$ Farads/meter and a conductivity of $0.5\text{E}-1$ to $1\text{E}-4$ Siemens/meter [16].

Faes and Meij found skin to have a specific resistance of $329\text{ Ohms}\cdot\text{cm}$ [20].

One can see that there seems to be little agreement about the specific resistances of skin and other tissues. This can be attributed to variations in the measurement apparatus, measurement frequencies, and experimental procedures used by each researcher. Other factors such as in vivo versus in vitro, temperature, and time after excision could have caused the differences in results. In addition, these measurements of tissue resistance were taken in order to learn about different characteristics of the tissue, such as hydration. For some, the measurements were taken with the purpose of being compared to other tissues, instead of just investigating the properties of the tissue themselves.

Experimental Methods

Introduction to Experimental Methods

The following sections will outline the thought process and the steps that were taken in measuring the electrical properties of human skin analogues. The purpose for measuring the electrical properties of human skin analogues is to illustrate the concept that a bipolar measuring system can reliably distinguish between normal and cancerous skin tissue.

Purpose of Measuring Electrical Properties of Skin Analogues

The purpose of measuring the resistance and reactance (which will also sometimes be referred to as, “electrical properties”) of skin analogues for this thesis is to attempt to conclude if skin with melanoma cells has a measurable difference of electrical properties compared to healthy, non cancerous skin. If a difference can be reliably detected between the two tissue types, a device can be made that diagnoses cancer by measuring the electrical properties of the tissue. Measurable different electrical properties could also let a device map out the border of the lesion against healthy tissue. Being able to map out the border of where healthy and cancerous tissue meet would allow the device to apply treatment only to the cancerous tissue and avoid an invasive procedure for both diagnosis and treatment.

A melanoma diagnosis system that functions by measuring the electrical properties of the suspected tumor is desirable because, as was shown earlier, all current diagnosis methods are invasive to the patient. Surgery and scarring of the skin are a result of the melanoma diagnosis techniques. A technique that compares the measured

electrical properties of the suspected tumor to known values of melanoma and healthy skin to make a diagnosis would be less invasive to the patient and cause no lasting effects.

Experimental Measurement Materials

The following sections detail the experimental setups that were used for each experiment that was performed to gather data for this thesis.

Electrode Fixture

Since the measured resistance and capacitance of a tissue sample is a function of the amount of tissue being measured (as evident by Equation 1), the distance between the electrodes must be the same for each trial. In order to provide a consistent electrode setup for measuring the electrical properties of skin tissue analogues between samples and trials, an electrode fixture had to be designed and manufactured. The fixture allowed the electrodes to be held at a consistent distance away from each other.

Several design considerations went into the design of the electrode fixture in order to ensure that the fixture functioned as needed. These considerations included: ease of manufacture, material, suitable dimensions, ability of replace electrodes as needed, and usability.

In order to ensure that the electrode fixture could be easily and quickly manufactured, a cylindrical design was chosen, allowing the fixture to be made on a lathe. The main body of the fixture consists of a solid cylinder with a post protruding from one face (see part labeled 1 on Figure 17). Through the body of the cylinder are two through holes that allow the wires of the electrodes to pass through. A cylindrical tube goes over the post (see part labeled 2 on Figure 17). This tube has two grooves on the

inner diameter where the electrodes are held. Screws on the tube allow the tube to be tightened onto the post; securing the electrodes in place and also allowing the tube to be removed to access the electrodes (see Figure 18 for a picture of the fixture with electrodes). The ability of the electrode holding tube to be able to slide off the body of the fixture allowed the electrodes to be easily replaced in the event of breakage. SolidWorks drawings of the electrode fixture can be found in the Appendix.

Figure 17 – Electrode Fixture

**The electrode fixture used to make electrical property measurements.
The parts of the fixture are labeled 1 and 2.**

The electrode fixture is made out of delrin. Delrin was chosen because it is non-conductive and would not interfere with the electrical measurements. Delrin is also inexpensive which allowed for the costs associated with this thesis to be kept low. Other benefits of using delrin include allowing the fixture to be non-corrosive and biocompatible.

Figure 18 - Electrode Fixture with Electrodes

A picture of the electrodes in the electrode fixture

Dimensions were chosen so that when the electrodes were inserted into the fixture, they would be spaced 1 cm apart. This dimension was chosen to make it easy to convert the measured values into units of Specific Resistivity ($\text{Ohm}\cdot\text{m}$). Units of Specific Resistivity will allow the electrical property measurements found in the following experiments to be compared with data from the literature. Using units of $\text{Ohm}\cdot\text{m}$ cancel out any effects from the size of the specimen tested, and will give values that pertain to the inherent electrical properties of the material being tested. An electrode spacing of 1 cm also allows the electrodes to be close enough to measure the tissue analogues that are to be used. Too great of a distance between the electrodes could also cause unnecessarily high resistance measurements, since more material would be taken into account during the measurement, which could lead to measurement errors. All the other dimensions were chosen to minimize the amount of material necessary to make the fixture but still allow it to be usable.

After preliminary tissue and equipment validation measurements were made, it became apparent that it would be helpful if the electrode fixture was attached to another fixture that would lower it and the electrodes down onto the sample and hold it steady. This would allow the same pressure to be placed on the sample for each trial, and keep the electrode fixture from moving during the measurement. A height gauge was modified for this purpose. The electrode fixture was secured to the height gauge, which could then be lowered onto the tissue sample (see Figure 19). Since the electrode fixture was not secured in the vertical direction, the electrodes could only be pushed into the sample with the weight of the electrode fixture. This allowed the pressure of the electrodes on the sample to be consistent for each measurement.

Figure 19 – Height Gauge

**The height gauge after it was modified
to hold the electrode fixture**

Measurement Electrodes

The electrodes that were used to make electrical properties measurements of the skin analogues were made of a Silver-Chloride (AgCl) compound (see Figure 20). AgCl electrodes are the most common type of electrode used when taking electrical measurements of biologic tissue because the compound does not create a charge density around the electrode. A charge density occurs when ions in the sample are attracted to the electrode due to the alternating current. These ions accumulate at the electrode-tissue interface, and interfere with the measurement. AgCl electrodes are also commonly used to make biologic measurements because they themselves do not exhibit polarization when a voltage is applied.

Figure 20 – AgCl Electrodes

The electrodes used to perform electrical property measurements

The AgCl electrodes that were chosen for this thesis were Warner Instruments pellet electrodes, model E255. This electrode was chosen because it had the smallest diameter available (0.8 mm). A small diameter allows the electrodes to make more accurate measurements because less tissue is under the electrode and a smaller area of tissue is between the two electrodes (see Equation 1). The smaller measurement area allows for the measurement resolution to be increased and also prevents too large of values from being measured. The electrodes are also described as “suitable for probing tissue” by the manufacturer.

Because the electrodes have a small diameter, they were brittle and subject to bending and breaking. When this occurred, the broken electrodes were switched out for new electrodes. This was facilitated by the fixture designed to allow the switching of electrodes.

A bipolar, 2-electrode setup was used for several reasons. As it has been stated earlier, and will be further explored later in the “Next Steps” section of this thesis, part of the objective of this thesis was to investigate the possibility of using bipolar radiofrequency tissue ablation to treat skin cancer. If the cancer is going to be treated with a bipolar setup, it would be beneficial to also diagnose the cancer in the same fashion. Bipolar electrodes also provide other benefits for making measurements. A bipolar setup only measures the tissue directly in-between the electrodes. This leads to more accurate measurements and thus a more accurate diagnosis because only the suspected cancerous tissue in question is examined.

National Instruments ELVIS

To perform the actual measurements of electrical properties for this thesis, a National Instruments Educational Laboratory Virtual Instrumentation Suite (or ELVIS) was used. ELVIS is a data acquisition device that uses a combination of hardware and software to allow the user to perform experiments that require measurements, automation, and control [26]. To perform the experiments in this thesis without ELVIS would have required the additional purchase of a separate power generator, oscilloscope, and function generator. Instead, ELVIS uses virtual equivalents of these built into the software, with a bench-top breadboard to allow the physical experimental materials to interface with the software. This allowed the costs of running these experiments to be greatly reduced.

The data acquisition device that was used for this thesis was the Impedance Analyzer. The NI ELVIS Impedance Analyzer can measure the specific impedance characteristics, which is a combination of resistance and reactance, of the device or material being tested. The NI ELVIS system accomplishes this by inputting an AC sine wave current source from the CURRANT HI pin to “excite” the material. The resulting sine wave is measured on the CURRANT HI and CURRANT LOW pins and then broken down into: phase, magnitude, resistance, and reactance of the material [26]. A sample output is shown in Figure 16. NI ELVIS system allows a researcher to easily investigate the electrical properties of a sample by inserting the electrodes into the CURRANT HI and CURRANT LOW pins, creating a Schwan electrode setup. All the researcher must do is select the measurement frequency.

The Impedance Analyzer allows for the user to select the frequency for the AC sine wave current source. A value of 10 kHz was chosen to perform these experiments because it was the highest possible value that could be produced by the NI ELVIS system. A high value was chosen because tissue ablation often uses signals in the 100s kHz range (see the “Tissue Ablation” section for more), and it was believed to be helpful to perform the measurements at a frequency similar to possible ablation frequencies. A high frequency was also chosen because higher frequencies are better at preventing charge densities from building up in the material and result in lower impedances in biologic tissues.

For each measurement, the Impedance Analyzer was turned on, the bipolar electrodes placed on the sample, and then the signal output would be allowed to settle. This settling could take anywhere from 10-30 seconds. Once the output had resolved, the resistance and reactance would be recorded, along with a screen shot of the graphical output (see Figure 21 for an example of the graphical output) for archiving.

Figure 21 – Sample ELVIS Output

An example output of the ELVIS impedance analyzer

Reactance and resistance are the two components that make up a material's electrical impedance. Resistance is the material's opposition to current flow on the real number line, and is measured in Ohms. Reactance is the material's opposition to current flow on the imaginary number line, and is also measured in Ohms. Resistance and reactance can be used to find a material's total impedance (also with units of Ohms) using Equation 2:

Equation 2-Impedance as a Function of Resistance and Reactance:

$$I = (R^2 + X_r^2)^{1/2}$$

Where:

I = Impedance

X_r = Reactance

R = Resistance

Therefore, a material's impedance can be seen as the magnitude of the resistance and reactance, separated by an angle, or phase shift. The capacitance of a material can be found if the reactance and measurement frequency are known using Equation 3:

Equation 3-Capacitance as a Function of Frequency and Reactance:

$$C = -1 / (2 * \pi * F * X_r)$$

Where:

C = Capacitance

X_r = Reactance

F = Frequency

Validation and Experimental Samples

The main purpose of this thesis is to investigate a new method of skin cancer diagnosis. This method would involve measuring the electrical properties of the suspect tumor, comparing it to known average values of healthy skin tissue and cancerous skin tissue, and making a diagnosis based on the results of the comparison. In order to decide if this is a viable diagnosing method, it must be first established that there is a measurable difference between healthy skin and cancerous skin. This will be the main objective for the experiments of this thesis: to build a database of the electrical properties of healthy and cancerous tissue, and to determine if there is a statistical difference between the two groups. To do this analysis, experiments were performed with the previously mentioned fixture, electrodes, and data acquisition device on tissue samples to determine if a difference between the electrical properties of the samples could be seen. The following section will outline the different samples tested and the reasoning behind why there were chosen. Some of the samples were tested to first validate the experimental methods and NI ELVIS system, while other samples were tested for the purpose of creating the

aforementioned database. To see the results of the experiments, please see the section titled “Data.”

Elvis Validation

The purpose of the first experiments performed for this thesis was to validate the ELVIS system. The author wanted to make sure that the values reported by the ELVIS system were accurate over the range of impedance values expected to be seen with tissue. This validation was performed by measuring various resistors and capacitors and comparing the measured values to the stated values of the circuit elements. The circuit elements were plugged directly into the CURRENT OUT and CURRENT IN pins (the electrode fixture and electrodes were not used) on the ELVIS data acquisition device and the impedance analyzer was used at a frequency of 10 kHz. The values of the resistors tested were: 10, 100, 1,000, 10,000, 100,000, and 1M Ohms. Three different resistors for each value were tested. The values for the capacitors tested were: 1E-5, 1E-6, 1E-7, 1E-8, and 1E-9 Farads. Three different capacitors for each value were tested. It should be noted that all the circuit elements had a stated error of +/- 5% by the manufacturer.

Bipolar Electrode and Electrode Fixture Validation

The purpose of the next experiments that were performed was to validate the experimental setup of the silver-chloride bipolar electrodes, electrode fixture, and ELVIS system. This validation experiment was also performed to ensure that the small size of the AgCl electrodes would not skew the electrical property measurements. This experiment was performed in a similar manner to the ELVIS validation experiments, by measuring sets of resistors and capacitors, and comparing the measured values to the

stated values of the circuit elements. To perform these tests, the electrodes and electrode fixture were set up how they would be for a tissue sample test on the ELVIS data acquisition system and then the circuit elements were connected to the electrodes. The values and number of resistors and capacitors tested was the same for the previous validation test.

Raw Chicken

After the experimental system had been validated, the next set of experiments consisted of using the ELVIS data acquisition system, bipolar electrodes, and electrode fixture to measure the electrical properties of different tissue sections of a raw chicken thigh (see Figure 22). The different sections of the chicken thigh that were tested were the skin, thigh meat, and fat. The purpose of testing different types of tissues was to evaluate whether or not the experimental methods used could distinguish between different tissue types by measuring the electrical properties. Granted, the physical and visual differences between chicken skin, fat, and thigh meat are quite large, but if the system can distinguish a difference between them by only examining their electrical properties, it may be possible that it can also distinguish a difference between healthy and cancerous skin tissue. For the testing of raw chicken thigh meat, skin, and fat, each type of tissue was measured 10 times at 10 kHz. After a measurement of one type was taken, the bipolar electrodes were moved to another area of the same tissue and the measurement repeated, until all 10 measurements had been recorded.

Figure 22 – Raw Chicken Measurements

**An example of a measurement being taken for
raw chicken meat**

Raw Chicken versus Cooked Chicken

After the raw chicken electrical property measurements had been made, the chicken samples that were used were cooked in a convection oven for 35 minutes at 350 degrees Fahrenheit. The same measurements that were previously taken were repeated and recorded. The purpose of cooking the chicken and retaking the measurements was that since a major contributor to the electrical properties of a biologic tissue (and one of the main differences between normal tissue and tumors) is the water content of the tissue, cooking the tissue should remove a large proportion of the water, causing the electrical property values to change. These values were compared to the values obtained from the same tissue before the sample was cooked, to investigate if water content made a difference in the electrical properties. This experiment allowed the researcher to validate that the experiment setup of ELVIS data acquisition system, bipolar electrodes, and electrode fixture could distinguish between the different sample types (raw fat vs. cooked fat, raw skin vs. cooked skin, raw thigh meat vs. cooked thigh meat).

Human Skin Analogues

The final set of experiments that were preformed for this thesis involved measuring the electrical properties of several skin tissue cultures from MatTek, Corp (see Figure 23). Two different sets of skin tissue cultures were tested: normal skin tissue (EpiDerm™) and skin tissue with malignant melanoma integrated into the sample (Melanoma™). The purpose of testing two different sets of human skin cultures was to compare the results of the electrical property measurements for each set. Since one set contains malignant melanocytes while the other does not, if a statistical difference can be found between the two sets, the objective of this thesis will have been met: that melanoma skin cancer can be diagnosed by measuring the electrical properties of the suspected tumor and comparing those values to known values of healthy skin and cancerous skin tissue.

Figure 23 – Skin Analogue Measurements

An example of an electrical property measurement for a skin tissue analogue

EpiDerm™ skin model cultures were obtained from MatTek Corp. to be used as a human skin analogue for healthy, non-cancerous skin. EpiDerm™ has many features that make it ideal for this purpose. The cultures are made from normal human epithelial keratinocytes and take the form of 3-D, highly dimensional tissue (see figure 24). The cultures are metabolically active and have an in vivo-like lipid profile. The samples have been cultured on specially prepared cell culture inserts. MatTek Corp. claims that EpiDerm™ closely parallels human skin ultra structurally, and exhibits in vivo-like morphological and growth characteristics. EpiDerm™ consists of organized granular, spinosum, and basal tissue layers, similar to those found in vivo [27]. It is important to note that the EpiDerm™ samples have an even distribution of cells, which is visible in the figure.

Figure 24 - EpiDerm™ Histology

A slide of an EpiDerm™ sample showing the different keratinocyte morphologies

The electrical properties of nine EpiDermTM samples were measured, with each sample measured four times at a 90 degree rotation from each other. A total of 36 individual tests were used to build the database for “normal skin tissue”.

MelanomaTM skin model cultures were obtained from MatTek Corp. to be used as human skin analogues for cancerous skin. MelanomaTM has many features that make it ideal for this purpose. The cultures contain human malignant melanoma cells embedded in 3-D, highly differentiated and human-like structure (see figure 25). The normal tissue that the melanoma is seeded in consists of human-derived epidermal keratinocytes and normal dermal fibroblasts, closely resembling the EpiDermTM samples. These cells have been cultured to form a multilayered, highly differentiated epidermis. The epidermis of the cultures consists of organized granular, spinosum, and basal epidermal layers, similar to those found in vivo. Structurally, the model closely parallels the progression of melanoma in vivo. The cultures also have a dermal component that is composed of a collagen matrix and human dermal fibroblasts [27]. It is important to note that unlike the EpiDermTM samples, the MelanomaTM samples do not have a uniform distribution of cells. The melanoma cells project down into the dermal layer of the sample, similar to the progression of melanoma in vivo.

Figure 25 - MelanomaTM Histology

A slide of a MelanomaTM sample showing the different keratinocyte morphologies and melanoma cells

The electrical properties of six MelanomaTM samples were measured, with each sample measured eight times at a 45 degree rotation from each other. A total of 48 individual tests were used to build the database for “cancerous skin tissue”.

Data

After the validation and electrical property measurements were taken as outlined in the “Validation and Experimental Samples” section, the data was entered into Minitab for graphical and statistical analysis. It was used to create the charts, graphs, and statistical hypothesis testing seen below. The following sections will present the data gathered during the experiments. For a discussion of the data and analysis, please see the “Conclusions” section.

ELVIS Validation Results

Table 3 contains the measured data for the ELVIS validation for resistance. The face value of each resistor is listed, along with the measured value for each resistor. The 3rd column shows the percent error of the measured resistance to the listed value of resistance. The final column shows whether the experimental error falls within the 5% error that is reported by the manufacturer.

Table 3 – ELVIS Resistance Validation Data

Face Value of Resistor (Ohms)	Measured Resistance (Ohms)	Experimental Error (%)	In Tolerance (Y/N)
10	12.37	23.7	N
10	12.44	24.4	N
10	18.28	82.8	N
100	101.19	1.19	Y
100	101.11	1.11	Y
100	100.17	0.17	Y
1000	982.41	-1.759	Y
1000	979.66	-2.034	Y
1000	982.62	-1.738	Y
10000	9840	-1.6	Y
10000	9900	-1	Y
10000	9810	-1.9	Y
100000	97190	-2.81	Y
100000	97720	-2.28	Y
100000	97240	-2.76	Y
1000000	360630	-63.937	N
1000000	354960	-64.504	N
1000000	366200	-63.38	N

Table 4 is the measured data for the ELVIS validation for capacitance. The face value for each capacitor is listed, along with the measured reactance value for each capacitor. The measured reactance values are then converted to capacitance using Equation 3 so the measured values can be compared to the listed capacitance of each capacitor. The 4th column shows the experimental error of the measured capacitance to the listed capacitance. The final column shows whether the experimental error falls within the 5% error that is reported by the manufacturer.

Table 4 – ELVIS Capacitance Validation Data

Face Value of Capacitor (F)	Measured Reactance (Ohms)	Calculated Capacitance (F)	Experimental Error (%)	In Tolerance (Y/N)
1.00E-005	1.27E-002	-1.25E-03	-12631.89	N
1.00E-005	3.51E-002	-4.53E-04	-4634.33	N
1.00E-005	5.39E-002	-2.95E-04	-3054.97	N
1.00E-006	-14.09	1.13E-06	12.96	N
1.00E-006	-14.07	1.13E-06	13.12	N
1.00E-006	-13.78	1.15E-06	15.50	N
1.00E-007	-157.01	1.01E-07	1.37	Y
1.00E-007	-165.36	9.62E-08	-3.75	Y
1.00E-007	-149.69	1.06E-07	6.32	N
1.00E-008	-1.60E+003	9.95E-09	-0.53	Y
1.00E-008	-1.59E+003	1.00E-08	0.10	Y
1.00E-008	-1.57E+003	1.01E-08	1.37	Y
1.00E-009	-1.53E+004	1.04E-09	4.09	Y
1.00E-009	-1.57E+004	1.01E-09	1.37	Y
1.00E-009	-1.62E+004	9.82E-10	-1.82	Y

Below are two graphs (Scatterplot of ELVIS Resistance Validation and Scatterplot of EVLIS Capacitance Validation) that show the measured ELVIS data for the resistors and capacitors versus the theoretical listed values for both resistance and capacitance. Where only one data point is visible is a result of a tight grouping of the data compared to the scale of the graph.

Please note: the measured reactance of the 1.00E-005 capacitors was left out because the ELVIS machine could not properly measure such a strong capacitor.

Including this data on the graph would have made the graph difficult to read. However, this data is still used in the analysis in the “Conclusions” section.

Bipolar Electrode and Electrode Fixture Validation Results

Table 5 contains the measured data for the electrode and fixture validation for resistance. The listed value of each resistor is shown in column 1, along with the measured value for each resistor in column 2. The 3rd column shows the experimental error of the measured resistance to the listed resistance. The final column shows whether the experimental error falls within the 5% error that is reported by the manufacturer.

Table 5 – Bipolar Electrode and Electrode Fixture Resistance Validation Data

Resistor Face Value (Ohms)	Measured Resistance (Ohms)	Experimental Error (%)	In Tolerance (Y/N)
10	12.69	26.90	N
10	12.9	29.00	N
10	28.89	188.90	N
100	101.57	1.57	Y
100	101.36	1.36	Y
100	100.5	0.50	Y
1000	984.93	-1.51	Y
1000	983.07	-1.69	Y
1000	985.16	-1.48	Y
10000	9860	-1.40	Y
10000	9930	-0.70	Y
10000	9840	-1.60	Y
100000	95860	-4.14	Y
100000	96250	-3.75	Y
100000	95940	-4.06	Y
1000000	215290	-78.47	N
1000000	215560	-78.44	N
1000000	215790	-78.42	N

Table 8 is the measured data for the electrode and fixture validation for capacitance. The listed value for each capacitor is shown in column 1, along with the measured reactance for each capacitor in column 2. The measured reactance values are then converted to capacitance so they can be compared to the listed capacitance of each capacitor. The 4th column shows the experimental error of the measured capacitance to

the listed capacitance. The final column shows whether the experimental percent error falls within the 5% error that is reported by the manufacturer.

Table 6 – Bipolar Electrode and Electrode Fixture Capacitance Validation Data

Capacitor Face Value (F)	Measured Reactance (Ohms)	Calculated Capacitance (F)	Experimental Error (%)	In Tolerance (Y/N)
1.00E-06	-13.96	1.14E-06	14.01	N
1.00E-06	-13.92	1.14E-06	14.34	N
1.00E-06	-13.65	1.17E-06	16.60	N
1.00E-07	-155.33	1.02E-07	2.46	Y
1.00E-07	-163.78	9.72E-08	-2.82	Y
1.00E-07	-148.08	1.07E-07	7.48	N
1.00E-08	-1580	1.01E-08	0.73	Y
1.00E-08	-1560	1.02E-08	2.02	Y
1.00E-08	-1550	1.03E-08	2.68	Y
1.00E-09	-14930	1.07E-09	6.60	N
1.00E-09	-15370	1.04E-09	3.50	Y
1.00E-09	-15810	1.01E-09	0.70	Y

Below are two graphs (Scatterplot of ELIVS and Electrode/Fixture Resistance Validation and Scatterplot of ELVIS and Electrode/Fixture Capacitance Validation) that show the measured ELVIS and electrode/fixture data versus theoretical face values for both resistance and capacitance. Where only one data point is visible is a result of a tight grouping of the data compared to the scale of the graph.

Scatterplot of ELVIS and Electrode/Fixture Resistance

Scatterplot of ELVIS and Electrode/Fixture Capacitance

Raw Chicken Results

Below are the results from the electrical property measurements of raw chicken using the bipolar electrodes, electrode fixture, and ELVIS as outlined in the

“Validation and Experimental Samples” section. Table 7 contains the measured resistance, reactance, and calculated capacitance of raw chicken skin. Table 8 contains the measured resistance, reactance, and calculated capacitance of raw chicken thigh meat. Table 9 contains the measured resistance, reactance, and calculated capacitance of raw chicken fat.

Table 7 – Raw Chicken Skin Data

Raw Chicken Skin Resistance (Ohms)	Raw Chicken Skin Reactance (Ohms)	Calculated Raw Chicken Skin Capacitance (F)
4280	-267.12	5.96E-08
3730	-244.66	6.51E-08
3110	-192.55	8.27E-08
3400	-251.03	6.34E-08
3630	-353.94	4.50E-08
4040	-435.22	3.66E-08
4970	-569.07	2.80E-08
4470	-366.45	4.34E-08
3480	-296.9	5.36E-08
3700	-428.73	3.71E-08

Table 8 – Raw Chicken Thigh Meat Data

Raw Chicken Thigh Meat Resistance (Ohms)	Raw Chicken Thigh Meat Reactance (Ohms)	Calculated Raw Chicken Thigh Meat Capacitance (F)
2150	-335.22	4.75E-08
1660	-254.2	6.26E-08
1280	-195.71	8.13E-08
2120	-388.78	4.09E-08
1770	-320.58	4.96E-08
1550	-260.78	6.10E-08
1700	-345.63	4.60E-08
1550	-297.47	5.35E-08
1820	-392.4	4.06E-08
2110	-493.7	3.22E-08

Table 9 – Raw Chicken Fat Data

Raw Chicken Fat Resistance (Ohms)	Raw Chicken Fat Reactance (Ohms)	Calculated Raw Chicken Fat Capacitance (F)
2920	-139.39	1.14E-07
1920	-92.53	1.72E-07
2130	-105.43	1.51E-07
2180	-104.61	1.52E-07
3720	-167.75	9.49E-08
3310	-231.6	6.87E-08
3190	-30.73	5.18E-07
2830	-146.11	1.09E-07
3690	-57.98	2.74E-07
3530	-12.13	1.31E-06

Table 10 contains the calculated impedance of each raw chicken tissue type using Equation 2.

Table 10 – Raw Chicken Calculated Impedance

Calculated Raw Chicken Skin Impedance (Ohms)	Calculated Raw Chicken Thigh Meat Impedance (Ohms)	Calculated Raw Chicken Fat Impedance (Ohms)
4288.33	2175.98	2923.33
3738.02	1679.35	1922.23
3115.95	1294.88	2132.61
3409.25	2155.35	2182.51
3647.21	1798.8	3723.78
4063.38	1571.78	3318.09
5002.47	1734.78	3190.15
4485	1578.29	2833.77
3492.64	1861.82	3690.46
3724.76	2166.99	3530.02

The following boxplots show the resistance, reactance, and impedance of each raw chicken tissue compared to each other. Boxplots break data up into quartiles. The two vertical lines show the 1st and 4th quartiles, while the shaded box shows the 2nd and 3rd quartiles. The horizontal line through each box shows the 50th percentile, or the mean average. Boxplots that are on a different horizontal level with each other would suggest

that different values are measured for each type of tissue, and thus a difference between the electrical properties between the tissues.

The following boxplot, “Boxplot of Raw Chicken Skin vs. Meat vs. Fat Resistance” shows the measured resistance data for raw chicken. The average resistance measurements for skin, meat, and fat are: 3,881 Ohms, 1,771 Ohms, and 2,942 Ohms respectively.

Boxplot of Raw Chicken Skin vs. Meat vs. Fat Resistance

The following boxplot, “Boxplot of Raw Chicken Skin vs. Meat vs. Fat Reactance” shows the measured reactance data for raw chicken. The average resistance measurements for skin, meat, and fat are: -340.6 Ohms, -328.4 Ohms, and -108.8 Ohms respectively.

Boxplot of Raw Chicken Skin vs. Meat vs. Fat Reactance

The following boxplot, “Boxplot of Raw Chicken Skin vs. Meat vs. Fat Impedance” shows the calculated impedance data for raw chicken using Equation 2. The average impedance values for skin, meat, and fat are: 3,897 Ohms, 1,801 Ohms, and 2,945 Ohms respectively.

Boxplot of Raw Chicken Skin vs. Meat vs. Fat Impedance

The following scatterplot, “Scatterplot of Raw Chicken Skin vs. Meat vs. Fat Electrical Properties” shows each measurement for each raw chicken tissue sample on the same plot. Separate grouping of the measurements would suggest that there are fundamental differences of the electrical properties between the tissue types.

Scatterplot of Raw Chicken Skin vs. Meat vs. Fat Electrical Properties

A One-Way ANOVA (or Analysis of Variance) can be used to conclude whether data from two or more sets are statistically different from each other. ANOVA returns a test statistic which can be used to reject or accept a null hypothesis.

A One-Way ANOVA analysis was performed with Minitab on the raw chicken impedance data. If by using the ANOVA analysis we can conclude that the tissues had statistically different electrical properties, we can conclude that the experimental setup was successful in detecting the different electrical properties of the tissues. We may also conclude that different types of tissues have statistically different electrical properties. The Minitab output, along with the ANOVA p-value, is shown below. A discussion about

what conclusions can be reached, if any, from this output will be discussed in the “Conclusions” section.

One-way ANOVA: Skin Impedance (, Thigh Meat Imped, Fat Impedance (O

Source	DF	SS	MS	F	P
Factor	2	22003739	11001869	38.77	0.000
Error	27	7662734	283805		
Total	29	29666472			

S = 532.7 R-Sq = 74.17% R-Sq(adj) = 72.26%

Level	N	Mean	StDev
Skin Impedance (Ohms)	10	3896.7	565.4
Thigh Meat Impedance (Oh	10	1801.8	294.6
Fat Impedance (Ohms)	10	2944.7	667.0

Individual 95% CIs For Mean Based on
Pooled StDev

Pooled StDev = 532.7

Cooked Chicken Results

Below are the results from the electrical property measurements of cooked chicken using the bipolar electrodes, electrode fixture, and ELVIS as outlined in the “Validation and Experimental Samples” section. Table 11 contains the measured resistance, reactance, and calculated capacitance of cooked chicken skin. Table 12 contains the measured resistance, reactance, and calculated capacitance of cooked chicken thigh meat. Table 13 contains the measured resistance, reactance, and calculated capacitance of cooked chicken fat.

Table 11 – Cooked Chicken Skin Data

Cooked Chicken Skin Resistance (Ohms)	Cooked Chicken Skin Reactance (Ohms)	Calculated Cooked Chicken Skin Capacitance (F)
6480	-742.27	2.14E-08
6220	-665.59	2.39E-08
5950	-804.37	1.98E-08
9280	-848.65	1.88E-08
12140	-991.42	1.61E-08
12970	-2440	6.52E-09
9270	-1530	1.04E-08
6650	-1250	1.27E-08
11400	-2040	7.80E-09
3300	-468.88	3.39E-08

Table 12 – Cooked Chicken Thigh Meat Data

Cooked Chicken Thigh Meat Resistance (Ohms)	Cooked Chicken Thigh Meat Reactance (Ohms)	Calculated Cooked Chicken Thigh Meat Capacitance (F)
2840	-670.08	2.38E-08
2580	-624.3	2.55E-08
2870	-771.73	2.06E-08
3280	-733.05	2.17E-08
2920	-764.47	2.08E-08
2650	-781.86	2.04E-08
2590	-715.52	2.22E-08
2220	-642.91	2.48E-08
2380	-821.99	1.94E-08
2540	-724.78	2.20E-08

Table 13 – Cooked Chicken Thigh Mean Data

Cooked Chicken Fat Resistance (Ohms)	Cooked Chicken Fat Reactance (Ohms)	Calculated Cooked Chicken Fat Capacitance (F)
22190	-1770	8.99E-09
22220	-2310	6.89E-09
26340	-5050	3.15E-09
17010	-1690	9.42E-09
34620	-1440	1.11E-08
15930	-654.13	2.43E-08
27670	-2380	6.69E-09
32440	-513.76	3.10E-08
28640	-3040	5.24E-09
44280	-5390	2.95E-09

Table 14 contains the calculated impedance of each cooked chicken tissue type using Equation 2.

Table 14 – Cooked Chicken Calculated Impedance

Calculated Cooked Chicken Skin Impedance (Ohms)	Calculated Cooked Chicken Meat Impedance (Ohms)	Calculated Cooked Chicken Fat Impedance (Ohms)
6522.37	2917.98	22260.48
6255.51	2654.46	22339.75
6004.12	2971.95	26819.73
9318.72	3360.92	17093.75
12180.42	3018.41	34649.94
13197.52	2762.93	15943.42
9395.41	2687.02	27772.17
6766.46	2311.22	32444.07
11581.09	2517.95	28800.89
3333.1	2641.38	44606.84

The following boxplots show the resistance, reactance, and impedance of each cooked chicken tissue compared to each other. Boxplots that are on a different horizontal level with each other would suggest that different values are measured from each type of tissue, and thus a difference between the electrical properties between the tissues.

The following boxplot, “Boxplot of Cooked Chicken Skin vs. Meat vs. Fat Resistance” shows the measured resistance data for cooked chicken. The average resistance measurements for skin, meat, and fat are: 8,366 Ohms, 2,687 Ohms, and 27,134 Ohms respectively.

Boxplot of Cooked Chicken Skin vs. Meat vs. Fat Resistance

The following boxplot, “Boxplot of Cooked Chicken Skin vs. Meat vs. Fat Reactance” shows the measured reactance data for cooked chicken. The average reactance measurements for skin, meat, and fat are: -1,178 Ohms, -725.1 Ohms, and -2,424 Ohms respectively.

Boxplot of Cooked Chicken Skin vs. Meat vs. Fat Reactance

The following boxplot, “Boxplot of Cooked Chicken Skin vs. Meat vs. Fat Impedance” shows the calculated impedance data for cooked chicken using Equation 2. The average impedance values for skin, meat, and fat are: 8,455 Ohms, 2,784.4 Ohms, and 27,273 Ohms respectively.

Boxplot of Cooked Chicken Skin vs. Meat vs. Fat Impedance

The following scatterplot, “Scatterplot of Cooked Chicken Skin vs. Meat vs. Fat Electrical Properties” show the measurements for each cooked chicken tissue sample on the same plot. Separate grouping of the measurements would suggest that there are fundamental differences of the electrical properties between the tissue types.

Scatterplot of Cooked Chicken Skin vs. Meat vs. Fat Electrical Properties

A One-Way ANOVA analysis was performed with Minitab on the cooked chicken impedance data. If by using the ANOVA analysis we can conclude that the tissues had statistically different electrical properties, we can conclude that the experimental setup was successful in detecting the different electrical properties of the tissues. We may also conclude that different types of tissues have statistically different electrical properties. The Minitab output, along with the ANOVA p-value, is shown below. A discussion about what conclusions can be reached, if any, from this output will be discussed in the “Conclusions” section.

One-way ANOVA: cooked skin impe, cooked meat impe, cooked fat imped

Source	DF	SS	MS	F	P
Factor	2	3286532094	1643266047	58.53	0.000
Error	27	758069173	28076636		
Total	29	4044601267			

S = 5299 R-Sq = 81.26% R-Sq(adj) = 79.87%

Level	N	Mean	StDev
cooked skin impedance	10	8455	3187
cooked meat impedance	10	2784	295
cooked fat impedance	10	27273	8601

Pooled StDev = 5299

Raw Chicken versus Cooked Chicken Results

The following scatterplots compare the electrical properties for each chicken tissue type between raw and cooked chicken. Again, separate groupings would suggest that the experimental system was able to determine a difference between the electrical properties that occurs when a biological tissue is cooked and the water content is lowered.

The following scatterplot, “Scatterplot of Chicken Skin Raw vs. Cooked Electrical Properties” shows the measured reactance and resistance of raw and cooked chicken skin on the same graph.

Scatterplot of Chicken Skin Raw vs. Cooked Electrical Properties

The following scatterplot, “Scatterplot of Chicken Meat Raw vs. Cooked Electrical Properties” shows the measured reactance and resistance of raw and cooked chicken meat on the same graph.

Scatterplot of Chicken Meat Raw vs. Cooked Electrical Properties

The following scatterplot, “Scatterplot of Chicken Fat Raw vs. Cooked Electrical Properties” shows the measured reactance and resistance of raw and cooked chicken fat on the same graph.

Scatterplot of Chicken Fat Raw vs. Cooked Electrical Properties

T-tests were performed using Minitab to compare the differences in raw and cooked chicken impedance results for each tissue type (skin, meat, and fat). T-tests are used to conclude whether or not two groups of data are statistically different from each other. T-tests are the equivalent of an ANOVA when data from only two set are being compared. If by using a T-test we can conclude that each group of tissue (raw vs. cooked) is statistically different from each other, we can conclude that the experimental setup was successful in detecting the difference in electrical properties between the tissues based on water content. We may also conclude that different types of tissues have statistically different electrical properties. The Minitab output for each comparison, along with the T-test p-value, is shown below. A discussion about what conclusions can be reached, if any, from this output will be discussed in the “Conclusions” section.

Two-Sample T-Test and CI: skin impedance, cooked skin impedance

Two-sample T for skin impedance vs cooked skin impedance

	N	Mean	StDev	SE Mean
skin impedance	10	3897	565	179
cooked skin impedance	10	8455	3187	1008

Difference = mu (skin impedance) - mu (cooked skin impedance)

Estimate for difference: -4559

95% CI for difference: (-6875, -2243)

T-Test of difference = 0 (vs not =): T-Value = -4.45 P-Value = 0.002 DF = 9

Two-Sample T-Test and CI: thigh meat impedance, cooked meat impedance

Two-sample T for thigh meat impedance vs cooked meat impedance

	N	Mean	StDev	SE Mean
thigh meat impedance	10	1802	295	93
cooked meat impedance	10	2784	295	93

Difference = mu (thigh meat impedance) - mu (cooked meat impedance)

Estimate for difference: -983

95% CI for difference: (-1261, -705)

T-Test of difference = 0 (vs not =): T-Value = -7.45 P-Value = 0.000 DF = 17

Two-Sample T-Test and CI: fat impedance, cooked fat impedance

Two-sample T for fat impedance vs cooked fat impedance

	N	Mean	StDev	SE Mean
fat impedance	10	2945	667	211
cooked fat impedance	10	27273	8601	2720

Difference = mu (fat impedance) - mu (cooked fat impedance)

Estimate for difference: -24328

95% CI for difference: (-30500, -18157)

T-Test of difference = 0 (vs not =): T-Value = -8.92 P-Value = 0.000 DF = 9

Human Skin Analogue Results

Table 15 contains the results from the electrical property measurements of EpiDermTM tissue sample from MatTek Corp. using the bipolar electrodes, electrode fixture, and ELVIS as outlined in the “Validation and Experimental Samples” section.

Table 15 – EpiDerm™ Data

Tissue Sample	Resistance (Ohms)	Reactance (Ohms)	Calculated Impedance (Ohms)
A	14350	-776.63	14371.00
A	15030	-939.91	15059.36
A	45330	-6460	45788.00
A	30770	-2370	30861.14
B	1920	-126.9	1924.19
B	2680	-123.05	2682.82
B	4440	-239.66	4446.46
B	6670	-668.26	6703.39
C	9640	-655.55	9662.26
C	13340	-2300	13536.82
C	7820	-359.14	7828.24
C	Not available	Not available	Not available
D	5900	-460.65	5917.96
D	6030	-449.12	6046.70
D	6210	-362.41	6220.57
D	6060	-423.76	6074.80
E	1500	-93.05	1502.88
E	1120	-109.88	1125.38
E	2140	-231.09	2152.44
E	1810	-168.81	1817.86
F	21540	-1610	21600.09
F	8820	-544.96	8836.82
F	12680	-651.23	12696.71
F	16790	-906.72	16814.47
G	1790	-123.77	1794.27
G	2110	-100.53	2112.39
G	2160	-93.26	2162.01
G	2150	-87.05	2151.76
H	2990	-124.27	2992.58
H	2340	-105.57	2342.38
H	2500	-109.27	2502.39
H	2210	-96.3	2212.10
I	2470	-114.54	2472.65
I	2390	-131.1	2393.59
I	2170	-118.93	2173.26
I	2180	-118.54	2183.22

Below is the scatterplot, “Scatterplot of EpiDerm™ Electrical Properties” that shows the measured electrical properties of the EpiDerm™ samples.

Scatterplot of EpiDerm™ Electrical Properties

Below is the Boxplot, “Boxplot of EpiDerm™ Impedance” that shows the calculated impedance values for each EpiDerm™ sample.

Boxplot of EpiDerm™ Impedance

As one can see, there appear to be some outliers in the data that are skewing the results. These data points (specifically samples: A, C, and F) have such a greater variance and average than the other samples, it can be assumed that errors occurred during the measurement of these samples. These samples have averages that are more than two standard deviations from the mean of the rest of the data. These errors could have be a result of the individual tissue samples drying out before they could be measured. Since the samples were used in previous, unrelated experiments before given to the author, it is rational to assume that they had been compromised. To stop these outliers from skewing the data and following analysis, they will be removed from the normal tissue dataset. The modified EpiDerm™ data that will be used for the remainder of this thesis is presented below in Table 16.

Table 16 – EpiDerm™ Data W/O Outliers

Tissue Sample W/O Outliers (Ohms)	Resistance W/O Outliers (Ohms)	Reactance W/O Outliers (Ohms)	Calculated Impedance W/O Outliers (Ohms)
B	1920	-126.9	1924.189079
B	2680	-123.05	2682.823383
B	4440	-239.66	4446.463417
B	6670	-668.26	6703.392531
D	5900	-460.65	5917.955595
D	6030	-449.12	6046.702306
D	6210	-362.41	6220.565972
D	6060	-423.76	6074.798148
E	1500	-93.05	1502.88333
E	1120	-109.88	1125.377099
E	2140	-231.09	2152.441077
E	1810	-168.81	1817.855004
G	1790	-123.77	1794.273951
G	2110	-100.53	2112.393496
G	2160	-93.26	2162.012356
G	2150	-87.05	2151.761535
H	2990	-124.27	2992.581333
H	2340	-105.57	2342.380205
H	2500	-109.27	2502.386847
H	2210	-96.3	2212.097125
I	2470	-114.54	2472.654325
I	2390	-131.1	2393.59295
I	2170	-118.93	2173.256622
I	2180	-118.54	2183.220495

Below is the scatterplot, “Scatterplot of EpiDerm™ W/O Outliers Electrical Properties” that shows the resistance and reactance of the EpiDerm™ samples with the outliers removed.

Scatterplot of EpiDerm™ W/O Outliers Electrical Properties

Below is the boxplot, “Boxplot of EpiDerm™ W/O Outliers Impedance” that shows the calculated impedance values of the EpiDerm™ samples with the outliers removed.

Boxplot of EpiDerm™ W/O Outliers Impedance

Please note: from this point on, the EpiDerm™ data will no longer be referred to with the qualifier “W/O outliers.”

Below in Table 17 are the results from the electrical property measurements of Melanoma™ tissue samples from MatTek Corp. using the bipolar electrodes, electrode fixture, and ELVIS as outlined in the “Validation and Experimental Samples” section.

Table 17 – Melanoma™ Data

Tissue Sample	Resistance (Ohms)	Reactance (Ohms)	Calculated Impedance (Ohms)
Mel 1	21600	-5810	22367.75
Mel 1	33480	-8800	34617.20
Mel 1	25360	-9390	27042.59
Mel 1	29890	-6940	30685.11
Mel 1	28120	-9480	29674.99
Mel 1	4710	-455.12	4731.94
Mel 1	6390	-1030	6472.48
Mel 1	24840	-10270	26879.33
Mel 2	36340	-14300	39052.34
Mel 2	4230	-303.68	4240.89
Mel 2	4990	-776.39	5050.04
Mel 2	5840	-754.28	5888.51
Mel 2	5400	-597.93	5433.00
Mel 2	5910	-926.34	5982.16
Mel 2	4580	-485.33	4605.64
Mel 2	4200	-352.69	4214.78
Mel 3	26760	-6290	27489.30
Mel 3	32940	-7010	33677.64
Mel 3	37160	-10810	38700.41
Mel 3	32750	-7360	33566.83
Mel 3	37480	-9140	38578.36
Mel 3	34780	-9020	35930.61
Mel 3	35610	-6690	36232.97
Mel 3	32520	-4330	32807.00
Mel 4	767.78	-25.25	768.20
Mel 4	887.54	-27.46	887.96
Mel 4	941.05	-36.56	941.76
Mel 4	1020	-35.98	1020.63
Mel 4	1190	-39	1190.64
Mel 4	1210	-46.54	1210.89
Mel 4	1340	-61.87	1341.43
Mel 4	1630	-102.43	1633.22
Mel 5	1190	-86.14	1193.11
Mel 5	1280	-95.35	1283.55
Mel 5	1460	-121.03	1465.01
Mel 5	1320	-100.92	1323.85
Mel 5	1350	-100.07	1353.70
Mel 5	1310	-104.23	1314.14
Mel 5	1370	-113.21	1374.67
Mel 5	1450	-126.97	1455.55
Mel 6	5040	-659.75	5083.00
Mel 6	4770	-580.54	4805.20
Mel 6	11930	-3830	12529.72
Mel 6	11180	-4180	11935.86
Mel 6	11410	-4580	12294.90
Mel 6	5920	-961.16	5997.52
Mel 6	5560	-858.22	5625.85
Mel 6	5080	-742.57	5133.99

Below is the scatterplot, “Scatterplot of Melanoma™ Electrical Properties” that shows the measured electrical properties of the Melanoma™ samples.

Scatterplot of Melanoma™ Electrical Properties

Below is the Boxplot, “Boxplot of EpiDerm™ Impedance” that shows the calculated impedance values for each EpiDerm™ sample.

Boxplot of Melanoma™ Impedance

Comparison of MelanomaTM and EpiDermTM

For the following graphs and analysis, the data recorded from the measurement of MelanomaTM and EpiDermTM were added to the same Minitab file. This allowed comparisons between the two sets of data. Comparing the EpiDermTM and MelanomaTM data is the primary test performed for this thesis. A statistical difference between the two sets of data would suggest that melanoma tissue can be distinguished from normal tissue.

Below is the scatterplot, “Scatterplot of EpiDermTM and MelanomaTM Electrical Properties” which shows the measured resistance and reactance values of the two different tissue types on the same graph.

Scatterplot of EpiDermTM and MelanomaTM Electrical Properties

Below is the boxplot, “Boxplot of EpiDermTM and MelanomaTM Impedance” which shows the measured calculated impedance values of the two different tissue types on the same graph. The average impedance for EpiDermTM and MelanomaTM are: 3,088 Ohms and 12,856 Ohms respectively.

Boxplot of EpiDerm™ and Melanoma™ Impedance

A One-Way ANOVA analysis was performed with Minitab on the EpiDerm™ and Melanoma™ data. If by using the ANOVA analysis we can conclude that the tissues had statistically different electrical properties, we can conclude that the experimental setup was successful in detecting the different electrical properties of the tissues. We may also conclude that different types of tissues have statistically different electrical properties. The Minitab output, along with the ANOVA p-value, is shown below. A discussion about what conclusions can be reached, if any, from this output will be discussed in the “Conclusions” section.

One-way ANOVA: Impedance (Ohms) versus Sample

Source	DF	SS	MS	F	P
Sample	1	1526660835	1526660835	11.64	0.001
Error	70	9184007210	131200103		
Total	71	10710668045			

S = 11454 R-Sq = 14.25%

R-Sq(adj) = 13.03%
Individual 95% CIs For Mean Based on
Pooled StDev

Level	N	Mean	StDev
EpiDerm	24	3088	1736
Melanoma	48	12856	13926

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(-----*-----)
                                         (-----*-----)
-----+-----+-----+-----+-----+-----+-----+-----+-----+-----+
      0       5000      10000      15000

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Pooled StDev = 11454

Conclusions

The following sections will discuss the data that was gathered from the experiments presented earlier in Table 3 through Table 17. When possible, the author will come to a conclusion about what the data means in relation to the purpose of the experiment and the objective of this thesis: to build a database of the electrical properties of healthy and cancerous tissue, and determine if there are statistical differences between the two types.

ELVIS Validation Discussion

The resistance and capacitance data gathered during the validation of the ELVIS data acquisition system was presented in Tables 3 and 4. It is important that ELVIS accurately and precisely measured resistance and capacitance over a range of values that is possible with biologic tissues, since the system would be later used to measure chicken tissue and human skin analogues.

From the data in Table 3, ELVIS accurately measured the resistance of the resistors tested (within a 5% margin of error that was reported by the manufactures) between the values of 100 to 100k Ohms. If the measured values of resistance of the different tissue values fell within this range, we can conclude that the ELVIS system can accurately measure resistance. The measured resistance values for raw chicken fell between 1k and 5k Ohms, the measured resistance values of cooked chicken fell between 2k and 50k Ohms, and measured resistance values of the EpiDermTM and MelanomaTM tissue analogues from MatTek Corp. fell between 1k and 40k Ohms. Since all the measured tissue resistance values fell within the accurate range for ELVIS, we can be

confident in concluding that the ELVIS system accurately reported the resistance measurements that were inputted during these experiments.

Looking at the ELVIS validation data for capacitance in Table 4, one can see the ELVIS system accurately measured the reactance of the capacitors tested (within a 5% margin of error that was reported by the manufacturers) approximately between the values of -100 and -16k Ohms (remember reactance is on the imaginary plane for impedance, and a negative value for reactance converts to a positive value of capacitance. See Equation 3). If the measured values of reactance of the different tissue values fell within this range, we can conclude that the ELVIS system can accurately measure reactance, and therefore capacitance. The measured reactance values for raw chicken fell between -12 and -600 Ohms (with only 2 measurements out of 30 outside of the acceptable range), the measured reactance values of cooked chicken fell between -600 and -5.5k Ohms, and the measured reactance values of the EpiDermTM and MelanomaTM tissue analogues from MatTek Corp. fell between -100 and -14k Ohms (with only 3 measurements out of 60 outside the acceptable range for the entire dataset). Since most of the measured tissue reactance values fell within the accurate range for the ELVIS system, one can be confident in concluding that ELVIS accurately reported the reactance measurements that were inputted during these experiments.

Since the possible measured values of resistance and reactance both fall in the range of what is accurately measured by the ELVIS data acquisition system, one can conclude that conclusions made about impedance (which is a combination of resistance and reactance. See Equation 1) may be made from the data gathered using ELVIS and that the data is valid.

Bipolar Electrode and Electrode Fixture Validation Discussion

The resistance and capacitance data gathered during the validation of the bipolar electrodes and electrode fixture was presented in Tables 5 and 6. It is important that the bipolar electrodes and electrode fixture did not cause the measured electrical properties to be skewed. If the bipolar electrode and electrode fixture did not affect the electrical properties measured by ELVIS, the resistance and capacitance values reported by ELVIS should be similar to the listed values of the resistors and capacitors used during the ELVIS validation.

From the bipolar electrode and electrode fixture validation data presented in Table 5, ELVIS accurately measured the resistance of resistors (within a 5% margin of error that was reported by the manufactures) between the values of 100 to 100k Ohms (note that this is the same range for the ELVIS validation above). Since the addition of using the bipolar electrodes and electrode fixture did not affect the range of resistance values that the ELVIS system accurately reported, one can conclude that the bipolar electrodes and electrode fixture did not significantly affect the resistance measurements.

From the bipolar electrode and electrode fixture validation data presented in Table 6, ELVIS accurately measured the reactance of capacitors (within a 5% margin of error that was reported by the manufactures) between the values of approximately -100 and -1.6k Ohms (note that this is the same range for the ELVIS validation above). Since the addition of using the bipolar electrodes and electrode fixture did not affect the range of reactance values that the ELVIS system accurately reported, one can conclude that the bipolar electrodes and electrode fixture did not significantly affect the reactance measurements.

Since the bipolar electrodes and electrode fixture did not affect the range of accurate values of resistance and reactance that is measured by the ELVIS data acquisition system, one can conclude that conclusions about impedance may be made from the data gathered using ELVIS and that the data is valid.

Raw Chicken Discussion

The resistance and reactance data for the raw chicken experiments was presented in Tables 7 through 10. The purpose of these measurements was to do a preliminary investigation of whether or not the experimental setup could distinguish different raw chicken tissues types based only on their electrical properties. If the system was able to measure differences in the electrical properties of the different raw chicken tissue types (skin, meat, and fat), separate groupings of the resistance and reactance measurements should be visible, and there should be a statistical difference between the average impedance for each group.

By visually examining the raw chicken data presented in the boxplots of raw chicken and the stated mean averages in the “Data” section, one can see that the resistance measurements for each tissue type are grouped separately. The average resistance for each tissue type is different, and there is little overlap between the first and third quartiles for each tissue type. Examining the boxplots for reactance, one can see that the measured reactance for skin and meat are similar, but the reactance for fat is different for both. When the impedance is calculated for the tissue types using Equation 2, resistance dominates and the impedance measurements are different for each tissue sample. Examining the scatterplot of raw chicken data confirms that the electrical properties are separately grouped.

Although the raw chicken data seems to show visually that the experimental setup was able to find differences in the electrical properties of the three tissue types, it is important to make sure that any difference is statistically significant, and not due to random variations. To illustrate that the differences between the tissue types are statistically significant, an ANOVA test was performed on the impedance values using Minitab. The null hypothesis was chosen to be that there is no difference between the mean impedance values and the alternative hypothesis was chosen to be that there is a difference between at least one impedance mean. A significance value of 0.05 (meaning there will be a 5% chance that the conclusion is wrong) was also chosen. Minitab calculated a p-value of 0.000. Since $0.000 < 0.05$, the null hypothesis is rejected and the alternative hypothesis is concluded to be true.

It makes sense that the different raw chicken tissues have different impedance values. Skin, muscle (or meat), and fat are all different structurally. The different structures cause differences in the ability of ions to flow through the tissues. Also, some tissues may have more ions and water available to transport an electrical current.

From this analysis, one can conclude that a statistical difference in the impedance values between the raw chicken tissue types was recorded by the experimental setup and the system was able to distinguish between tissues. This means that it is possible to differentiate between tissues by examining their electrical properties.

Cooked Chicken Discussion

The resistance and reactance data for the cooked chicken experiments was presented in Tables 11 through 14. The purpose of these measurements was to do a secondary investigation of whether or not the experimental setup could distinguish different tissues types based only on their electrical properties, and also to create a database of cooked tissue measurements to later compare with the raw chicken tissue data (see “Raw Chicken versus Cooked Chicken Discussion” section). A secondary purpose for cooking the chicken tissue was to simulate tissue with lower water content and examine how this affects the electrical properties (this discussion will take place in the next section, “Raw Chicken versus Cooked Chicken Discussion”). If the system was able to measure differences in the electrical properties of the different cooked chicken tissue types (skin, meat, and fat), separate groupings of the resistance and reactance measurements should be visible, and there should be a statistical difference between the average impedance for each group.

By visually examining the cooked chicken data presented in the boxplots for cooked chicken, one can see that the resistance measurements for each tissue type are grouped separately. The mean average resistance for each tissue type is different, and there is no overlap between the first and third quartiles for each tissue type. Examining the boxplots for reactance, one can see that there is also a difference in the reactance measurements for each tissue. When the impedance is calculated for the tissue types using Equation 2, the impedance measurements are different for each tissue sample. Examining the scatterplot of cooked chicken data confirms that the electrical properties are grouped separately. It is interesting to note the different amounts of variance between

the tissue types. The measurements for meat are tightly grouped and have a small variance, the measurements for skin have a larger grouping, and the measurements for fat have a very large grouping. This is probably due to the fact that the chicken meat cooked the most uniformly, with an even distribution of water content throughout the tissue. The skin and fat may not have cooked as uniformly, and contained areas of both high and low water content.

Although the cooked chicken data seems to show visually that the experimental setup was able to find differences in the electrical properties of the three tissue types, it is important to make sure that any difference is statistically significant, and not due to random variations. To show that the difference between tissue types is statistically significant, an ANOVA test was performed on the impedance values using Minitab. The null hypothesis was chosen to be that there is no difference between the mean impedance values and the alternative hypothesis was chosen to be that there is a difference between at least one impedance mean. A significance value of 0.05 (meaning there will be a 5% chance that the conclusion is wrong) was also chosen. Minitab calculated a p-value of 0.000. Since $0.000 < 0.05$, the null hypothesis is rejected and the alternative hypothesis is concluded to be true.

From this analysis, one can conclude that a statistical difference in the impedance values between the cooked chicken tissue types was recorded by the experimental setup and the system was able to distinguish between tissues. This reinforces the previous conclusion found during the raw chicken experiments that the experimental system was able to distinguish the differences between tissues by examining only the electrical properties of the tissue.

Raw Chicken versus Cooked Chicken Discussion

The conclusion has been reached that the experimental setup was able to detect differences in the electrical properties between different tissue types for both raw and cooked chicken. To even further validate the fact that the experimental setup is able to distinguish between tissues, the electrical property data for each tissue type will be compared against each other for the raw and cooked chicken groups. If there is a statistical difference, one can conclude that the setup was able to detect a difference in the electrical properties of a tissue type based on the water content of the tissue (cooking the tissue was done in order to remove water content), for the same type of tissue. This is important because one of the primary differences between normal and cancerous tissue is water content. If a diagnosis system based on electrical properties is going to be able to detect the difference between normal and cancerous tissue, it will have to do so at least in part by detecting a difference in water content.

Scatterplots for the electrical properties of each tissue type (for raw vs. cooked) were presented above. By visually inspecting these graphs, one can see that there seems to be separate groupings between raw and cooked tissue. This suggests that cooking tissue causes a change in electrical properties due to a loss of water content in the tissue.

To show that there is a statistical difference between the raw and cooked chicken impedance measurements for each tissue type, 2 Sample Student's T-tests were performed for each tissue type (2 Sample Student's T-tests are the same as ANOVA tests when comparing data from two samples). The null and alternative hypotheses for each grouping were chosen to be that there is no difference between the impedance means and that there is a difference between the impedance means, respectively. A significance

value of 0.05 (meaning there is only a 5% chance the conclusion is wrong) was chosen.

Minitab calculated the following p-values:

Table 18 – P Values

Test	P-Value
Raw vs. Cooked Skin	0.002
Raw vs. Cooked Meat	0.000
Raw vs. Cooked Fat	0.000

Since $p\text{-value} < 0.05$ for each test, each null hypothesis is rejected and each alternative hypothesis is concluded to be true.

From the analysis, we can conclude there is a statistical difference of the electrical properties between raw and cooked for each tissue type. Thus, we can conclude that the experimental setup was able to detect differences in the electrical properties of a tissue based on a change in water content. This further reinforces the conclusion that the experimental setup is capable of detecting different tissue types by examining the electrical properties of the tissues. Since these methods have worked to distinguish different chicken tissue types, it may be possible that they can distinguish between healthy and melanoma tissue.

EpiDermTM and MelanomaTM Discussion

Now that it has been shown that the experimental methods can detect differences in tissue via measured electrical properties, what conclusions, if any, can one come to about the human skin analogues data? The data gathered from the measurement of EpiDermTM and MelanomaTM skin analogues was presented in Tables 15 through 17. The purpose of these measurements was to determine if there is a statistical difference between the two types. If there is, melanoma could be diagnosed in the future by

measuring the electrical properties of the suspected tumor and comparing the results to known ranges for healthy and cancerous skin.

By visually examining the scatterplots of resistance and reactance for EpiDermTM, one can see that a large amount of the data points are grouped together, which suggest reliable measurement. By visually examining the scatterplot and boxplot of the MelanomaTM data, one can see that there is one group of data points that is tightly grouped, while other data points are widely scattered. However, the data for each tissue type is not meant to be examined on its own, they should be compared with each other. When the data from EpiDermTM and MelanomaTM is put on the same scatterplot, one can see that the tight grouping of the MelanomaTM data lies directly over the EpiDermTM data, while the other grouping of MelanomaTM data is distinctly separate.

The question arises: why are there two separate groupings of the MelanomaTM data, and what can be concluded from it? It has already been shown that the measurements made by the ELVIS system, bipolar electrode, and electrode fixture system are accurate, so it unlikely that the two groupings is due to measurement error. Also, the large number of data points in the second MelanomaTM group (18 out of 48 total data points) suggests that they are not a random occurrence, but rather an actual property of the MelanomaTM samples. The main difference between the EpiDermTM and MelanomaTM samples is that the MelanomaTM samples have melanoma cells (see the “Validation and Experimental Tissues” section). It is possible that the melanoma was not evenly distributed throughout the tissue samples. It is important to remember that the tissue samples were rotated 45 degrees between each measurement, meaning a different portion of the sample was recorded for each measurement. We can therefore confidently

assume that the two distinct groupings of the MelanomaTM data was caused by the electrodes sometimes measuring the normal tissue cells (which were the same as the EpiDermTM samples), while at other times, the measurements were affected by the melanoma cells. Now that the reason for the separate groupings of the MelanomaTM data has been found, we can investigate if whether or not there is a statistical difference between the EpiDermTM and MelanomaTM data.

To show that the difference between the EpiDermTM and MelanomaTM data is statistically significant, an ANOVA test was performed on the impedance values using Minitab. The null hypothesis was chosen to be that there is no difference between the mean impedance values and the alternative hypothesis was chosen to be that there is a difference between at least one impedance mean. A significance value of 0.05 (meaning there will be a 5% chance that the conclusion is wrong) was also chosen. Minitab calculated a p-value of 0.001. Since $0.001 < 0.05$, the null hypothesis is rejected and the alternative hypothesis is concluded to be true.

Using Minitab, it has been shown that there is a statistical difference between the electrical properties of EpiDermTM and MelanomaTM data measured by the experimental setup.

It is interesting to note that the resistance of the MelanomaTM samples where cancer was detected the resistance was higher than the non-cancerous EpiDermTM samples. This trend conflicts with the previous research done by Rigaud, B, et al (see the “Electrical Properties of Skin” section). A possible explanation for this discrepancy is that Rigaud performed his measurements and analysis on in vivo samples, whereas the data collected for this thesis used in vitro samples.

Final Conclusions

Using the gathered data and statistical analysis, the ELVIS data acquisition system, AgCl bipolar electrodes, and electrode fixture have been validated and can be used to reliably and accurately measure a material's electrical properties. Once the validity of the experimental system was established, it was shown that the system could detect significant differences in the electrical properties of different chicken tissue types. It was shown that the system could also distinguish between the same tissue types when the water content of one sample had been lowered. Finally, it was shown that the system was able to distinguish differences between healthy and cancerous human skin tissue analogues (when enough data points are taken so that the melanoma cells can be measured). This means that it may be possible to diagnose melanoma by examination of the electrical properties of the suspected tissue.

Now that it has been established that this type of system can distinguish between normal and melanoma human skin analogues, the next step would be to test this system on actual human skin samples, in vitro and then in vivo. Although the skin analogue data provided clear differences between healthy and cancerous tissue, the differences for actual human tissue may not be as great. Human skin is more complex (the dermis contains nerve, blood vessels, and hair follicles), which may make the differences between healthy and cancerous skin not as significant. However, this does not mean that this method cannot be used to diagnose melanoma in vivo. As long as a database with a large amount of data points is constructed, and enough data points of the suspected tumor are taken, a statistical conclusion and diagnosis could still be made.

The main goal of this thesis has been achieved; measurable differences in the electrical properties of healthy and cancerous tissue have been recorded. A larger and more complete database of healthy and cancerous tissue electrical properties can now be established, and ranges for each tissue can be defined. Then, when a new measurement is taken of a suspected tumor, the new data point can be compared to known values for healthy and cancerous skin, and a diagnosis can be made.

Next Steps: Diagnose and Treat Melanoma

The following sections are meant to be suggestions for future research and experimentation to build on the work of this thesis. The author believes that the research and data gathered for this thesis can be expanded and further investigated in the areas of in-vivo cancer diagnosis and treatment. Since the diagnosis method of melanoma has already been thoroughly examined, the following sections will focus on a novel melanoma treatment method using radiofrequency tissue ablation. How such a device might look and function will be discussed along with previous uses of radiofrequency tissue ablation to treat cancer. The actual building of such a device is out of the scope for this thesis, and will be reserved for a student at a later time. The purpose of the following sections is to facilitate the next steps in the project. Further research, testing, and analysis will need to be performed to continue this work.

Tissue Ablation

Introduction to Tissue Ablation

Since the one of goals of this thesis was to also investigate a method of skin cancer treatment, radiofrequency tissue ablation is also investigated. Radiofrequency tissue ablation uses an alternating current delivered to the target tissue to cause localized heating of the tissue, which destroys a small volume of tissue without affecting other surrounding structures beyond the treatment site [8]. Radiofrequency tissue ablation has already been approved by the Food and Drug Administration to treat some diseases such as: liver cancer, kidney cancer, and lung tumors [1]. It is a preferred method of treatment when a patient has co-morbidities or is not healthy enough for a more invasive treatment

[28]. The following sections will provide information on: how radiofrequency tissue ablation works, how it treats cancer, and also previous studies where radiofrequency tissue ablation was used to treat liver and breast cancer. No previous uses of radiofrequency tissue ablation to treat skin cancer were found in the literature.

What is Tissue Ablation?

Ablation is a term that is used to describe a procedure performed on the body to destroy diseased or damaged structures [8]. Ablation can use heat, cold, or chemicals to destroy tissue. This thesis will focus on radiofrequency tissue ablation, which uses the direct application of electrical energy to a specific area in an attempt to cause thermal injury and necrosis of the tissue [29].

How Radiofrequency Tissue Ablation Works

Radiofrequency tissue ablation creates heat in the targeted tissue by applying a current to the tissue using electrodes. A generator creates a sinusoidal alternating electrical current. The signal is generally in the 375 kHz to 500 kHz range, which corresponds to the radiofrequency area of the electromagnetic spectrum. Most devices that are currently used are monopolar. This means that a single electrode delivers the alternating current signal to the tissue, and the signal returns to the generator through a large grounding pad attached to the patient [29]. The current must travel through the patient in order to complete the circuit. For devices that are bipolar, the current is delivered to the tissue using an electrode and returns to the generator via a nearby electrode.

The treatment thermal heat is generated by friction. As the alternating current oscillates back and forth between the electrode and grounding pad or other electrode, charged ions and water molecules in the tissue in the current path vibrate back and forth trying to follow the oscillation of the current. This ionic agitation leads to frictional heating of the tissue [21]. Thermal injury of the tissue starts at 41 degrees Celsius, and necrosis of cells occurs at 46 degrees Celsius [19]. Necrosis occurs because of the denaturing of proteins vital to cell life and the loss of intracellular fluid [21].

Radiofrequency Tissue Ablation and Cancer

Radiofrequency tissue ablation is considered a reliable treatment method to destroy some types of tumors because it can be used to cause cell necrosis in a small, targeted area without affecting structures beyond the treatment site [1]. Radiofrequency tissue ablation is considered safer than other ablation and treatment methods because excess energy is absorbed in nearby tissues as simple heat [8]. Radiofrequency tissue ablation treats cancer by killing the cancerous cells, which stops the ability of the cells to replicate and spread. Radiofrequency tissue ablation also has the ability to kill healthy cells. To stop the treatment from damaging healthy tissue, the treatment must be monitored by the doctor or generator supplying the electrical current.

As the current is applied to a tumor, changes occur in the tissue. A decrease in the ability of the soft tissue to conduct current occurs (see the previous “Practical Observations” section). This leads to an increase in resistance seen by the generator. This allows for the progress of the treatment to be monitored by monitoring the increase in impedance [21].

The two types of cancer that are often treated with radiofrequency tissue ablation are liver and breast cancer. The following section will provide information on studies conducted using radiofrequency tissue ablation on these cancers. Again, it is important to note that no previous investigations into using radiofrequency tissue ablation for the treatment of skin cancer were found.

Liver Cancer

In a 1998 study entitled “Ablation of Liver Tumors Using Percutaneous RF Therapy,” Goldberg, Gazelle, et al. treated 29 patients who had a total of 44 hepatic metastases. The purpose of the study was to determine what, if any, effects internally cooled electrodes had on the volume of ablated tissue.

The researchers used a 500 kHz monopolar generator which not only provided output energy but also measured output to the tissue, tissue impedance, and electrode tip temperature. The current supplied by the generator was delivered to the liver metastases with 18 gauge needles that were insulated except for the last 1-3 inches. The researchers' experimental group of electrodes was internally cooled, where cooled perfusate was circulated through the center of the electrode. The purpose of internally cooled electrodes is to lower the temperature of the tissue at the tip of the electrode, in an attempt to prevent burning of the tissue and to increase the volume of the ablated tissue. The tip of the electrode was placed directly in the center of the tumors under the guidance of ultrasound or CT scan.

After performing the treatment, the volume of ablated tissue was measured with a CT scan. The volume of ablated tissue with traditional electrodes was limited to an average of 1.6 cm diameter (see Figure 26 [30]). To create a larger volume with standard

electrodes, the power to the tissue must be increased which results in tissue vaporization and charring. Internally cooled electrodes however can ablate an average volume of 2.4 cm diameter. This is because since the electrode tip is cooled, more energy can be deposited into the tissue [31]. The researchers also noticed that the volume of ablated tissue is affected by the presence of large blood vessels in the vicinity of the treatment site. The flow of blood acts as a heat sink and keeps the tissue from reaching the required temperature for necrosis.

Figure 26 – Radiofrequency Ablation of the Liver

An example of liver tissue after treatment with radiofrequency tissue ablation

Overall, the researchers were able to create volumes of necrosis of 1.5 to 4.5 cm in diameter. Of the 29 patients treated, 94% were alive after 12 months. 50% of the patients were still disease free after 12 months [30].

Other research by Solbiati, et al., also showed that radiofrequency tissue ablation could be used to effectively treat liver cancer. Solbiati's group used ultrasound imaging techniques to guide the ablation electrode to the tumor [32].

Breast Cancer

In the 1999 study entitled, “Radiofrequency Ablation of Breast Cancer,” Jeffrey, Birdwell, et al, treated 5 women with breast cancer with radiofrequency energy right before the resection of their tumors. They were attempting to determine if radiofrequency tissue ablation is an acceptable treatment method for breast cancer.

The patients were treated with a 15 gauge multiple needle electrode for 30 minutes using a monopolar generator. The generator continuously monitored the power applied to the tissue and the impedance seen by the electrodes. As the treatment progressed, the impedance increased by a factor of ten and the power declined. The researchers used this phenomenon to monitor the treatment. After the treatment, the breasts were resected and the tumor was examined with an enzyme histochemical analysis. The researchers noticed that the ablated tissue appeared the same to the naked eye as the non-treated tissue. Under the histochemical analysis however, there was a clear and defined line separating treated and non-treated tissue.

The researchers found evidence of cell death in all patients. The enzyme histochemical analysis showed that the radiofrequency tissue ablation caused a volume of necrosis with a diameter of 0.8 cm to 1.8 cm. From these results, the researchers were able to conclude that radiofrequency tissue ablation of breast cancer results in cell death [19].

Other research by Livraghi, et al., has also shown that radiofrequency tissue ablation can be an effective treatment method for breast cancer [33].

Skin Cancer and Radiofrequency Tissue Ablation

Currently, there are no published papers on the use of radiofrequency tissue ablation to treat skin cancer. The author believes that this lack of previous treatment or experimentation allows for a good opportunity to investigate the ability of radiofrequency tissue ablation to treat skin cancer. Also, since radiofrequency tissue ablation has been shown to be effective for treating other types of cancer, there is reason to believe that it would also be effective for treating skin cancer.

Bipolar versus Monopolar Electrodes

Tissue ablations that are currently used employ monopolar electrode systems. In a monopolar electrode system, the alternating current from the generator is delivered to the tissue by a single electrode (although this single electrode may have multiple leads). This electrode is inserted through the skin and directly into the tissue and placed in the center of the area that is to be treated. A grounding pad is placed on the thigh or back of the patient. The therapeutic current disperses through the body before traveling to the grounding pad to complete the electrical circuit. Since the current is delivered by one electrode and spreads out from that electrode toward the grounding pad, the volume of ablated tissue spreads out in a spherical fashion from the tip of the electrode. The longer the current is applied, and the stronger the current, the larger the treatment volume. Because the treatment volume of ablated tissue spreads in a spherical fashion and evenly from the electrode, it is difficult to control what tissue is ablated besides by controlling the size of the sphere.

Another type of tissue ablation method uses bipolar electrodes. In a bipolar electrode system, the alternating current from the generator is delivered to the tissue by

two closely spaced electrodes. The current alternates back and forth between the two electrodes, instead of returning to grounding pad. Because the treatment current only travels between two electrodes, only the tissue that is between the two electrodes is ablated. This allows for much greater control over the ablated tissue. The volume of ablated tissue depends on the amount of time the current is applied, the strength of the current, and the configuration of the electrodes. Having this greater controls allows for some structures to be treated, while other structures nearby are not treated.

The author believes that a bipolar electrode system should be used when treating skin cancer with radiofrequency tissue ablation. Since melanoma lesions are relatively small compared to other cancers (<4 mm diameter), bipolar electrodes would allow greater control to ensure that only cancerous tissue is ablated and healthy tissue is not. The following sections will go into greater depth on how this can be achieved.

How Tissue Ablation will be used to treat Skin Cancer

The following sections will outline how the author believes skin cancer can be diagnosed and treated using a bipolar electrode system. These sections will include information on: the difference between healthy and cancerous tissue and how this may allow for a new method of cancer diagnosis, the electrode setup for such a device, and the generator which will provide the treatment current. Please note that the following sections are the opinions of the author, and will need to be validated by future experimentation and research.

Difference between Healthy and Cancerous Tissue

The differences between healthy tissue and cancerous tissue will play a large role in the treatment of skin cancer using tissue ablation. It has been established by this thesis (see the “Conclusions” section) that a difference between the impedance of normal tissue and tissue containing melanoma cells is measurable. This fact will not only be important in the diagnosis of a tumor, but it can also be used to facilitate the treatment of the tumor using tissue ablation.

The data gathered for this thesis established the fact that melanoma tissue has higher impedance than normal tissue. This fact can be used to diagnose and selectively treat only tissue that matches the criteria of melanoma tissue. To do this, a “scan” of the electrical impedance of the suspected tumor and the surrounded area can be made using a device and electrode setup that is described below. A model of the scanned tissue can be made in a computer and the area of cancer that needs treatment can be identified and highlighted. Once the specific area of skin that needs treatment has been identified, the tissue ablation treatment can progress. This can be done by selectively targeting the highlighted cancerous areas. By only treating the cancerous skin, the surrounding healthy tissue can be left alone. This will decrease scarring and healing times by minimizing the treatment area.

Electrodes

The electrodes of the ablation device should be configured in a way that will allow for the most control over the treatment area. Using a matrix of bipolar electrodes will allow the system to analyze skin electrical properties and to map healthy and cancerous tissue, and then apply the treatment electrical current only to the tissue that has

been determined to be cancerous. A matrix of electrodes will allow the system to analyze and treat a two dimensional area of tissue, instead of just a one dimensional area between two point electrodes. Measurements of the skin's electrical properties will be measured between each electrode, creating a “map” of the scanned tissue. The data will be processed by a computer in the generator to determine the area of cancerous tissue. Once this area has been determined, the generator can supply the electrical current to the electrodes that touch the area of cancerous tissue. This will cause the cancerous tissue to be ablated, while leaving tissue that has been determined to be healthy untreated.

The electrodes will be bipolar. This means that the electrical current for both diagnosis and treatment will only travel from one electrode to another on the device. There will not be a grounding pad. Bipolar electrodes will allow the treatment area to be much more controlled because the treatment will only be applied between electrodes, instead of spreading out from one electrode toward the grounding pad.

The density of electrodes used in the matrix will affect the resolution of the system to both diagnose melanoma and the area that can be treated with radiofrequency tissue ablation. In other words, the more electrodes per unit of area, the more accurate the system will be able to build a model of the cancerous tissue and the better it will be at applying a treatment current to only the identified tissue. The resolution should be small enough to detect the smallest structures of skin cancer that can be detected through other diagnosis techniques. The optimum electrode density will have to be investigated in later experimentations.

The electrodes will be made of an AgCl compound. The reasons to use this material are the same for why AgCl was used to gather the data earlier in this thesis.

AgCl does not create a charge density around the electrode. A charge density occurs when ions in the sample are attracted to the electrode due to the alternating current. These ions accumulate and interfere with the measurements at the electrode-tissue interface. AgCl electrodes also do not exhibit polarization when a voltage is applied.

Generator

To create the electrical signal that is needed to ablate the cancerous tissue, an electrical generator is needed. The generator creates the electrical signal with the appropriate voltage and frequency. The signal travels from the generator to the electrodes via conductive wires.

Certain signal properties are often used for the ablation of human tissue. A generator used for tissue ablation will have an output power of approximately 100 Watts and a frequency of 490 kHz. This frequency corresponds to the radiofrequency section of the electromagnetic spectrum. These power and frequency values correspond to previous uses of Radiofrequency tissue ablation to treat other types of cancers.

Generators also have the ability to monitor the progress of the treatment while the treatment signal is being applied. The generators accomplish this by monitoring the impedance of the tissue at the treatment site. As the tissue is treated, the impedance measured by the generator changes. When the impedance reaches a determined level that corresponds to successful tissue ablation, the generator will automatically stop the treatment. This capability allows treatment to be completed without the possibility of over treating the tissue, which could lead to burning.

The generator can also contain the necessary computer hardware and software to build the tissue model from the diagnosis data. This model is used to identify the

cancerous tissue that needs treatment. Once this tissue has been identified, the computer will program the generator to only apply the treatment current through the electrodes that are over the melanoma.

Summary of Future Work

The fundamentals of radiofrequency tissue ablation, the previous uses of this treatment method to treat cancer, and the possible look of a system that could be used to treat melanoma have been outlined. A radiofrequency tissue ablation system could be used alongside a diagnosis method that distinguishes between normal and cancerous skin by examining the electrical properties of the tissue to treat melanoma. Such a system would have the benefits of being less invasive to the patient and make more accurate diagnoses over current diagnosis and treatment methods.

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Appendix

Drawing of electrode fixture, labeled as “Part 1” in “Electrode Fixture” section.

The drawing includes the following views and dimensions:

- Isometric View:** Shows the 3D shape of the doughnut.
- Top View:** A circle with an outer diameter of $\phi .50$ and an inner hole diameter of $\phi .20$. Section lines A-A are indicated.
- Section A-A:** A cross-sectional view showing the thickness of the doughnut as $.11$. The inner hole is also shown in section.
- Front View:** A rectangle with a height of $.50$ and a width of $.50$.

Section A-A SCALE 4 : 1

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Assembly drawing of electrode fixture.

[illegible]