A COMPREHENSIVE STUDY OF THE EFFECTS OF CHEMOTHERAPY
ON FRICTION RIDGE DETAIL

By

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Chapter 1—Introduction

**Exclusivity of Friction Ridge Skin**

Fingerprint impressions are exclusive to each individual, allowing for an efficient mode of identification. In a medical context, categorically, oncology, friction ridge degradation has the capacity to contribute to reduction of patient quality of life. As patients undergoing chemotherapy administration must manage unfavorable side effects as a result of their condition, determining the factors associated with ridge degradation in response to chemotherapy drugs may alert medical professionals to needed adjustment of treatment plans or, in the very least, provide essential information for patient notification. As friction ridge skin is a characteristic method of identification, degradation would lessen both the exclusivity and efficiency of this mode of recognition, causing significant issues for patients who must provide identification for business or traveling purposes. Therefore, the proposed study seeks to validate prior longitudinal studies of chemotherapy drugs associated with print degradation as well as determine the effects of additional chemotherapy drugs known to also cause skin abnormalities. This allows for comparison between degradation levels in relation to drug classes and treatment cycles. Characteristics associated with reduced ridge visibility, including age, weight, height, race, and physical activities are useful informative data that may promote research implications. Higher levels of degradation in individuals of a certain age or race could call for further analysis of genetic factors by which individuals are pre-disposed to print deterioration in response to chemotherapy drugs.

**Prior Research Initiatives**

Various research studies attest that a chemotherapy drug, capecitabine, is known to cause fingerprint loss. The majority of articles were written in response to individuals who were
discovered to have no friction skin ridge detail when asked to provide identification for traveling purposes.\textsuperscript{1,2} After subsequent investigation into each individual, all were chemotherapy patients who exhibited side effects of this singular chemotherapy drug. Building off of these reports, a longitudinal study was conducted in order to isolate the effects of capecitabine on a singular patient throughout the treatment process. Research on this front attested to a directional relationship between capecitabine and ridge degradation, with ridge detail returning to relatively normal levels approximately 65 days following cessation of treatment.\textsuperscript{3}

**Distinctiveness of Study and Brief Methodology**

The intent of this proposed study is to further the previous research initiative by verifying the longitudinal study and incorporating additional chemotherapy drugs known to cause skin abnormalities. Data collected will substantially contribute to the existing knowledge base, providing for additional factors for medical consideration when formulating treatment plans and informing the patient on potential side effects. Data will be collected from chemotherapy patients who have been prescribed the aforementioned drug types at the University of South Alabama Mitchell Cancer Institute in Mobile, Alabama.
Skin Layers

Throughout the litigation process, exclusivity is a favorable evidentiary trait that augments the position on which a case is founded. Fingerprint impressions, more commonly referenced in forensic science as friction ridge skin, are singular to every individual and are grounded in the dermis, the second of three skin layers.\(^4\) The outer layer of skin, the epidermis, functions primarily as a barrier between lower levels of tissue and foreign substances in the surrounding atmosphere. Though the epidermis is comprised of a multitude of cellular varieties, all of which serve a specialized function, keratinocytes are the primary type of cell in the epidermis, constituting 90-95 percent of the layer.\(^4\,^5\) Figure 1.1 illustrates the five distinct layers of keratinocytes characteristic of the epidermis of the hand. Each layer is distinct based upon cellular structure and rigidity. As cells in the basal layer undergo mitosis and are propelled upward, the cells are subjected to increased differentiation through each progressive layer.\(^4\,^5\) This process, also known as keratinization, describes the production of the stable protein keratin, a fortifying cellular agent, the addition of which corresponds to the perfunctory tasks and daily strain sustained by the epidermis. Fully differentiated layers are sloughed off at the surface, creating a continuous balance of production, keratinization, and depletion.\(^4\,^6\)
The dermis is the second skin layer, serving as a structural foundation for the superficial epidermis and a regulation site for temperature and sensory reaction. Rooted in the dermis are subjacent projections of tissue, as illustrated in Figure 1.1 that correspond to the ridges and plains of friction ridge patterns. Primary ridges support the elevated regions of a skin pattern, while secondary skin ridges support depression areas of a given pattern. Each ridge provides structural support for keratinocytes located in upper layers of friction ridge skin. Extending from primary ridges are eccrine sweat glands, the singular supplement to friction ridge skin. Functioning to regulate body temperature, eccrine sweat glands, dependent on their length, originate in the dermis or hypodermis, with their ducts extending to the surface of friction ridge skin. Beneath the dermis lies the hypodermis, which is made up of fatty tissue that provides for flexibility. The hypodermis also provides for skin contouring and is composed of adipose tissue, a tissue variety that reserves additional lipids for energy production.

**Formation of Friction Ridge Patterns and Minutiae**

The exclusivity of friction ridge skin is the result of natural biological development. Though the formation of tissue and organs is a customary process, formation does not yield identical products; all biological processes are inherent, yet uncertain, allowing for singularity. During gestation, friction ridge skin is formed between 10.5 and 16 weeks. The fundamental concepts of cell proliferation as well as the development of volar pads are underlying factors in the construction of friction ridge skin. Volar
pads form as a result of inflammation of tissue beneath the epidermis. The swelling of tissue begins at the thumb at approximately 7 weeks, slowly progressing to each adjacent finger, as depicted in Figure 1.2. After ten weeks, volar pads cease to exhibit uniformity and change shape as cells present in surrounding tissue rapidly divide and combine with volar pad tissue, effectively creating a recognizable delineation of the hand and fingers at approximately 16 weeks.4, 7

The predominant theory of friction skin formation holds that basal cells in the epidermis rapidly divide at approximately 10.5 weeks, at which point, cell aggregations join for randomized pattern development.4, 8-10 Figure 1.3 illustrates initial cell proliferation, whereby cells in the basal layer aggregate to form patterns. As each finger increases in size, developed ridges are distanced, resulting in subsequent ridge formation to maintain consistency.4, 11

Consistency maintenance is directly correlated to minutiae formation. Minutiae, or, defining locales present on friction ridge skin, distinguish individual impressions of friction ridge skin, yielding the favorable evidentiary trait of exclusivity. Essentially, minutiae are discontinuations of ridge structure, and fall under two distinct categories, ridge endings and bifurcations.12

In addition to these defining locales on friction ridge skin, each impression can be divided into three classes of ridge patterns: loops, whorls, and arches, all of which are dependent on volar pad size and regressionary behavior.4 Specifically,
the height of the pad and the shape it takes as surrounding areas of tissue begin to slowly grow may affect the size and orientation of the pattern. Loops are the most common type of pattern, occurring in approximately 60 percent of the population. They originate from one side of the print, curve around, and continue toward the side from whence it came. Whorls are circular in shape, and are the second most common type of pattern, occurring in approximately 35 percent of the population. The last pattern type, arches, are the least common pattern, with a 5 percent occurrence. Arches begin on one side of the print and exit on the opposite side. Patterns of friction ridge skin can be classified according to two singular points, known as core and delta points. Core points can be described as the location at which central ridges are at their steepest, while a delta can be defined as the point at which ridges diverge. Each pattern has a core; loops have one delta while whorl patterns have two deltas.

**Case Report Studies Depicting Hand-Foot Syndrome**

The proposed research study is both original and comprehensive in nature, aiming to measure the degradation of friction skin ridge detail in conjunction with prescribed chemotherapy drugs and other plausible dependent variables. As denoted previously, friction ridge skin is distinct for every individual, allowing for exclusivity in identification. However, in an oncological context, the loss of friction ridge skin adversely affects patients whose quality of life has already been diminished. According to Al-Ahwal, clinicians should place greater focus on the potential loss of friction ridge detail, which could add significantly more stress to cancer patients whose lives have already been severely altered. The author describes the case report of a 53-year old male patient diagnosed with stage IV adenocarcinoma metastasized to the liver, lungs, and rectum. The patient was administered capecitabine, an anti-metabolic drug that prevents the growth of cancer cells by preventing cells from producing DNA and RNA, as part
of a palliative care regimen. After fifteen days of treatment, the patient presented with grade 1 Hand-Foot Syndrome (HFS) following the second and third cycles of chemotherapy. Following the fifth and sixth chemotherapy administration cycles, the patient exhibited grade 3 HFS and fingerprint loss, preventing the patient from completing documentation that required fingerprint impressions.²

HFS, also known as palmar-plantar erythrodysesthesia (PPE), is characterized as being a common disadvantageous response to chemotherapy drug administration. HFS manifests as erythema (reddening) and dysesthesia (numbing sensation) localized to the skin of the palms of the hands and the soles of the feet. Patients with severe cases of HFS present with swelling of the skin accompanied by blistering and desquamation (the shedding of skin layers).² The National Cancer Institute classifies erythrodysesthesia into three distinct grades that conform to the severity of skin response.² Grade 1 HFS is characterized as erythema with no pain or discomfort; Grade 2 HFS represents a significant shift in severity in which the skin exhibits peeling, blistering, and bleeding, accompanied by edema (fluid build-up); Grade 3 HFS presents as ulceration in conjunction with previous grade symptoms, significantly affecting routine activities.²

A separate report, published by Wong, Choo, and Tan, presents the case of a 62-year old male patient diagnosed with metastatic nasopharyngeal carcinoma. Doctors placed the patient on a capecitabine regimen in July 2005 to sustain remission status following treatment and prescribed a continuation of the dosage after follow-up appointment confirmed the positive outcome of the regimen. In December 2008, three years following the initial capecitabine treatment, the patient was detained for several hours at airport customs, impeded from entering the country on account of the individual’s lack of ridge detail.¹ The authors note that many
patients who undergo long-term capecitabine administration may experience loss of prints and should be notified to avoid inconvenience.1

Capecitabine and Ridge Degradation

Capecitabine, or Xeloda, is an anti-metabolic drug that is orally administered to catalyze the effectuation of Fluorouracil, a substance that contests cancerous growths by preventing the production of DNA and RNA in cells.3,18-19 Without DNA and RNA, the nuclei of cells are unable to properly function and divide. While the prevalence of HFS is markedly higher with capecitabine administration, there are additional drugs that are also associated with HFS, including Cytaribine (Cytosar-U), Floxuridine (FUDF), Fluorouracil (5-FU, Adrucil), Idarubicin (Idamycin), Liposomal doxorubicin (Doxil), Doxorubicin (Adriamycin), Sunitinib (Sutent), Sorafenib (Nexavar), Pazopanib (Votrient), and Vemurafenib (Zelboraf).3,20-21

The developmental process of HFS as associated with capecitabine is not explicitly known.3,19,22-23 Current hypotheses on the subject speculate that HFS is a result of the susceptibility of both cancerous cells and keratinocytes to capecitabine toxicity.3,19,22 Other hypotheses suggest skin changes occur when small amounts of a given chemotherapy drug seep out of the blood vessels present in the extremities and are introduced to surrounding tissue.3,20 Friction and heat are two factors associated with increased issuance of the drugs from the vessels.20 Still other hypotheses suggest that in addition to waste products such as excess water and salts, chemotherapy drugs are also emitted from the body by way of pores that are linked to sweat glands.3,24

Several of these hypotheses appear to be plausible based on cell proliferation sites and the process of converting Fluorouracil into an effective cancer targeting substance.3,5 The introduction of capecitabine into the system causes numerous reactions to take place, leading to
the eventual conversion of Fluorouracil to 5-FU. The enzyme thymidine phosphorylase, or TP, aggregates at cancerous sites in large quantities and converts Fluorouracil to 5-FU, thereby limiting its toxic effects to cancerous tissue. Studies have shown that TP is more prevalent in friction ridge skin than other areas of the body, allowing for deduction that the increased proliferation of keratinocytes in the epidermis draws 5-FU to these areas in much the same way that the substance is drawn to areas with high proliferation of cancerous cells.

**Longitudinal Study of Ridge Degradation**

A longitudinal study conducted by Schenck documented the effects of capecitabine on a single patient from initial administration to final treatment. The study evidenced diminished friction ridge skin distinctly associated with capecitabine treatment. The study also attested to the permanency of friction ridge skin; though ridges were exposed to toxic medication, detail was restored to relative initial condition approximately 65 days after treatment, with no change in pattern or minutiae arrangement. These results are depicted in Figure 1.4. Section “A” displays quality of ridge detail at beginning of capecitabine treatment, “B” showcases quality throughout duration of treatment, “C” is indicative of quality at cessation of treatment, and “D” signals the return of normal ridge detail. The study evidences a direct result between capecitabine and a decline in impression quality. These findings verify previous literature, which estimates keratinocyte maturation to be between 30 to 40 days. The suspension of observed quality increase is in direct correlation to a significant disruption in basal layer proliferation, suggesting that these rapid areas of growth were susceptible to 5-FU in much the same way as cancerous growth and required approximately 30 to 40 days for friction ridge detail to be apparent on the upper epidermal layer.
The author challenges researchers to build upon the former research initiative by documenting the results of not only capecitabine treatments with regard to modified dosage, but also additional chemotherapy drug treatments on friction ridge skin detail. The proposed research initiative aims to address this challenge, calling for validation of the aforementioned longitudinal study, while simultaneously determining the effects of additional chemotherapy drugs on friction ridge skin.

**Taxane Class Drugs and Anti-Microtubule Mechanism**

Taxane class drugs are a variety of anti-microtubule reagents whose principle mechanism is the stabilization of guanosine diphosphate (GDP)-bound tubuline in the microtubule. The protein tubulin polymerizes in vitro to form microtubules, fibrous cellular projections that support cellular activity, including spindle fiber formation during mitosis. Many anti-microtubule reagents stem cellular growth by inhibiting polymerization; however, taxane class drugs operate utilizing a reverse mechanism. Taxane class drugs are mitotic inhibitors, binding to tubulin to create a hyperstabilization dynamic, which leads to subsequent division inhibition as the tubules are unable to depolymerize.
Taxane drugs, derived from the plant genus *Taxus*, include Paclitaxel (Taxol) and Docetaxel (Taxotere). These drugs are administered by injection, with common side effects including swelling, rash, and painful separation of the nail from the nail bed. Hand-foot syndrome is also a reported side effect of chemotherapy drug concoctions, including paclitaxel at 10 percent occurrence, and docetaxel at 5 percent occurrence. Taxane-induced HFS appears more frequent in conjunction with relatively large doses that are administered in quick succession.

Several case reports detail both paclitaxel and docetaxel-induced HFS. The first case report in study details a 72-year old patient diagnosed with stage T1 breast cancer and prescribed a weekly injection of paclitaxel over a span of 12 weeks. Following the sixth dosage of paclitaxel, the patient was diagnosed with grade 3 HFS, characterized by redness, desquamation, and dysesthesia. The patient was instructed to wear long articles of clothing and generously apply sun block to the affected areas, causation for improvement and continuation of 12-week treatment. The second and final case report details a 52-year old patient diagnosed with metastatic breast carcinoma. The patient was administered two weekly cycles of docetaxel, after which, the patient presented with grade 3 HFS characterized by severe redness and swelling. Although the patient was prescribed a dosage that has not presented HFS in the past, professionals are certain that the patient’s metastatic condition altered metabolism of the drug, causing symptoms at a lower dosage. However, despite the incidence of HFS, no reports exist describing the potential effect of taxane chemotherapy on friction skin ridges.

**Liposomal Doxorubicin (Doxil) and Anthracycline Mechanism**

Liposomal Doxorubicin, or Doxil, is an antitumor anthracycline, a drug class derived from the *Streptomyces* fungus species. The drug is composed of doxorubicin encased in a
liposome, or lipid, to allow for direct contact with cancerous tumor growths upon injection, without detection by the immune system.\(^3\) Though the exact targeting mechanism of the drug is currently unclear, scientists Denard, Lee, and Ye of the University of Texas Southwestern (UTSW) Medical Center have contributed to previous research which evidences that viral infection prompts the detachment of a protein, CREB3L1, and its corresponding amine group, from the cellular membrane to the nucleus, where genetic code for the inhibition of cellular proliferation is transcribed.\(^3\)\(^4\)–\(^3\)\(^5\) The UTSW group has found that doxorubicin introduction prompts the formation of lipid molecules known as ceramides, which aid in detaching CREB3L1 from the membrane.\(^3\)\(^4\),\(^3\)\(^6\) Though the exact mechanism of cellular breakdown by doxorubicin is unclear, these findings provide information that can be built upon through further analysis. There are several noted changes in the skin as a result of doxorubicin administration; hand-foot syndrome is a common side effect of doxorubicin, occurring five to six weeks following treatment in approximately 30 percent of cases. In approximately 10 to 29 percent of all patients, the drug darkens and discolors the nail bed.\(^3\)\(^3\)
Chapter 3—Methodology

Overview of Academic Partnership and Objectives

Collection of fingerprints will take place in the Chemotherapy Infusion Suite of the University of South Alabama Mitchell Cancer Institute (USAMCI), located at 1660 Springhill Avenue in Mobile, Alabama. Michael A. Finan, M.D., Interim Director of the Mitchell Cancer Institute, and Dr. Rodney P. Rocconi, M.D., Associate Director for Clinical Research, have agreed to an academic research partnership with the University of Southern Mississippi’s School of Criminal Justice following in tandem approval of the University of Southern Mississippi and South Alabama Internal Review Boards. Following approval, Dr. Jenna Wildman, a resident enrolled at the University of South Alabama College of Medicine, will be assisting with data collection.

Primary objectives of study protocol are to conduct a comprehensive study of the effects of taxane class drugs, liposomal doxorubicin, and capecitabine on friction ridge skin. Pending evidenced degradation, principal aims include alerting the medical field of a confirmed side effect of various chemotherapy drugs to provide essential information for patient notification. Secondary objectives include analysis of patient traits and diagnostic variables in conjunction with generated quality scores to determine statistical trends.

Study Population

In order to narrow the scope of the proposed study to be conducive to time constraints, partnership with the USAMCI shall be utilized to identify three groups of five patients each, with groups corresponding to the chemotherapy drugs under analysis—taxane class drugs, doxorubicin, and capecitabine. As such, the study population is dependent upon the patients who meet qualifications of the study. Chemotherapy combinations containing the studied drugs may
be admitted to the study; however, additional drugs present will be noted in the study. Following determination of these patients, the researcher will collect ridge detail impressions from these individuals for further analysis and interpretation. The researcher aims to gather impressions throughout their chemotherapy treatment period that typically lasts 6 months. Impressions will be gathered prior to first chemotherapy cycle, at the halfway point (3 months), and at completion of chemotherapy (6 months). Additionally, a post-chemotherapy impression will be obtained to assess resolution of ridge detail at 90 days +/- 14 days.

Exclusion criteria include individuals who are not being administered the antitumor drugs being studied. No individual who meets inclusion criteria shall be excluded from the proposed study as a result of race, ethnicity, socioeconomic status, or gender. Patients will be provided with a consent form and may refuse participation. Prior to collection and at the discretion of the guidelines for Human Subjects Research and the researcher, all probable participants must have understood the extent of the study, including any and all potential benefits and harm. If the individual is unable to write but is deemed competent, verbal consent will be obtained and documented.

**Research Design**

Friction ridge skin impressions will be collected utilizing the powder/label technique.$^3$ A relatively common postmortem lift technique, this method showcases clearer ridge detail in comparison to the traditional ink method, as indicated in Figure 1.5.$^{37}$ The powder/label technique necessitates the direct
application of black fingerprint powder to the friction ridge skin by a fingerprint brush. Following the light coating of powder onto the skin, the adhesive side of a white mailing label is slowly applied to one side of the friction ridge skin to reduce doubling the impression and is then flattened onto the remainder of the skin. The label is applied to the backside of a clear acetate ten-print card, correspondent to the appropriate finger from which the impression was collected. Residue will then be cleared from the skin using isopropyl alcohol and paper products.

During the collection period, the researcher and all collaborators will maintain a central logbook in which patient name will correspond to a unique study identification number. This logbook will be stored at USAMCI in a locked cabinet within a locked room with access provided only by the clinical trial staff of the USAMCI, which does not have access to the clinical trial study thereby limiting potential bias. All investigators and clinical trial staff will have completed and maintain HIPPA training and certification. Dr. Wildman will assist with clinical data collection, will be informed and educated of both collection technique and the study identification number, which will remain prevalent throughout the study. All clinical data will be de-identified and maintained on a password-protected spreadsheet on a single computer at USAMCI. Considering that the impression interpretation must be completed at the University of Southern Mississippi School of Criminal Justice Fingerprint Laboratory, these de-identified impressions will be labeled with the study number and transported by hand by the investigators of this study. Furthermore, manila envelopes will serve as patient data kits, containing acetate cards and a brief survey detailing a list of common physical activities that may worsen or increase the risk of HFS symptoms.
Data Analysis and Interpretation

Collected data will be analyzed in accordance with a scoring system existent within a database known as AFIX Tracker. The software has the capability to allow for both comparison of a collected print to a database, or individual analysis of a single impression. The latter capability will be utilized, particularly, the “Auto-Extract” feature, which acts as an assessor of impression quality. AFIX Tracker allows impressions to be scanned and uploaded to the database, at which time minutiae points are automatically identified and a quality score between 0-80 generated. To ensure the scoring mechanism is analyzing similar surface area, the white mailing labels will be identically cut to negate higher scores proportional to greater surface area.

In order to organize data, a password-protected excel spreadsheet will be maintained throughout the collection and scoring process, with corresponding unique study identifier number forming the “y” axis and the chemotherapy drugs forming the “x” axis. De-identified clinical data will be available for analysis. Under each study number and chemotherapy drug, a section will be created to organize subsequent data collection. Additional room will be provided for patient traits, including age, race, weight, height, and physical activities.

Statistical analyses will be performed to evaluate impression quality, percentage of disrupted impressions, impression scores correlated to chemotherapy agents received and associated clinical factors, as well as chemotherapy administration details such as dosage, length of chemotherapy duration, and delays or reductions in chemotherapy.

Discussion of Timeline

The timeline of the proposed study is dependent upon the treatment cycles of the chemotherapy drugs in question and the posed research design to gather impressions at beginning, duration, cessation, and following treatment. Treatment schedules are determined by
labeled use of each agent for each tumor type. Considering different types of cancer might have different dosages, timing, and frequency of the same agent. As such there are limitations on the study in the form of time frame and limited sample size.
General Timeline

Spring 2015
April 15th, 2015………Prospectus Submission to Thesis Advisor and Mitchell Cancer Institute
May 1st, 2015…………………..Prospectus Submission to Honors College

Summer 2015
June 2015……………………………..in Tandem Submission of Research Design to the University of Southern Mississippi and South Alabama Internal Review Boards
June/July 2015…………………………………………….Data Collection Begins Pending Internal Review Board Approval and Alignment of Patient Schedules to Inclusion Criteria

Fall 2015
August-December 2015……………………Continued Collection and Analysis of Data for Duration and Cessation of Treatment
October 15th, 2015………………………..Progress Report/Thesis Draft to Advisor
November 1st, 2015………………………..Progress Report/Thesis Draft to Honors College

Spring 2016
January-March 2016…………..Final Collection and Analysis of Data for Treatment Follow-up
March 15th, 2016………………………………….Thesis Draft to Advisor
April 1st, 2016………………………………….Final Thesis to Advisor and Honors College
April 15th, 2016……………………….Final Thesis to Department Chair and Honors College
Literature Cited


