

AN INVESTIGATION OF TIME SINCE INJURY:
A RADIOGRAPHIC STUDY OF FRACTURE HEALING

A Thesis

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Kevin B.D.P. Hufnagl
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Abstract

Working at the junction of medicine and physical anthropology, this research investigates the rate of fracture healing. The ability to assign ages to fractures based on the degree of remodeling could be a valuable tool for identifying skeletal remains. This ability could differentiate between individuals with similar fractures and could also narrow the search of medical records for matches. Multiple radiographic images from 62 individuals were collected from the Baton Rouge Orthopaedic Clinic, including information on sex, ancestry, age of the individual, and age of the fracture. Breaks in the x-rays are categorized into one of six stages, defined on the basis of observable characteristics in radiographs. Variables of age, sex, ancestry, and type of fixation (ie, internal or external) are tested against the stage of the fracture and the time since the initial diagnosis of the fracture. Univariate analysis of variance shows that age is the only variable investigated in this study that repeatedly shows a significant correlation to the age of a particular fracture. Further research is needed to draw concrete conclusions and develop acceptable ranges for dating fractures.

Chapter 1: Introduction

Physical anthropology focuses its study on the biological evolution and development of humans and other primates. One of the specialized fields within the realm of physical anthropology is forensic anthropology. Members of this discipline utilize the information, knowledge, and principles established in anthropology to analyze and solve legal problems pertaining to human skeletal remains. One of the major roles of forensic anthropologists is the identification of individuals from their skeletal remains (Byers, 2002). In order to accomplish this task, anthropologists construct biological profiles of individuals based on their osteological remains. Numerous studies have been conducted to establish and refine methodologies to estimate ancestry, sex, age, and height from a skeleton, as well as identify trauma exhibited by the bone (Giles and Elliot, 1962; Phenice, 1969; Todd, 1920; Trotter and Gleser, 1952). The ability to tell when an antemortem traumatic incident occurred could be a valuable tool in the identification process of skeletal remains for forensic anthropologists and other medico-legal professionals.

Analysis of trauma with respect to time is only established in reference to the time of death—if the injury occurred before, during, or after death. Once an incident has been designated as antemortem (before death), no further temporal information is determined. However, antemortem trauma can provide valuable information that may aid in the identification of a nameless individual. Such trauma can be externally evident and be recalled as a distinguishing feature by witnesses. Furthermore, medical files of antemortem trauma can be used to verify the identity of skeletal remains.

Comparing dental x-rays is one of the most reliable methods to make a positive identification by matching filling shape and location and tooth shapes in ante- and post-mortem images. Radiographic films of vertebral spinous processes and trauma to bone have also been used in a variety of cases to make identifications based on unique combinations of skeletal features (Angyal and Derczy, 1998; Hogge et al., 1994; Riddick, 1998).

If it were possible to determine when the traumatic event occurred, another piece of information could be added to the biological profile of a person that could prove valuable in identifying or differentiating among several individuals. For example, in a setting of war, where mass casualties take place, injuries are not uncommon, and the demographic profile of most individuals is similar (e.g., young to middle-aged male). The ability to date fracture healing could potentially prove of significant value in the identification of conflict casualties.

The current research represents a pilot study to investigate the possibility of determination of age-since-trauma—alternatively, the post-trauma interval (PTI)—based on the degree of repair and remodeling evident in radiographic images. This study also investigates the variation in fracture healing rates caused by factors of age, sex, ancestry, medical treatment, and weight-bearing capacity of bones. Furthermore, it examines the degree of consistency in bone repair and considers the feasibility of further studies of the same subject matter with narrower research questions.

This research falls somewhere in the area where the interests of pathologists and forensic anthropologists intersect with the concerns of medical doctors and surgeons. The latter are concerned with trauma diagnosis and speedy treatment, while the former

focus on questions of causality. Doctors study osteological trauma and its progress forward in time. The current study attempts to transfer such medical knowledge of fracture healing to a pathological setting and trace an injury's development backward to its point of inception.

A variety of factors (e.g., age, type of bone, fracture severity, treatment, and nutritional status of the individual) exert influence on fracture healing (Ortner, 2003). By controlling some of these factors, patterns of fracture healing for a certain skeletal population could be established. This study provides baseline data to be utilized and tested in other skeletal samples.

Chapter 2: Literature Review

A review of the literature on the subject of bone healing yields little information from an anthropological point of view on the subject matter at hand. What is mentioned in anthropological texts are basic overviews of post-fracture activity of osteological materials imported from the medical literature in order to present the information (White, 2000). Roberts (1988) is one of the few authors applying knowledge of fracture healing from medicine to the field of anthropology. In some texts, those focusing more on pathology and forensic anthropology, the topic of trauma is addressed. However, under the topic of trauma, little attention is given to the process after fracture. Ortner (2003) and Byers (2002) touch lightly on processes occurring after fracturing and the speed at which they occur. Nonetheless, they focus on the factors and circumstances involved in the cause of fracturing.

However, in order to find extensive information on histological and morphological changes after trauma along with associated time frames, one has to refer to the medical literature (Birzle et al., 1978; Frost, 1989; Hendrix, 2002; Hulth, 1989). The texts of multiple articles and chapters on osteological trauma only agree on the grand picture. The details, on the other hand, are often in disagreement. While no obvious conflict emerges, issues such as stages of bone healing and remodeling speeds are not consistent enough to allow formation of a coherent picture. Definitions of the pertinent stages of bone healing differ from author to author, and, as such, any related time frames tend to be associated with a particular article and will exhibit inconsistencies if transferred to another author's remodeling outline.

The literature yields limited information about time since injury. The writings that mention information pertinent to an investigation of the interval since trauma focus on the processes of healing and remodeling, bringing up the temporal factor merely in passing. The following sections present basic information on bone histology, fracture mechanics, and treatment pertinent to understanding later discussion on the subjects of this study. Additionally, information on the various stages of bone healing and the times that have been associated with some of them are organized and outlined.

Histology of Bone

Bone has a unique structure that gives it both tensile and compressive strength as well as flexibility and light weight. Its structure also makes it “one of the most dynamic and metabolically active tissues in the body” (Nordin and Frankel, 1989:3). Bone is composed of both inorganic minerals, that produce its strength, and organic components, that contribute to its resilience. The two major organic components of bone are collagen and the ‘ground substance,’ which is a mixture of proteins, polysaccharides, and glycosaminoglycans. The minerals forming the primary part of the inorganic portion of bone are calcium and phosphate forming hydroxyapatite crystals (Nordin and Frankel, 1989).

At the microscopic level, bone is built from osteons. Each osteon is a system of concentric interconnected rings of bone matrix, called lamellae, with a central Haversian canal containing nerves and blood vessels. The bone cells, or osteocytes, located in the spaces between adjacent lamellae, receive their nutrients from these blood vessels through extensive networks of tiny canaliculi within each osteon, and through Volkmann’s canals that form bridges between osteons.

Four types of bone cells are found throughout the bone, each at particular locations, depending on their function. Osteocytes are the basic bone cells that compose the osteons. These cells are located between the concentric lamellae in small hollow spaces, or lacunae. Osteocytes appear mostly inactive and generally seem to maintain the bone matrix around them. They are supplied with nutrients by the system of canaliculi. Osteoblasts are the bone-building cells and are found in areas where active remodeling or other bone growth occurs. They create bone by synthesizing and releasing organic osteoid into the surrounding extracellular spaces. There, the osteoid becomes calcified and entraps the osteoblast, which becomes an osteocyte. Osteoblasts arise from osteoprogenitor cells, thought to be the only one of the four bone cells capable of division and multiplication. These progenitors are found on or near all free bone surfaces (Fawcett, 1994). They multiply to maintain their numbers and will change into osteoblasts when new bone is required. The fourth type of bone cell is the osteoclast, which is found in Howship's lacunae, located throughout the bone matrix. Osteoclasts are responsible for the resorption of bone in locations where it is not needed or has died.

Macroscopically, two types of mature (lamellar) bone can be identified, compact and cancellous bone. Compact bone is dense bone found on the external surfaces of bones. It consists of many osteons layered next to one another. Cancellous or trabecular bone is less dense, as it consists of a tight network of criss-crossing trabeculae, or thin bony spicules, that are about as thick as a single osteon. Together, the trabeculae form a spongy-looking mesh of bone that is permeated by red blood marrow. Cancellous bone is found in the interior of most bones, under a sheet of compact bone, except in the diaphyses of long bones, which contain no bone matrix. Covering the compact bone

layer surrounding the bones is a thin connective tissue called the periosteum. On the inside of long bone shafts is another tissue termed the endosteum. Both of these connective tissues are layered with a high concentration of osteoblasts and progenitor cells, since the surface of bone is a likely locale for necessary bone growth.

Biomechanics of Fractures

The term trauma refers to any injury induced by an outside force. While multiple types of skeletal trauma occur, the most recognizable trauma is fracturing. Fractures are produced by excessive or abnormal forces on the bone. Bone, like every other material, has a breaking point and will fracture when the forces acting on it exceed its specific failure point (Nordin and Frankel, 1989).

The five general modes of loads or stresses are compression, tension, shear, torsion, and bending. Each of these places a different set of forces on the bone and causes a different distortion, measured as strain, which is the ratio of the change in dimension relative to the original size (Rogers, 2002a). The type of fractures produced by each of these is often predictable from the type and location of the applied stressor. Fractures of long bone shafts, the focus of this study, commonly occur from bending and torsional loading. Alternatively, fractures resulting from compression, tension, and shear occur more frequently in cancellous bone (Nordin and Frankel, 1989). Fracture mechanics are based in the realm of physics, and the type of fracture produced from any external force can be anticipated by the principle that the weakest structure will break first. Furthermore, compact bone is generally stronger than cancellous bone. The structure of compact bone makes it particularly resistant to compressive and tensile stresses. It withstands more compressive load than tensile load, and more tensile load

than shear load (Nordin and Frankel, 1989). Due to its unique structure and combination of compact and cancellous bone, every bone is able to withstand different modes of load to differing degrees.

For a bone to fracture, the stresses exerted on it have to exceed the bone's elastic and plastic limit. A load on a bone initially causes the bone to bend under the stress. If the load does not surpass the elasticity of the bone, when removed, the bone will return to its original shape. However, if the load goes beyond the elasticity of a bone, the subject will become permanently deformed. The range of load that causes permanent deformation of osteological material is termed the region of plasticity of the bone. When the load tops this range, fracturing occurs. Since cortical bone is stiffer than cancellous bone, the former is able to withstand greater degrees of stress, while the latter can handle more strain. This means that compact bone has a higher elastic region, but cannot deform as much as cancellous bone. While cancellous bone may appear brittle and weak, its multi-angular organization actually allows it to absorb a large amount of energy. Since cancellous bone lacks stiffness, it has a smaller elastic region (Nordin and Frankel, 1989).

Age, disease, repetitive loading, and other factors may weaken bone and cause it to fracture under lower stresses than it would normally. Fortunately, bone is one of the body's tissues with a remarkable potential for repair (Ortner, 2003).

Fracture Healing

Once a bone is broken, especially in the case of a complete fracture, the bone is usually unable to continue functioning properly. Strength and stability have to be restored quickly and correctly. Healed bone has to be strong so that repeated fracturing is unlikely to occur.

According to Hendrix (2002), the process of healing is only partially understood. It can be studied at the clinical, radiographic, biochemical, or histologic level. Hendrix reveals one reason that the literature shows little consistency in terms of stages of bone healing, when he states that “the healing process is ... separated only arbitrarily into phases for the purposes of study... and such separation is an abstraction” (203).

Before looking at how various authors divide the process of healing, the actual process needs to be understood. When bone fractures, generally, three events happen. First, blood vessels within the Haversian canals rupture. When bone separates at the fracture line, osteons separate and blood vessels are stretched or squeezed, resulting in their dissociation. Also, during a fracturing incident the tissue surrounding the bone is usually injured, either by the bone segments or the external force that caused the fracture. In any case, some blood vessels will be ruptured, and the blood will pool in the fractured area. There, the blood will coagulate once flow to the area ceases when the vessel ends become sealed. This blood forms a hematoma between the two fractured sections. Collins (1966) and Schenk (1973) have both suggested that the formation of the hematoma is not part of the actual healing process. Nevertheless, the blood clot is usually included as part of the fracture-repair period.

The second event that takes place during the initial fracturing is the disruption of the osteogenic tissues lining the bone. Both the endosteum and the periosteum are lined with a high concentration of osteoblasts and osteoprogenitor cells. Disruption of the connective tissue signals to these cells that a traumatic event has occurred and bone needs to be repaired. The disruption of the periosteum is the initial signal for the proliferation of more osteoblasts, which will be deposited on the surfaces of the bone segments in

order to form new bone. The third event that takes place at the time of the traumatic event is the separation of a certain amount of bone cells from the vascular system. Any loose bone fragment will no longer have a connection to the vascular system of the body, and many cells at the edges of the fracture also will be cut off from the blood vessels permeating the bone. Without the proper nutritional connections, the osteocytes will become necrotic since blood supply is unlikely to be restored to the cell through the canaliculi (Ortner, 2003). Such dead bone has to be resorbed before the healing process can be complete. However, the resorption of necrotic bone does not necessarily begin immediately after fracturing. Necrotic bone at the ends of the bone fragments, as well as necrotic fragments in the fracture space, can become incorporated into the subsequent healing processes (Collins, 1966).

After fracturing occurs, some osteoprogenitor cells differentiate into fibroblasts and other supporting cells. These cells form soft fibrous granulation tissue at either end of the fracture segments and extend into the blood clot. This tissue represents the first organization at the fracture site. The granulation tissue is a mixture of a variety of different cells that will be needed during the course of fracture repair. Three of the four bone cells will be represented. Osteocytes will not be present since no actual new bone has formed at this point in time. Osteoblasts are present to begin formation of new bone. Osteoclasts in the granulation tissue will sometimes begin resorption of some necrotic bone in the area during this stage. Not all necrotic bone is resorbed, however. Often, if the location of the necrotic bone is suitable, it will be incorporated into the fibrous bridging between the broken ends that occur at this time. Progenitor cells are needed in order to continually keep producing new osteoblasts. Other things in the granulation

tissue include fibroblasts, macrophages to eat away the hematoma, supporting cells, and other intercellular materials. The area also becomes newly vascular during this stage as new blood vessels, usually from the surrounding muscles, extend into the fracture space and create a fibrous union between fracture fragments (Birzle et al., 1978; Frost, 1989; Hendrix, 2002; Paton, 1992; Sevitt, 1981).

The next stage in bone repair is the formation of a primary bony callus across the fracture that provides great stability to the bone once it is complete. As the cells in the granulation tissue pursue their individual activities, osteoid is laid down rapidly. The primary callus that forms initially is made up of woven, immature bone and is not heavily calcified. This callus is still slightly soft and can be cut by a sharp knife (Collins, 1966). Three types of calluses form across a fracture site. The intermediate or sealing callus joins the actual ends of the broken bones. The endosteal callus is the part of the callus that unites the opened marrow spaces, and the periosteal callus forms around the outside of the fracture and bridges over the site. This third callus is usually the most visible in radiographic images, as it is the most exterior layer of newly produced bone and has a distinguishing bulging shape that makes it easier to locate than either of the other two calluses. The only real difference between these three calluses is their origin. The periosteal callus is formed by osteoblasts on the periosteum that was distorted during the fracturing event. Similarly, the endosteal callus is formed primarily by the osteoblasts on the endosteum inside the break. The sealing callus is between these two and is most likely created by osteoblasts in the granulation tissue that deposit their osteoid along the fibrous connective tissues and become ossified there. Thus, the intermediate callus follows the orientation of the fibrous connections between the bone ends and has a

cancellous appearance. Otherwise, no obvious structural differences exist between these three types of calluses. Therefore, the differential naming of these parts of the primary callus appears to serve a descriptive and conceptual purpose (Hendrix, 2002; Ortner, 2003).

Eventually, the woven bone has to be turned into lamellar bone. When lamellar bone begins replacing woven bone, the callus is referred to as secondary, if such a distinction is made at all. The creation of a secondary lamellar callus is accomplished through a combination of osteoblastic and osteoclastic activity. As osteoblasts deposit their osteoid, it now becomes highly mineralized and the structure of the resulting osteocytes is orderly and structured into circular lamellae, characteristic of mature lamellar bone. As new bone is created, the osteoclasts are responsible for resorbing unused bone. Osteoclasts remove the remaining necrotic bone within the callus and at the fracture ends. Once the fracture location has been strengthened by lamellar bone formation, the woven bone from the first callus is also resorbed. Frost (1989) names the unit composed of these different types of cells that are responsible for conversion of calcified cartilage to woven bone and woven bone to lamellar bone the “basic multicellular unit,” or BMU (287).

Once the callus has matured completely, the bone is basically as strong as it will get. Based on the stresses and loadings imposed on the fracture site, most of the callus, especially the unnecessary bulge of the periosteal callus, will be resorbed and will restore the bone to a smooth outline. The bone will also be remodeled according to the stresses it experiences and in subsequent years may look similar to the original. If the original fracture was small or set well, possibly no trace of the break will remain in later life. One

final item of note is that the possibility exists that some of the endosteal callus trabeculae may persist indefinitely in the medullary cavity at the locations of long bone shaft fractures (Collins, 1966).

These stages represent the major histological phases that have been identified in the process of bone healing. Depending on the research questions or designs, some researchers disregard some phases as insignificant to the healing process, while others combine phases to suit their methodology. Since the phase designation is arbitrarily determined by the researcher, phases used by different researchers rarely match exactly with one another (Hendrix, 2002).

Rate of Bone Remodeling

Various researchers divide healing stages differently, or commonly assign different names to them. In conjunction with this individual phase definition, times associated with the various stages are variable, even if the stages appear to refer to the same state of bone repair. For instance, Frost (1989) defines five stages of bone repair as fracture, granulation tissue, callus formation, lamellar bone remodeling and recontouring of the bone. According to Frost, the granulation process begins seven days after fracture and continues for approximately two weeks. After that, the callus continues to mineralize and finishes in four to sixteen weeks. For Frost's fourth stage, his BMUs remodel the bone. Each BMU needs about three to four months to complete the resorption-ossification sequence per cylindrical section. With this speed as his basis for approximation, Frost writes that the healing process may take from one to four years for a whole woven bone to be converted to lamellar bone.

Paton (1992), on the other hand, defines bone healing stages slightly differently and barely mentions any associated time frames. He also uses five phases: hematoma formation, organization of hematoma (i.e. granulation), callus formation, mature bone consolidation, and remodeling. The only temporal information he provides is that in adults cortical bone requires three months to heal and cancellous bone only six weeks. Children take about half as long. A problem with Paton's time frames is that he does not define what age range defines childhood, and, furthermore, he does not specify exactly what is meant by "healed." Some use callus completion as point of healing, and in clinical settings the term "healed" actually refers to the point in time when the bone is strong enough to function on its own and the fixation devices can be safely removed. This is usually before the callus is completely formed (Toal and Mitchell, 2002).

Collins (1966) does not even designate particular phases in the healing process of bone. However, he is one of the first writers to attach some time frames to the healing process. According to him, the granulation tissue begins formation on the second day after injury. On the fifth day, the earliest signs of osteogenesis (bone building) can be seen. Fibrous union between fragments takes three weeks to occur, and the callus is not complete until six weeks after injury.

Frost (1989), Paton (1992), and Collins (1966) all based their classification of stages on the level of histology. The current research investigates the same process from the radiographic level. At this level of inquiry, both Toal and Mitchell (2002) and Hendrix (2002) provide good outlines of what characteristics are observable in radiographic images during the healing process of bones.

Initially, the edges of the fractured segments are clearly delineated. Subsequently, the edges of the fragments begin to blur on the radiographic images, indicating the beginning of necrotic bone resorption. Hendrix states that this stage is seen between 10 and 14 days, while Toal and Mitchell assign a five- to ten-day range to the appearance of resorption on x-ray films. From day 10 to 20, according to Toal and Mitchell, extra bone begins to appear on the radiographs. Initially, a cloudy, or as Hendrix states, “fluffy,” callus extends from both ends of the fragments. With time, this callus mineralizes and becomes more radiopaque. Then, the fracture line begins to disappear as the callus begins spanning over the fracture gap. Toal and Mitchell state that this initial bridging of the fracture gap begins after about a month. Gradually, the callus continues to grow and bridge more and more of the fracture line. Eventually, the fracture line becomes obliterated. Toal and Mitchell attribute a time of three months to the point when the callus is mostly done and begins resorbing to re-establish the continuity of the cortex and the medullary cavity. After this point, remodeling takes a long time to reform the bone and return it to a resemblance of its former self. However, neither Toal and Mitchell nor Hendrix state any particular time ranges beyond the beginning of callus formation. Nevertheless, their description of bone remodeling observable in radiographs provides a valuable starting point for the evaluation of fracture healing in the current study.

Last, a vast variety of factors have been cited as influencing the rate of bone healing. Age, nutritional status, chronic disease (e.g., anemia, diabetes), fracture location and type, degree of motion and apposition, type of bone, and infection are just a few of the many factors that hypothetically or actually influence the rate of bone remodeling (Hendrix, 2002; Ortner, 2003; Toal and Mitchell, 2002).

In summary, this project combines information from the field of medicine and anthropology. In order to study the rate of fracture healing and bone remodeling, even at a radiographic level, the histological and biochemical processes that contribute to the healing process of bone have to be considered.

Chapter 3: Materials and Methods

Before the materials for this research project could be gathered, permission to conduct study of human subjects was sought from the Institutional Review Board of Louisiana State University (see Appendix). After the research was exempted, the radiographic materials could be gathered.

The radiographic films originated at the Baton Rouge Orthopedic Clinic from an electronic database the clinic has had in operation since 2003. The x-rays were gathered by clinic personnel after permission was obtained from clinic management. The database was searched for specified injury codes recorded with each file so that only specific kinds of fractures were collected.

From the beginning, the research was limited to fractures of long bone shafts. Further restrictive categories were that first priority should be given to fractures without internal fixation. Due to modern medicine and hospital policy, however, such fractures were relatively rare. Thus, later in the data collection phase, x-rays with internal fixation were pulled as well. Nevertheless, these were limited to those in which the fracture and any healing would be minimally obscured by the plates, screws, or intramedullary nails. The radiographic films were not sampled randomly in order to keep the sample size large enough. Therefore, the x-rays that were compiled for the data were the first ones that matched the specified categories.

Once selected, the x-rays were copied and identification criteria, such as names, removed. The final data set for this study consisted of 62 sets of radiographic films. For each set, demographic information on age, sex, and ancestry was recorded as well as the date of examination for each individual film. Each set consists of multiple x-rays,

minimally four. Since the x-ray protocol for medical examination of fractures is to take at least two radiographic images at right angles to one another—generally an anterior-posterior (AP) and a medial-lateral (ML) view—at least two images are present for each date. Additional oblique images and close-up images are part of highly comminuted fractures, fractures with extensive treatment structures, and fractures where one of the standard views is unusable (i.e., lateral view of a humeral fracture is usually indistinguishable from the torso behind it). Furthermore, since this research is investigating a temporal component to fracture healing, each set of radiographic films had to have at least a follow-up x-ray so that change in healing and bone remodeling could be observed and recorded. Hence, each set consists of minimally four separate films: two initial views and two subsequent views. However, all but two sets have four or more pairs of images.

The x-rays were then numbered (e.g., 3-11a) where the first number represents the case or a particular individual. The second number refers to the position of a particular film in the sequence of x-rays for a specific case with “1” designating the initial x-ray. The letter (i.e., a, b, or c) refers to a particular fracture. Since several individuals exhibited joint fractures of radius and ulna or of tibia and fibula, these letters were used to differentiate between such multiple fractures. In these cases the stage of healing of the radius would be recorded as “a” while the stage of healing of the ulna on the same x-rays would be differentiated with a “b.” Since this project was not designed to determine an individual’s average healing rate, the decision was made to record multiple fractures on the same individual separately, for possible analysis or deletion.

Subsequently, the data were entered into a Microsoft Excel 2003 file. The variables recorded were case number, date of birth, age, sex, ancestry, type of displacement of fracture, pattern of fracture, orientation of the fracture line, location of fracture on the bone, side and type of bone, type of treatment, date of service (DOS), and observed healing stage. The demographic variables and those detailing the kind of fractures were all independent variables possibly influencing the speed and effectiveness of fracture healing. These variables were recorded because they had possible effects on the healing rates of the fractures and because they would be identifiable on skeletal remains. Social factors like nutritional status or wealth that influence fracture healing were not recorded, since they are less readily discernible from skeletal remains. Further, by using data only from the Baton Rouge Orthopedic Clinic, a private institution, some of such social factors would remain relatively constant.

Age was calculated from date of birth and date of service. Ancestry or social race was obtained from the medical records. Displacement was recorded as displacement of alignment, apposition (AP or ML), or length. The pattern of fracture refers to categories of complete, comminuted, or incomplete. Fracture lines were classified as either transverse, oblique, or spiral, and the location of the fracture was on the distal end, the proximal third, or at midshaft. Clinical treatment of each fracture was recorded as two variables: 1) the type of fixation method used, and 2) if fixation of the bone was internal or external. Initial categories for stage of healing were fresh fracture, resorption, fluffy callus, mature callus, partial bridging, almost complete bridging, and complete bridging. However, due to the ambiguity of some x-rays and the resolution, the resorption stage was combined with the fluffy callus stage and renamed the granulation stage.

We will return to the choices of healing stages below, but first let us summarize the 62 cases. The demographics of the sample are given in Table 1.

Table 1: Demographic distribution of data sample

Sex	White	Black	Asian	Unknown	Total
Male	24	7	1	2	34
Female	21	7	0	0	28
Total	45	14	1	2	62

Their ages ranged from two to 93 with 46.7% under the age of 20. Due to recording errors, two individuals had no ages recorded with their films; however, due to the lack of epiphyseal fusion evident in the x-rays, they were classified as younger than 11 years of age. For the analysis of age, individuals were placed in two age categories. First, the sample was split equally into three groups based on their ages. The youngest group ranged from ages 2 to 10 and was designated as “age group A.” “Age group B,” the middle group, ranged from 11 to 45. Those individuals over the age of 45 were placed in “age group C.” The age range was also simply split into two groups of young and mature. Age 19 was chosen as the value to split the ages. At this age the long bones under investigation in the current study have generally fused. With the bones no longer growing at the epiphyseal plates, bone growth assumes a mature rate of metabolism at this point, which would influence the rate of fracture healing after age 19 (Rogers, 2002b).

A variety of fractures was also evident in the data. Of the 62 cases, 43 exhibited single fractures, two fractures were recorded for 18, and one case showed three distinctly separate fractures. The latter was a fracture of the distal tibia and the proximal tibia and fibula. Of the 18 double fractures, seven were radius-ulna fractures, 10 tibia-fibula fractures, and one was a left and right femoral fracture. For purposes of the analysis,

only one fracture was used per case, and the choice was made to use as primary fractures the fractures of the radius, the tibia, and the right femur for the double fracture cases, and the distal tibia for the triple fracture.

Table 2 presents a breakdown of the number of the different kinds of fractures that were recorded in the data sample. The first column shows the counts for the 62 primary fractures and the second column represents the counts for all 82 fractures, if each fracture is counted separately. All numbers refer to the initial radiographic films taken at the Baton Rouge Orthopedic Clinic.

Table 2: Summary table of counts of different fracture variables

Variable	Primary Count	Total Count	Variable	Primary Count	Total Count
Comminuted fracture	19	24	Femur	6	7
Complete fracture	36	49	Fibula	0	11
Incomplete fracture	7	9	Humerus	23	23
Distal third	20	29	Radius	9	9
Midshaft	31	40	Ulna	1	8
Proximal third	10	12	Tibia	23	24
External fixation	25	29	Oblique fracture line	17	20
Internal fixation	25	32	Spiral fracture line	15	16
“free”	12	21	Transverse fracture line	30	46

The category of “free” treatment refers to radiographs where no fixation or other treatment was visible on the x-ray. This category was commonly assigned to fractures of the fibula where the tibia was fixated and the fibula was allowed to heal on its own.

Compared to the tibia, the fibula has relatively little functional value in weight-bearing.

Due to its size and limited role in mobility, clinical treatment of fractures of the fibula are often limited to simple realignment without a fixation method. The corresponding tibia takes on the role of a splint (Helms and Major, 2002). The category of “free” fixation was also common for fractures of the humeral shaft for which isolated fractures are usually treated without invasive operations. (Lenchik, 2002).

The sets of radiographs are also variable in the amount of time they represent. The shortest case represents two pairs of x-rays spanning a period of 29 days, while several cases at the other end of the spectrum number 12 pairs of radiographs and span a time of 490 days, or over 16 months.

Methodology

This project investigates the healing rate of fractured bones. Hence, one necessary variable for the analysis is the degree of healing. The first step in the analysis of the data was the identification of particular stages of healing for each individual radiographic film. As noted previously, the literature is not in agreement as to what stages are useful or appropriate to study. Stages are generally chosen arbitrarily to suit the research interests of the moment. Toal and Mitchell (2002) and Hendrix (2002) give the best description and outlines of what stages of bone healing are observable in radiographs. Drawing primarily from Hendrix, with support from Toal and Mitchell, this researcher came up with the seven stages listed earlier, that have been reduced to six. Figure 1 presents a simple flowchart outlining the process of fracture healing and how it corresponds to the stages of bone healing visible in radiographs used in this study.

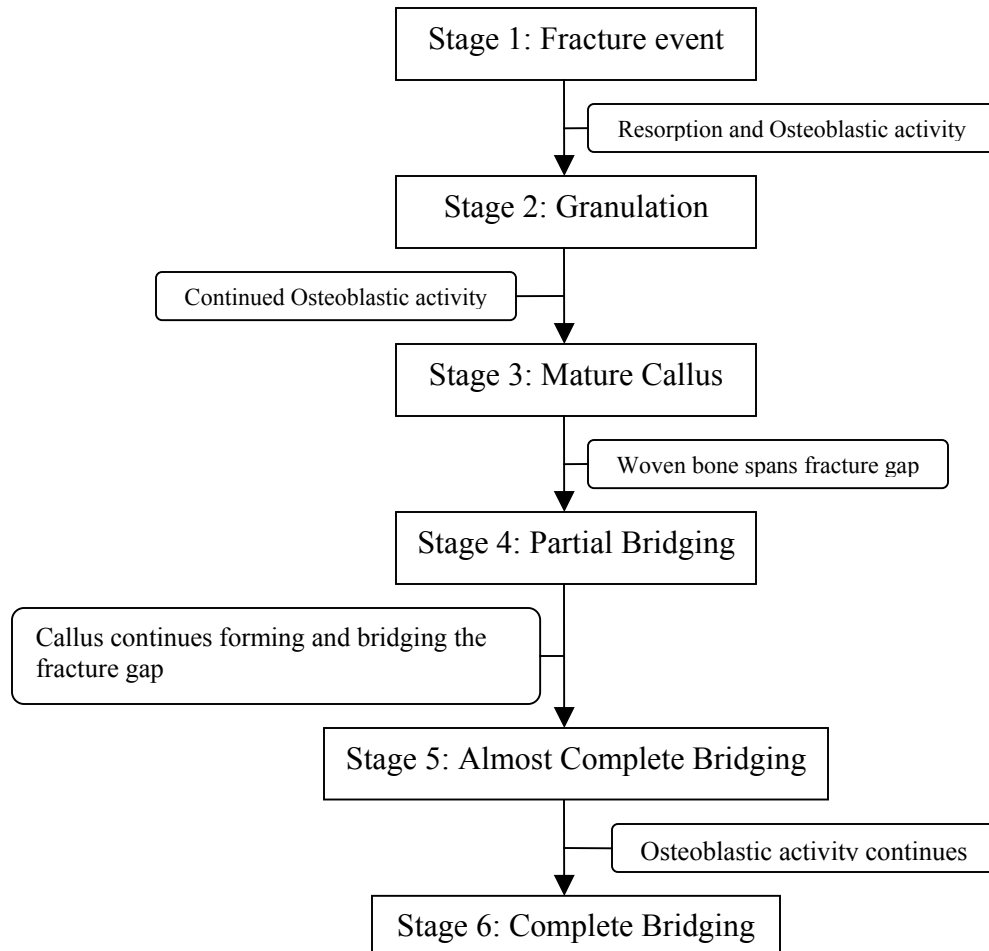


Figure 1: Flowchart outlining the fracture healing process and the stages utilized in this research

The first stage, illustrated in Figure 2, is not really a stage as it indicates the absence of observable bone healing. This initial state is designated “fracture event.” In this state, the fragment edges are sharply delineated. Stage two, “granulation,” refers to the beginning of resorption along the fracture fragments and the initial indicators of callus formation. Characteristics of this stage are widening of the fracture gap due to resorption, blurring of the fragment edges, and appearance of faintly mineralized buds of callus, indicated by the white arrows in Figure 3.



Figure 2: Example of Stage 1: *Fracture* is indicated by sharply delineated edges of the fracture fragments (arrows).

These buds are sometimes referred to as “cloudy,” “fluffy,” or “immature callus” in the literature. The third stage is “mature callus” and is illustrated in Figure 4 (Hendrix, 2002; Toal and Mitchell, 2002). The mature callus is identified because it is radiopaque and appears as dense as regular bone with the exception of its bulging out and over the fracture gap. At this stage the fracture line is still clearly delineated.

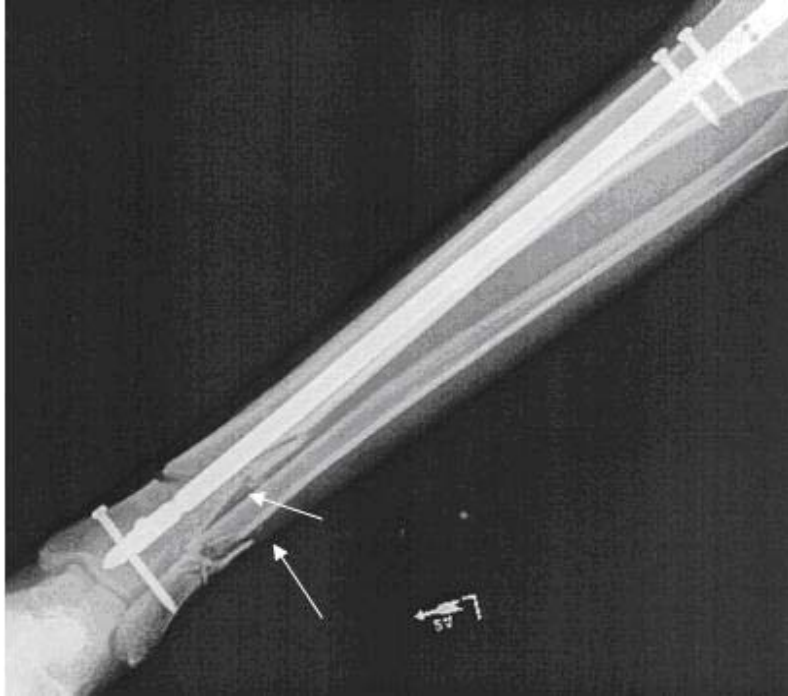


Figure 3: Example of Stage 2: *Granulation* indicated by fracture edges blurring and small buds of cloudy or fluffy callus becoming evident (white arrows).



Figure 4: Example of Stage 3: *Mature callus* is indicated by new bone growth of similar density as normal bone and the clear demarcation of the fracture line.

The fourth stage, illustrated in Figure 5, is called “partial bridging” and refers to the point in time when the callus is connected across the fracture gap in some areas. The radiographic characteristic of this stage is that the fracture line is beginning to blur and is not clearly evident along some portions of the fragments.



Figure 5: Example of Stage 4: *Partial bridging* is indicated by loss of the clear definition of the fracture line.

Stage five indicates the point in fracture healing when fractures are classified as clinical union. This fifth stage, exemplified by the tibial fracture in Figure 6 (left arrow), is referred to as “almost complete bridging” and is characterized by the fracture line being almost complete obscured. Only the faintest indication of the fracture line remains at this point, as the mature callus has nearly bridged the fracture completely. Lastly, stage six, or “complete bridging,” refers to the point when the fracture line is completely eradicated in the x-rays and evidence of the line is no longer observable. This stage is shown by the completed callus on the fibula in Figure 6 (right arrow).



Figure 6: Examples of Stages 5 and 6: The tibia shows *almost complete bridging* (Stage 5), which shows a bare hint of the fracture line. The fibula exhibits *complete bridging* (Stage 6) since all indication of the fracture line is gone.

Clinical union occurs when the fixation or stabilization apparatus can be safely removed and is normally identified before complete union of the fracture fragments is achieved (Hendrix, 2002; Toal and Mitchell, 2002). After clinical union, few radiographic follow-up images are taken. The lack of Stage six x-rays in the data illustrates this pattern. Classification of fracture healing was cumulative, such that the most advanced stage was identified, with the underlying assumption that all lower stages had already taken place.

The second essential variable to a study of bone healing rates is time. All of the radiographs from the Baton Rouge Orthopedic Clinic came with a date of imaging. However, the exact date of the traumatic incident was not recorded. Two methods were used to incorporate time periods for the healing of the fractures.

First, for part of the analyses, the initial x-ray date was taken to equal that of the date of injury. While this assumption may not be true for all cases, it is supported by the data. The initial x-ray for all cases showed clearly defined sharp edges on the bone fragments, indicative of a recent fracture event. Hence, the individuals incurred the injury no more than a couple of days before the initial radiograph was taken. Further, the unit of time for this study is more in the magnitude of weeks, rather than days. Therefore, a couple of days, especially if applicable to the majority of cases, should not cause significant problems with the results of the analysis.

The second method used to deal with the lack of dates of injury focused on the length of particular healing stages. By subtracting the amount of time that passed between subsequent stages of bone healing, the time necessary for one stage to radiographically transition into the next can be approximated. While this method does not provide an origin point for the fracture, or a time span for resorption to begin, it does provide approximations for stage lengths. Used together these two methods supplement each other as they focus on different questions. By taking the initial x-ray as the date of injury, the first method is able to answer when particular stages of healing begin after injury. On the other hand, by calculating lengths of healing stages relatively to each other, the second method is not bound to a fixed date of injury and eliminates the uncertainty between injury and initial radiograph. In conjunction, these two methods are able to circumvent the uncertainty of the date of injury. Lastly, any inconsistencies between their findings would indicate problems with the time of fracture origin or with the methods themselves.

The statistical analysis of the data was conducted using the student version of the Statistical Package for the Social Sciences (SPSS) 12.0 software. Time necessary per stage was estimated using the two methods outlined above. The means and associated coefficients of variation were calculated for the start of each stage and the whole stage as well. Subsequently, several univariate linear models were developed, testing the effect of different combinations of anthropological (i.e., age, ancestry, and sex) and medical (i.e., weight-bearing and location of treatment) factors on the variation of the healing period for the recorded stages of bone healing. Analyses of these variables are able to suggest which have a significant effect on the speed of fracture healing.

Several other factors were analyzed qualitatively due to their low respective subsample sizes. These include side-by-side healing of tibiae and fibulae and of radii and ulnae. Reports of these findings are based on observed patterns with low statistical strength due to limited sample sizes.

Boxplot graphs were also constructed to illustrate the range of time the individual stages were observable. These graphs, in conjunction with the accompanying statistics, were the basis used to discuss the possibility of establishing timelines for the dating of fracture healing.

Chapter 4: Results

Table 3 shows the means, standard deviations, and derived coefficients of variation pertaining to the lengths of each of the six different stages identified in this study. The coefficients of variation (CV) were calculated by dividing the standard deviations by their associated means. Therefore, the CVs are a measure of the spread of a variable relative to the size of its mean. The values in this table are calculated using every radiograph that exhibits the characteristics of the particular stage. Thus, the numbers represent the complete range of time that was observed for the six stages of fracture healing.

Table 3: Basic statistics for length of time each stage of healing was observed

Stages	N	Mean (days)	Std. Deviation	Coefficient of Variation
1	74	.22	1.317	5.97
2	130	22.37	17.195	.77
3	110	79.42	64.887	.82
4	107	116.96	78.919	.67
5	40	124.20	74.048	.60
6	28	260.86	114.570	.44

As expected, the mean age of more advanced stages of healing is greater. Furthermore, the standard deviation for later stages increases, indicating a greater degree of variation in the length of later stages of bone healing. The associated CVs however decrease with later stages. Thus, later stages take absolutely longer, but this increase is explained by the increase of the means.

Table 4 shows the same statistics based on the initial observation of each stage, excluding the first which would exhibit a mean value of 0. These measures show that later stages have an absolutely larger range of time when they start, but based on the coefficients of variation, the increase in the means explains this greater dispersion.

Table 4: Statistics for time of initial observations for the stages of fracture healing

Stage	N	Mean (days)	Std. Deviation	Coefficient of Variation
2	74	13.49	10.33	.77
3	68	52.99	31.55	.60
4	56	91.25	72.00	.79
5	29	125.34	81.70	.65
6	16	213.06	90.38	.42

Figures 7 and 8 are visual representation of the data used in Tables 3 and 4, respectively. The boxplot in Figure 7 illustrates the length of healing stages, and the graph in Figure 8 shows the variation in the beginning of the various stages. In both graphs the solid horizontal central line represents the median value, the boxes enclose the middle 50% of the data, and the T-shaped extensions express the range of all the values that are not statistical outliers.

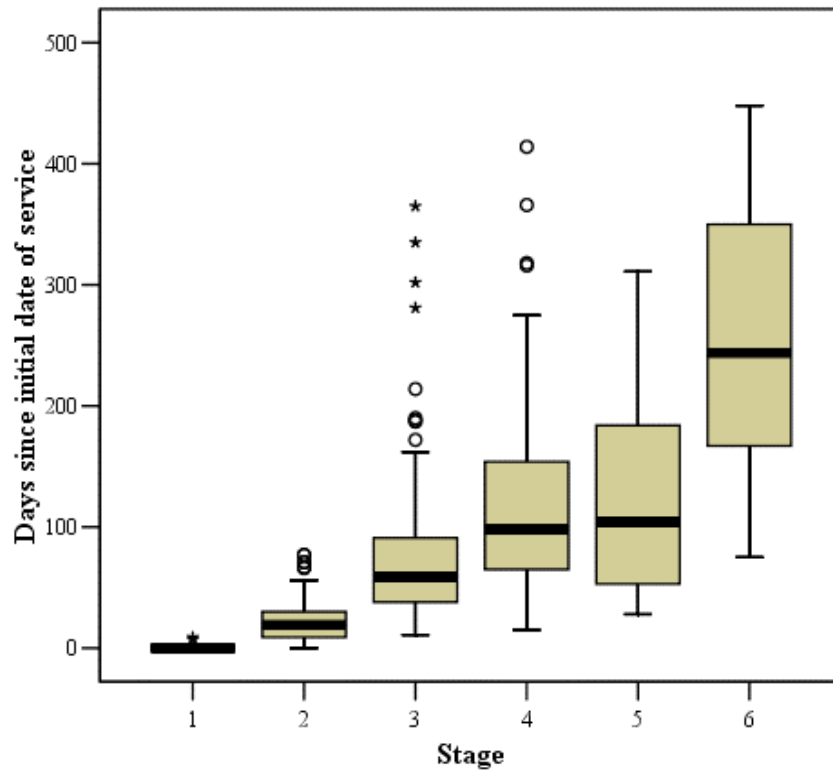


Figure 7: Boxplot showing range of time each stage is observed in the data set

Outliers, designated by small circles, are values lying outside 1.5 and within 3 times the box height. Asterisks designate extreme cases, which are further than three times the box height from the median value.

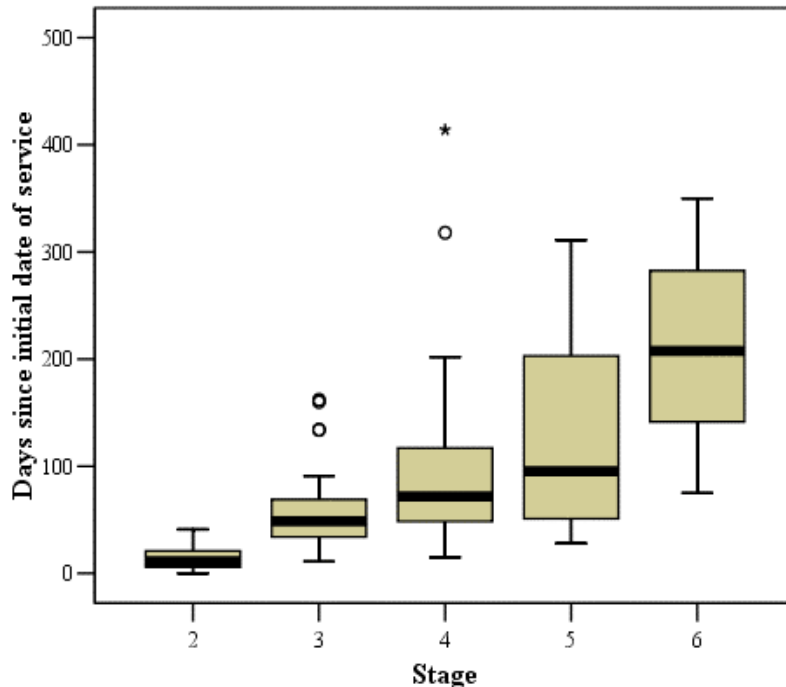


Figure 8: Boxplot showing range of time each stage is first observed

Tables 3 and 4 and Figures 7 and 8 illustrate how constant the rate of fracture healing is in this data set. The boxplot graphs show variation in the amount of time for the different stages. The two graphs and tables confirm that the longer the healing process continues, the greater the variation in stages that is expressed at a particular point in time. However, these four items indicate a limited degree of overlap between the earlier stages of fracture healing. “Granulation” (stage 2) has a comparatively narrow time period of occurrence, whereas subsequent stages have a tendency to overlap to a much greater extent. For example, stage 4 is almost completely within the range of values for stage 5.

Tables 5 and 6 show the mean amount of time between the initial radiographic image (DOS 1) and the first identification of stage 2 for a variety of subgroups of the data. Table 5 shows singular variables of age (trifurcated), age (split), sex, social race or ancestry in physical anthropology, weight-bearing, and location of fixation treatment. Table 6 shows the mean values for the data if the two age groups are separated by their sex. Lower means signify faster healing, so Table 5 shows that older individuals have a slower healing process. Males and non-weight-bearing bones heal faster than their opposites. Ancestry shows no difference in the start of healing and fractures treated with external or no fixation methods tended to heal faster than those fixated internally. Table 6 shows that the difference in stage 2 initiation does not become obvious until age group B, which starts at age 11.

Table 5: Mean values for the start of stage 2 divided by tested variables

Variable	Subgroup	Mean (days)	Variable	Subgroup	Mean (days)
Age Group	A (2-10)	10.58	Ancestry	Black	13.58
	B (11-44)	10.89		White	13.41
	C (>44)	21.74	Weight-bearing	Yes	16.05
Age	Young (<19)	10.56		No	12.23
	Mature (>19)	16.75	Fixation	Internal	17.20
Sex	Male	12.22		External	12.85
	Female	15.68		Free	10.70

Table 6: Mean values for the start of stage 2 for age groups separated by sex

Age Group	Sex	Mean (days)	Age Group	Sex	Mean (days)
A (2-10)	Male	10.93	Young (<19)	Male	9.51
	Female	10.00		Female	12.64
B (11-44)	Male	9.31	Mature (>19)	Male	16.02
	Female	12.77		Female	17.32
C (>44)	Male	19.61			
	Female	23.86			

Tamhane's T2 post hoc test confirms that the pattern seen with the age groups A, B, and C is statistically significant. At the 0.05 significance level Group C is significantly different from both groups A and B. Groups A and B show no significant difference between them.

Based on these patterns several linear models were generated. Tables 7, 8, and 9 show the results of the analysis of variance of three such models. This analysis tests the ability of the terms and the whole model to explain the variance of the dependent variable, time from DOS 1 to first observation of stage 2. Hence, a significance value of less than 0.05 indicates which factor explains a significant amount of the initial onset of stage 2—"granulation." The tables also give the coefficients of determination (R^2) for the model, which is a measure of the amount of variation explained by the model. The adjusted coefficient is a more accurate measure as it accounts for model complexity and relationships between the factors used.

Table 7 uses the age categories of "mature" and "young," where "young" range from ages 2 to 18 and mature from 19 to 93. In Table 8, the age factor refers to three different nominal categories: age groups A (2-10), B (11-44), and C (older than 44). Table 9 uses age as a scale variable, so that the actual ages were used. In this model, individuals of ages 25 and 40 are not equated to each other, as in the models represented in Tables 7 and 8, but analyzed separately.

In all three models, the age groups account for a statistically significant amount of the variation in the age of the fracture at the 0.05 level of significance. All three models as a whole also explain a significant amount of the variation in stage 2 onset.

Table 7: Analysis of variance results for model of stage 2 onset based on factors of age (split), sex, and race

Variable	F-value	Significance Level
Whole Model	3.12	.004
Age (y, m) ^a	6.86	.011
Sex	1.99	.164
Race	.97	.414
Age (y, m) ^a * Sex	.24	.629
Age (y, m) ^a * Race	3.16	.080
Sex * Race	3.92	.052
Age (y, m) ^a * Sex * Race	2.52	.118

^a. y is younger than 19 years; m is 19 years or older

^b. $R^2 = .305$; adjusted $R^2 = .207$

Table 8: Analysis of variance results for model of stage 2 onset based on factors of age (trifurcated), sex, and race

Variable	F-value	Significance Level
Whole Model	2.99	.002
Age (A, B, C) ^a	6.33	.003
Sex	3.35	.072
Race	.99	.403
Age (A, B, C) ^a * Sex	.41	.666
Age (A, B, C) ^a * Race	.59	.627
Sex * Race	5.01	.029
Age (A, B, C) ^a * Sex * Race	1.73	.186

^a. A is ages 2-10; B is ages 11-44; C is ages greater than or equal to 45

^b. $R^2 = .415$; adjusted $R^2 = .276$

Table 9: Analysis of variance results for model of stage 2 onset based on factors of age, sex, and race

Variable	F-value	Significance Level
Whole Model	5.72	.000
Age	4.56	.000
Sex	6.69	.017
Race	1.72	.193
Age * Sex	8.64	.001
Age * Race	3.57	.073

^a. $R^2 = .932$; adjusted $R^2 = .769$

Ancestry never shows significance to explain the age at initial observation of stage 2. Sex only contributes a significant amount to the explanation power of the model

in the model that uses age as a scalar variable. In this same model the “Age-Sex” combination factor also shows significance. These “combination” factors divide the factors into further subgroups. Thus, the “Age (y, m)-Sex” factor considers four groups and looks at the differences between mature males, mature females, young males, and young females. The first two models indicate an interesting interaction between the factor of ancestry and sex. This interaction approaches the 0.05 level of significance in the model with the binary age variable. In the model where age is separated into three groups, the combination factor of ancestry and sex actually accounts for a significant portion of the variation in the onset of stage 2. The only model of the three that explains a good proportion of the variation in the age of the beginning of “granulation,” is the model that uses age as a scale variable. This model has an adjusted R^2 value of 0.769. Neither of the adjusted R^2 values for the other two models, indicating the strength of the complete models, is impressively high, falling between 0.207 and 0.276 in these models.

Additional models with five factors of age, sex, ancestry, weight-bearing, and location of fixation treatment (results not presented here), showed less significance than the previous three. Their adjusted R^2 values did not exceed 0.31 and the age category lost its significant explanation power. However, in two of these models the combination factor of ancestry and sex again accounts for a significant portion of the variation in time when stage 2 is first observed.

Furthermore, analyses of variance of factors of age, sex, ancestry, weight-bearing of bones, and internal or external fixation of fractures show similar results (not presented here). Of these six variables—age being tested twice—only the two age variables show significant relationships to the variance in the time of initial stage 2 observation. Age

groups A, B and C have the highest significance at the 0.001 level of significance and this trifurcation of ages explains approximately 19% of the variance of the age of fracture. “Mature” and “young” age groups also show significance, explaining 8.5% of the variance. None of the other factors tested revealed a significant influence on the time when stage 2 is first observed in radiographic films.

Stage 3 is the *mature callus* stage. Tables 10 through 14 pertain to the initial observations of this stage in radiographic films. Tables 10 and 11 express mean values for the variety of variables under investigation in the current study. The patterns observed for stage 2 in Table 5 are repeated in Table 10. Once again younger individuals and males are faster to begin stage 3 of the healing process than older and female individuals. Weight-bearing bones healed faster than non-weight-bearing ones, and fractures with external and no treatments showed faster healing than those where internal fixation methods were used. Unlike for stage 2, where ancestry showed no difference, black individuals in this study healed faster than white individuals. Also, Tamhane’s T2 post hoc test shows significant difference at the 0.05 level between age group A and the other two, but no significant difference between the two older groups (B and C).

Table 10: Mean values for the start of stage 3 divided by tested variables

Variable	Subgroup	Mean (days)		Variable	Subgroup	Mean (days)
Age Group	A (2-10)	31.31		Ancestry	Black	47.65
	B (11-44)	51.70			White	51.54
	C (>44)	59.69		Weight-bearing	Yes	46.36
Age	Young (<19)	41.61			No	51.93
	Mature (>19)	57.73		Fixation	Internal	52.37
Sex	Male	45.56			External	45.04
	Female	54.09			Free	48.70

Table 11: Mean values for the start of stage 3 for age groups separated by sex

Age Group	Sex	Mean (days)		Age Group	Sex	Mean (days)
A (2-10)	Male	26.48		Young (<19)	Male	38.67
	Female	34.00			Female	48.09
B (11-44)	Male	51.91		Mature (>19)	Male	58.19
	Female	60.33			Female	57.42
C (>44)	Male	65.17				
	Female	48.57				

When the same factors as before (i.e., age, sex, race, weight-bearing, location of treatment) are used individually to construct models (results not presented here) to explain the variation in the time when first signs of mature callus formation are observed, only the three age factors explain a significant amount of the variation of stage 3 onset at the 0.05 level of significance. However, the amount of variance explained is still very low for the two nominal age variables. The “young” and “mature” categories explain only about 7.0% of the variance and the trifurcated age variable around 10.9%. In the model that used the scalar variable for age, the adjusted R^2 value increases to 0.348, but is still very low, indicating that age is not the sole variable to be considered.

In spite of the fact that age shows significance by itself, when age, sex, and ancestry are tested together, none of the factors or models show a significant tie to the fracture healing process, as can be seen in Tables 12, 13, and 14. In none of these Tables does any factor show significance. However, age is part of the factors that show the lowest levels of significance. None of the other factors or combinations between the three explains a significant amount of the variation in the time of onset of stage 3.

Table 12: Analysis of variance for model of stage 3 onset based on factors of age (split), sex, and race

Variable	F-value	Significance Level
Whole Model	1.39	.227
Age (y, m) ^a	1.24	.270
Sex	.90	.346
Race	.06	.943
Age (y, m) ^a * Sex	2.33	.132
Age (y, m) ^a * Race	1.34	.251
Sex * Race	.82	.368

^a. y is younger than 19 years; m is 19 years or older

^b. $R^2 = .139$; adjusted $R^2 = .039$

Table 13: Analysis of variance for model of stage 3 onset based on factors of age (trifurcated), sex, and race

Variable	F-value	Significance Level
Whole Model	1.75	.081
Age (A, B, C) ^a	1.51	.230
Sex	.32	.573
Race	.27	.767
Age (A, B, C) ^a * Sex	1.32	.276
Age (A, B, C) ^a * Race	.28	.838
Sex * Race	.56	.459
Age (A, B, C) ^a * Sex * Race	2.72	.105

^a. A is ages 2-10; B is ages 11-44; C is ages greater than or equal to 45

^b. $R^2 = .276$; adjusted $R^2 = .118$

Table 14: Analysis of variance for model of stage 3 onset based on factors of age, sex, and race

Variable	F-value	Significance Level
Whole Model	1.62	.139
Age	1.83	.091
Sex	.003	.958
Race	.183	.834
Age * Sex	.264	.850
Age * Race	.015	.904

^a. $R^2 = .814$; adjusted $R^2 = .312$

In two additional models (results not presented here) that were constructed where all five variables were used (i.e., one of two nominal age variables, sex, race, weight-bearing, and location of treatment), age only reached the point of significance in the

model using the trifurcated variable. However, neither of the models as a whole explained a statistically significant portion of the variation in stage 3 onset and both of the adjusted R² values were less than 0.30.

Stage 4 is the beginning of bridging between the two fracture fragments, and, according to the data, this process is observable as early as two weeks; however, generally, it appears more frequently after the second month post-injury. Tables 15 and 16 show the mean values for the time since DOS 1 when the mature callus was first observed on the radiographs. The same patterns that were observed for stage 2 and 3 are repeated here. Males, blacks, and weight-bearing bones produced mature callus faster than their counter-variables. Older individuals were slower to reach stage 4 in the healing process, and the extremely young age group A healed much faster than both age groups B and C. Tamhane’s T2 post hoc test confirms that this difference is significant between group A and the other two at the 0.05 level of significance. Yet, the difference between groups B and C is not significant. Table 16 restates the pattern that older individuals take longer to begin stage 4 of healing than younger ones. Lastly, fractures treated with external fixation methods or methods not visible in the x-rays showed faster creation of mature callus than fractures that were treated with internal fixation methods.

Table 15: Mean values for the start of stage 4 divided by tested variables

Variable	Subgroup	Mean (days)	Variable	Subgroup	Mean (days)
Age Group	A (2-10)	37.78	Ancestry	Black	71.40
	B (11-44)	93.23		White	93.17
	C (>44)	110.56	Weight-bearing	Yes	73.74
Age	Young (<19)	65.32		No	94.32
	Mature (>19)	106.39	Fixation	Internal	99.61
Sex	Male	78.23		External	76.60
	Female	93.82		Free	74.65

Table 16: Mean values for the start of stage 4 for age groups separated by sex

Age Group	Sex	Mean (days)	Age Group	Sex	Mean (days)
A (2-10)	Male	44.83	Young (<19)	Male	57.54
	Female	23.67		Female	76.97
B (11-44)	Male	73.27	Mature (>19)	Male	106.76
	Female	119.83		Female	106.06
C (>44)	Male	118.22			
	Female	102.89			

Tables 17, 18, and 19 show the results for models created using the variables of age, sex, and race. Once again, all three age variables explain a significant portion of the variation of the time at which stage 4 signs are first observed in radiographs, but none of the other variables tested showed significance.

The models outlined in Tables 17 and 18 exhibit low adjusted R^2 values of 0.086 and 0.093, respectively. Neither of these two models as a whole explains a significant amount of the variation in the onset of stage 4 of the healing process. The third model (Table 19), using the scalar age variable, however, does show significant explanation power. Furthermore, this model explains approximately 50% of the variance observed in stage 4 onset—a relatively high number compared to other models constructed during the data analysis.

Table 17: Analysis of variance for model of stage 4 onset based on factors of age (split), sex, and race

Variable	F-value	Significance Level
Whole Model	1.58	.150
Age (y, m) ^a	6.78	.012
Sex	.32	.575
Race	.91	.444
Age (y, m) ^a * Sex	.02	.894
Age (y, m) ^a * Race	.08	.776
Sex * Race	.32	.577
Age (y, m) ^a * Sex * Race	.00	.983

^a. y is younger than 19 years; m is 19 years or older

^b. $R^2 = .236$; adjusted $R^2 = .086$

Table 18: Analysis of variance for model of stage 4 onset based on factors of age (trifurcated), sex, and race

Variable	F-value	Significance Level
Whole Model	1.40	.196
Age (A, B, C) ^a	3.67	.034
Sex	.09	.772
Race	.62	.603
Age (A, B, C) ^a * Sex	.13	.882
Age (A, B, C) ^a * Race	.14	.937
Sex * Race	.01	.945
Age (A, B, C) ^a * Sex * Race	.51	.604

^a. A is ages 2-10; B is ages 11-44; C is ages greater than or equal to 45

^b. $R^2 = .324$; adjusted $R^2 = .093$

Table 19: Analysis of variance for model of stage 4 onset based on factors of age, sex, and race

Variable	F-value	Significance Level
Whole Model	2.42	.035
Age	2.55	.030
Sex	2.74	.119
Race	.22	.879
Age * Sex	3.74	.072
Age * Race	.04	.854

^a. $R^2 = .853$; adjusted $R^2 = .501$

None of the larger models that include five variables together explain a significant portion of the variation in stage 4 commencements (results not shown here).

Furthermore, only one factor, age, explains a significant portion of the variation in the model using “young” and “mature” individuals along with the four other variables of sex, race, weight-bearing, and location of treatment. None of these models as a whole are significant as is reflected in their low R^2 values that do not exceed 0.38.

For stage 4, individual models of the age of the fracture tested with factors of age, sex, ancestry, weight-bearing property, and internal or external fixation, the patterns observed for the previous stages repeats (results not shown here). Only the three age

variables exhibit a significant relationship to the variance of the time when stage 4 was first recorded. The models using “young” and “mature” groups explain about 14.1% of the variance and age groups A, B, and C explain 16.7% of the variance in the time of initial onset of partial bridging. The model using age as a continuous variable has an adjusted R^2 value of 0.404.

Small sample size did not allow for meaningful statistical analyses of stages 5 and 6. For stage 5 simple means for the different variables along with the associated number of individuals (N) are presented in Table 20.

Table 20: Mean values for the start of stage 5 divided by tested variables

Variable	Subgroup	N	Mean (days)
Age Group	A (2-10)	10	46.60
	B (11-44)	17	165.59
	C (>44)	2	177.00
Age	Young (<19)	22	110.27
	Mature (>19)	7	172.71
Sex	Male	18	124.39
	Female	11	126.91
Weight-bearing	Yes	11	157.36
	No	18	105.78
Fixation	Internal	12	157.33
	External	0	-
	Free	17	102.76
Ancestry	Black	7	148.71
	White	20	115.95

Unlike previously, for stage 5 no difference is observed between the sexes and for this data white individuals healed faster than black individuals. Also, weight-bearing bones were quicker to reach stage 5 characteristics than non-weight-bearing ones. However, the other patterns that were apparent from the first four stages are evident as well in the data for stage 5. Older individuals take longer to heal. Additionally, internally treated fractures were slower to reach this stage than those fractures no longer

using fixation at this advanced stage of bone repair. Only 16 cases were identified as showing characteristics of stage 6 and the majority of those were young white individuals. Hence, means of the small subsamples would not be able to tell any significant patterns and were not calculated.

Chapter 5: Discussion and Conclusion

This project investigated the time frames associated with identifiable features and corresponding stages of fracture healing. By separating the set of radiographic images into subsets of when the earliest instances of particular stages were observed, it was possible to investigate both the influence of a variety of factors on the healing rate as well as narrow the focus of the points of interest.

By comparing Tables 3 and 4, a difference in two ways to study bone healing stages becomes observable. Table 4 lists the means for the initial onset times for stages of healing, while Table 3 compiles all the images for a particular stage together. As a result, the variance, represented by the standard deviation, is consistently lower in Table 4 than Table 3. A smaller variance implies that the data is less spread out, than data with a high standard deviation and variance. By using the first instance of a particular stage, the period under investigation is narrowed. The values in Table 3 represent the whole range of time when a particular stage of bone healing can be expressed. On the other hand, the latter table focuses on the point of initial beginning of a stage, or the period of transition from one phase to the next. Thus, Table 3 is a representation of the uncertainty of assigning times to fractures based on the degree of healing, while the Table 4 narrows the range as much as possible.

According to the factors considered in this research (i.e., age, sex, social race, weight-bearing of bones, and location of treatment), the most influential variable for healing of fractures is the age of the individual. Younger individuals heal faster than older people. Since the age factor remains significant for both binary and trifurcated age categories as well as when age is used as a scalar variable, a strong relationship between

age and fracture healing is suggested. The decrease in healing capacity of bone does not appear to have a definite cut-off or leveling-off point—at least those ages used in the current study as cut-off points. Since the use of age as a continuous variable consistently provided better models for the prediction of the beginning of bone healing stages, the decrease of healing speeds with advancing age, may be gradual, rather than at any particular age. Yet, to be completely sure of the fact that healing speeds do not become more constant at a particular age, additional statistical tests and graphs need to be constructed on a larger data set than was part of this research. Such analysis may be able to test for particular ages when the potential for bone healing slows significantly.

The peculiar relationship between ancestry and sex that was expressed by the model in Table 8 and hinted at in Table 7 presents an interesting concept. It suggests that sex and race should not be treated separately, but jointly. Since both of these variables are strongly influenced genetically, this finding possibly suggests a more strongly expressed biological factor at the beginning of the fracture healing process that tapers off or is overshadowed by other factors as the fracture progresses farther along the repairing road. The initial response to bone fractures may be determined more on a biological basis. For instance, a higher density of osteoprogenitor cells in the periosteal and endosteal lining of bone would speed up the reaction time of these cells to stress, strain, and fracture, resulting in faster bone healing. However, current evidence does not suggest that individuals of different sexes or racial categories have different densities of osteoblasts on the periosteum and the endosteum. Yet, a large variety of factors are believed to contribute to the remodeling capacity of osteological materials, including vitamins and enzymes (Sevitt, 1981). The probability is high that one or more of these

proposed factors exhibit strong correlations with sexual and racial categories. Therefore, some social factors, like nutrition may be statistically related to biological categories like sex. Furthermore, “granulation” is a quick step and is unlikely to be influenced by medical factors, due to its speed. As a matter of fact, a couple of cases from this data set exhibited signs of granulation by the time the first radiographic image was taken. This verifies that granulation is a fast phase and further reiterates the problem of lag between the time of injury and the time of initial diagnosis in the medical clinic. However, the fact that this pattern is only observed in one of the analyses performed also possibly suggests that it may be an aberration in the data. Furthermore, only seven cases belong to the black female group and another seven to the black male group, while the white groups have much higher group sizes (24 males and 21 females). This lack of plentiful data and the uniqueness of the occurrence suggest that the significance exhibited by these four groups in Table 5 is an anomaly. Further exploration of this particular relationship will show if the relationship is real or a product of this sample.

When the mean values for the start of particular healing stages were calculated certain patterns repeatedly showed up. First, females healed slower than males. This difference in fracture repair can be attributed to hormone levels. Estrogens contribute to the resorption process in bone and high levels of estrogen may hinder the healing process. Second, weight-bearing bones healed slightly faster than non-weight-bearing bones. This pattern may be explained biologically or medically. In either case, weight-bearing bones are necessary for human locomotion. Therefore, evolution may have put greater emphasis on the healing of these bones, than non-weight-bearing ones, leading to some biological characteristic of weight-bearing bones allowing them to heal faster. Even if

evolution had nothing to do with the pattern in weight-bearing, doctors and patients would place more emphasis on the healing of a fracture that hindered mobility than one that did not. Hence, medical treatment of fractures of weight-bearing bones may be designed to facilitate faster healing. The last pattern observed from the mean times when healing stages were observed was that fractures treated externally healed faster than those treated internally. Internal fixation involves surgery that creates an open fracture. After surgery, not only does the body have to repair the bone, but the associated tissue as well. An open fracture also allows for the external environment to reach the fracture, and the introduction of foreign agents could further delay the body's repair of the fracture. Lastly, internal fixation involves the implantation of foreign materials in the form of metal plates, screws, or intramedullary nails. This fixation involves further destruction of the bone in order for these artificial measures to do their job. Hence, after the surgery bone has to heal the fracture, the additional damage done by the implanting process, and get used to the foreign material in and along the bone. These factors may explain why externally treated fractures healed faster than those treated with internal fixation methods.

The obvious problem with the current project is the high probability that the data are skewed. Several factors contribute to this skewing. First, the radiographic images were not initially collected to be able to address the research questions put forth in this study. They were taken according to medical protocols and hospital or clinic policies in order to serve their clientele efficiently and quickly. Radiographs were not taken at regular intervals. The type of fracture and the healing progress determined when radiographs were taken, according to the doctor's decision. Therefore, the intervals between x-rays utilized in this study are not constant across cases. Second, due to the

immense diversity of forces exerted on our bones, an even greater variety of fractures can occur, and each fracture is treated individually. Therefore, standardization of intervals at which x-rays are taken for further research on fracture healing in *Homo sapiens* would prove highly unviable, since such standardization would not be medically advantageous.

Once again the issue of the great number of factors influencing bone healing comes up. The plethora of factors influencing fracture healing is indicated by the consistently low R^2 values calculated for the models constructed in the analysis of the data. Even controlling for some factors, by only utilizing data from one clinic, the combination of factors investigated in this study explains only about 25% of the variance of the time required for different stages of fracture healing. The easiest way of including more factors is to expand the sample size, while controlling as many known and unknown factors as possible. In order to conduct standardized statistical research on fracture healing rates, a lot of attention to detail would be required in order to control for the majority of the variables possibly affecting the rate. However, such a tightly controlled research project would only answer a tiny portion of the vast topic of fracture healing.

Future research in this area needs to control for as many factors as possible. By keeping the majority of factors under control, future researchers will be able to focus their attention on a couple of variable factors. With an extensive data set, beginning and endings of stages as well as overall stage duration can be investigated. This will lead to important inferences about variation in healing and remodeling rates between different statistical sample populations. For instance, the healing rate can be compared between black men and women over the age of 45. A word of caution: if radiographs are pulled

from multiple sources, additional variables will be introduced into the data set based on the patient demographics of different hospitals and clinics and their particular treatment policies. Private clinics will treat a particular type of patient a particular way, while public hospitals will treat a different demography of patients. Patients at private clinics will consistently have insurance and belong to the middle and upper economic classes. Poorer individuals, without insurance would be found at public hospitals. However, treatment protocol between medical institutions and even between individual doctors may also differ. At some clinics a fracture of the humeral shaft may be treated with a cast and at other clinics the same fracture would be treated with internal fixation of a plate and screws. Therefore, factors such as patient demographics and fracture treatment protocols should not be overlooked if samples are drawn from multiple sources.

Future research, should also attempt to address the issue of how images of bone healing differ between live and decomposed bodies. The current study investigates living specimen in order to draw inferences about deceased individuals to be used by forensic anthropologists. Therefore, one future study needs to analyze how healing stages can be identified on forensic specimen and how these observations correlate to the stages observed in radiographic images of living individuals as in the current study.

The last issue to address is the one of inter- and intra-observer error during the identification of healing stages in the radiographs. The stages adopted in this study are well-defined and a keen eye for detail should have no problem in identifying the same stages of fracture healing in any subsequent studies of related topics. At such a point in time, inter-observer error can be tested. In this study, intra-observer error was minimal as the data set was staged twice and a subsample of two hundred x-rays a third time.

Conclusion

This project investigated the effect that age, sex, ancestry, if the fractured bone was weight-bearing, and where the method of treatment was located has on the speed of fracture healing and remodeling. The speed of bone remodeling was inferred from the characteristics of fractured long bones as they progress through a set of six predefined stages that are observable on radiographs. Of the factors considered in this study, only age consistently showed a significant degree of correlation in variance with the various stages of fracture repair.

This project found that there are a variety of different reasons that can be responsible for the degree of variation observed in fracture healing. To suggest a strong dating timeline for fractures from radiographic observations is not advisable at this point. Additional research is needed to investigate particular factors individually in settings where other factors influencing fracture healing are controlled. Hopefully, the current research will provide a basis from which such future studies will spring.

Eventually, several small scale projects and studies may be pulled together to establish a research-supported dating technique for post-traumatic healing. At such a point, physical anthropologists will be able to assign ages to partially healed fractures. In forensic anthropology dating of fractures may prove to be a valuable tool in the identification of unknown skeletal remains. We will be able to give names to bodies and eliminate worrisome uncertainty for families and friends of the deceased.

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Appendix

Application for Exemption from Institutional Oversight

IRB #: 2693 LSU Proposal #: _____ Revised: 03/24/2004

LSU INSTITUTIONAL REVIEW BOARD (IRB) for HUMAN RESEARCH SUBJECT PROTECTION

Study exempted by: David Boyd, Chair, Institutional Review Board, 203 B-1 David Boyd Hall, 225-578-8692

APPLICATION FOR EXEMPTION FROM INSTITUTIONAL OVERSIGHT

Unless they are qualified as meeting the specific criteria for exemption from Institutional Review Board (IRB) oversight, ALL LSU research/projects using living humans as subjects, or samples or data obtained from humans, directly or indirectly, with or without their consent, must be approved or exempted in advance by the LSU IRB. This Form helps the PI determine if a project may be exempted, and is used to request an exemption.

Instructions: Complete this form.

If it appears that your study qualifies for exemption send:

- (A) Two copies of this completed form,
(B) A brief project description (adequate to evaluate risks to subjects and to explain your responses to Parts A & B),
(C) Copies of all instruments to be used. If this proposal is a part of a grant proposal include a copy of the proposal and all recruitment material.
(D) The consent form that you will use in the study

to: ONE screening committee member (listed at the end of this form) in the most closely related department/discipline or to IRB office.

If exemption seems likely, submit it. If not, submit regular IRB application. Help is available from Dr. Robert Mathews, 578-8692, irb@lsu.edu or any screening committee member.

Principal Investigator Kevin B Hufnagl Student? [Y] N

Ph: (406) 780 1541 E-mail gyrosscope@yahoo.com Dept/Unit Dept of Geog + Anth

If Student, name supervising professor Mary Manheim Ph: _____

Mailing Address 835 Azalea ST, Apt #3 Baton Rouge, LA 70802 Ph _____

Project Title Radiographic Analysis of Fractures to Establish Time since Injury

Agency expected to fund project Self + Dept. of Geography & Anthropology

Subject pool (e.g. Psychology Students) Medical Patients

Circle any "vulnerable populations" to be used: (children <18; the mentally impaired, pregnant women, the aged, other). Projects with incarcerated persons cannot be exempted.

I certify my responses are accurate and complete. If the project scope or design is later changed I will resubmit for review. I will obtain written approval from the Authorized Representative of all non-LSU institutions in which the study is conducted.

PI Signature [Signature] Date 5/20/04 (no per signatures)

Screening Committee Action: Exempted [X] Not Exempted _____ Category/Paragraph 4

Reviewer Mathews Signature [Signature] Date 5/27/04

Part A: DETERMINATION OF "RESEARCH" and POTENTIAL FOR RISK

This section determines whether the project meets the Department of Health and Human Services definition of "research" and if not, whether it nevertheless presents more than "minimal risk" to humans that

makes IRB review prudent and necessary.

1. Is the project a systematic investigation designed to develop or contribute to generalizable knowledge?

(Note "systematic investigation" includes "research development, testing and evaluation"; therefore some instructional development and service programs will include a "research" component).

YES

NO

2. Does the project present physical, psychological, social or legal risks to the participants reasonably expected to exceed those risks normally experienced in daily life or in routine diagnostic physical or psychological examination or testing? You must consider the consequences if individual data inadvertently become public.

YES Stop. This research cannot be exempted--submit application for IRB review.

NO Continue to see if research can be exempted from IRB oversight

3. Are any of your participants incarcerated?

YES Stop. This research cannot be exempted--submit application for IRB review.

NO Continue to see if research can be exempted from IRB oversight.

4. Are you obtaining any health information from a health care provider that contains any of the identifiers listed below?

A. Names

B. Address: street address, city, county, precinct, ZIP code, and their equivalent geocodes. Exception for ZIP codes: The initial three digits of the ZIP Code may be used, if according to current publicly available data from the Bureau of the Census: (1) The geographic unit formed by combining all ZIP codes with the same three initial digits contains more than 20,000 people; and (2) the initial three digits of a ZIP code for all such geographic units containing 20,000 or fewer people is changed to '000'.

(Note: The 17 currently restricted 3-digit ZIP codes to be replaced with '000' include: 036, 059, 063, 102, 203, 556, 692, 790, 821, 823, 830, 831, 878, 879, 884, 890, and 893.)

C. Dates related to individuals

i. Birth date

ii. Admission date

iii. Discharge date

iv. Date of death

v. And all ages over 89 and all elements of dates (including year) indicative of such age. Such ages and elements may be aggregated into

- a single category of age 90 or older.
- D. Telephone numbers;
- E. Fax numbers;
- F. Electronic mail addresses;
- G. Social security numbers;
- H. Medical record numbers; (including prescription numbers and clinical trial numbers)
- I. Health plan beneficiary numbers;
- J. Account numbers;
- K. Certificate/license numbers;
- L. Vehicle identifiers and serial numbers including license plate numbers;
- M. Device identifiers and serial numbers;
- N. Web Universal Resource Locators (URLs);
- O. Internet Protocol (IP) address numbers;
- P. Biometric identifiers, including finger and voice prints;
- Q. Full face photographic images and any comparable images; and
- R. Any other unique identifying number, characteristic, or code; except a code used for re-identification purposes; and
- S. The facility does not have actual knowledge that the information could be used alone or in combination with other information to identify an individual who is the subject of the information.

YES Stop. This research cannot be exempted--submit application for IRB review.

NO Continue to see if research can be exempted from IRB oversight.

Part B: EXEMPTION CRITERIA FOR RESEARCH PROJECTS

Research is exemptible when all research methods are one or more of the following five categories. Check statements that apply to your study:

1. In education setting, research to evaluate normal educational practices.

2. For research not involving vulnerable people [prisoner, fetus, pregnancy, children, or mentally impaired]: observe public behavior (including participatory observation), or do interviews or surveys or educational tests:

The research must also comply with one of the following: either that

a) the participants cannot be identified, directly or statistically;

or that

b) the responses/observations could not harm participants if made public;

or that

c) federal statute(s) completely protect

all participants' confidentiality;

or that

3. For research not involving vulnerable people [prisoner, fetus, pregnancy, children, or mentally impaired]: observe public behavior (including participatory observation), or do interviews or surveys or educational tests:

d) all respondents are elected, appointed, or candidates for public officials.

4. Uses only existing data, documents, records, or specimens properly obtained.

The research must also comply with one of the following:

either that:

a) subjects cannot be identified in the research data directly or statistically, and no-one can trace back from research data to identify a participant;

or that

b) the sources are publicly available

5. Research or demonstration service/care programs, e.g. health care delivery.

The research must also comply with all of the following:

a) It is directly conducted or approved by the head of a US Govt. department or agency

and that

b) it concerns only issues under usual administrative control (48 Fed Reg 9268-9), e.g., regulations, eligibility, services, or delivery systems;

and that

c) its research/evaluation methods are also exempt from IRB review.

6. For research not involving vulnerable volunteers [see 2 & 3" above], do food research to evaluate quality, taste, or consumer acceptance.

The research must also comply with one of the following:

either that

a) the food has no additives;



or that

b) the food is certified safe by the USDA, FDA, or EPA.

NOTE: Copies of your IRB stamped consent form must be used in obtaining consent. Even when exempted, the researcher is required to exercise prudence in protecting the interests of research subjects, obtain informed consent if appropriate, and must conform to the Ethical Principles and Guidelines for the Protection of Human Subjects (Belmont Report), 45 CFR 46, and LSU Guide to Informed Consent; (Available from OSP or [http://aapl022.lsu.edu/osp/osp.nsf/\\$Content/LSU%20IRB%20Documents](http://aapl022.lsu.edu/osp/osp.nsf/$Content/LSU%20IRB%20Documents))

HUMAN SUBJECTS SCREENING COMMITTEE MEMBERS can assist & review:

COLLEGE OF ARTS AND SCIENCES:

MASS COMMUN/SOC WK/AG:

Dr. Lerman * (Psych) 578-4118	Dr. Nelson (Mass C) 578-6686
Dr. Geiselman * (Psych) 763-2695	Dr. Archambeault (Soc Wk) 8-1374
Dr. Beggs (Socio) 578-1119	Dr. Rose (Soc Wk) 578-1015
Dr. Honeycutt (Com.Stu) 578-6676	Dr. Keenan* (Hum Ecol) 578-1708
Dr. Dixit (Comm Sc./Dis) 578-3938	Dr. Belleau (Hum Ecol) 578-1535

ED/LIBRARIES/INFO SCI

BUSINESS

Dr. Kleiner (Middleton) 578-2217	Dr. Biswas (Marketing) 578-8818
Dr. Culross (Education) 578-2254	
Dr. Landin* (Kinesiol) 578-2916	
Dr. MacGregor (ELRC) 578-2150	
Dr. Munro* (Curric & I) 578-2352	

(* = IRB member)

Vita

Kevin Benjamin Dominic Peter Hufnagl was born in Wasserburg, Germany, and spent the first thirteen years of his life in Germany. In 1993 he moved to Lisbon, Iowa, where he received his high school education, graduating in 1998. In 2002, he received a Bachelor of Science in mathematics and archaeology from the University of Wisconsin at La Crosse. Following a year of anatomy and physiology courses at Montana State University, he entered the anthropology master's program at Louisiana State University (LSU) with a full-time graduate assistantship.

While at LSU, Kevin worked in the Forensic Anthropology and Computer Enhancement Services (FACES) Laboratory, assisting with casework and performing various laboratory duties. He was fortunate enough to be allowed to give several lectures in introductory courses of physical anthropology and participated in the Educational Outreach Program of the FACES laboratory. Kevin's future plans include beginning his doctoral studies at the University of Tennessee at Knoxville in the fall of 2005.