A PALEOPATHOLOGICAL INVESTIGATION ON THE PRESENCE OF MALARIA IN MEDIEVAL NUBIA AND THE ASSOCIATED SKELETAL LESIONS

By

Elena Ora Watson

A DISSERTATION

Submitted to
Michigan State University
in partial fulfillment of the requirements
for the degree of

Anthropology – Doctor of Philosophy

2024

ABSTRACT

The implementation of *saqia* water-wheel irrigation in ancient Nubia allowed for an expansion of cultivatable land and is considered a primary factor behind the settlement growth along the Middle Nile Valley prior to and over the course of the medieval period (~375–1500 CE). However, these anthropogenic influences are believed to have created conditions favorable to mosquito populations and concomitantly, may have resulted in elevated malaria during the medieval period. The first goal of the dissertation was to investigate this hypothesis in examining skeletal remains excavated from two cemeteries at the Fourth Cataract site of Mis Island. Towards this objective, a method was used that involved assessing the presence of five skeletal lesions that have been implicated in malarial infection. To build on current perceptions of these lesions, the second goal of this research was to examine the lesions' association with age of the individual and the association among the lesions. For one of these lesions—femoral cribra—there is a need to further understand variation in the lesion's external appearance and the bone processes underlying its expression. Therefore, the third focus of this dissertation explored several variables visible on the lesion's surface possibly associated with "activity" and "severity" which were also investigated using micro-computed tomography (micro-CT) methods.

A relatively high estimated prevalence of malaria was observed in the skeletal remains excavated from Mis Island. These findings are consistent with the hypothesis of elevated malaria in the region during the medieval period associated with the effects of settlement growth and expansion of irrigated land that accompanied *saqia* agriculture intensification. Comparisons were also conducted between the two Mis Island cemeteries to examine potential temporal differences, and between sex and age cohorts to investigate relative exposure and possible endemicity of malaria. In comparing the two cemeteries, no significant differences in estimated malarial

infection were found. Additionally, no significant differences in estimated malaria were observed between males and females. A significant association between estimated malaria and age was found, and the elevated frequencies across age groups may indicate a primarily endemic type of malaria in the region during the medieval period.

In examining the association between the suite of lesions studied in this dissertation and age of the individual, the observed age-related patterns of the porous lesions were consistent with the hypothesis that their formation may be related to anemia. Furthermore, significant associations were observed between these lesions in the subadult age groups, but not among adults. These significant associations were between most of the porous lesions included in the suite of lesions and suggest shared processes involved in their formation.

The results of femoral cribra's possible "activity" and "severity" based on its external appearance provided preliminary support for such interpretations. Femoral cribra lesions estimated to be active or healing from the surface followed an age-related pattern anticipated for such statuses. Additionally, micro-CT analyses demonstrated trabecular differences in lesions that appeared healing consistent with more bone-forming processes. Investigating the severity of femoral cribra suggested a possible lesion progression of increased trabecular exposure and size visible on the surface which may be associated with resorptive processes and/or marrow hyperplasia.

This work is dedicated to my parents.
Thank you for your incredible support throughout this journey.

ACKNOWLEDGEMENTS

The encouragement and assistance from my mentors, colleagues, family, and friends were integral to arriving at this milestone. First, I am immensely grateful for the guidance and support from my committee members, Drs. Todd Fenton, Joseph Hefner, Ethan Watrall, and Gabriel Wrobel, throughout this research process and over the course of my graduate career. My sincere thanks to my committee Chair, Dr. Fenton, for believing in me from the beginning and providing so many opportunities for me to grow as a scholar and individual. Your excitement for this research spurred me forward and our discussions about these topics were instrumental in its development and progression. Thank you, Dr. Hefner, for all the knowledge you shared with me that made me a better osteologist and researcher, for teaching me how to use R, and for all the humor over the years. Thank you, Dr. Watrall, for your guidance on topics regarding archaeology of ancient Nubia and for your support in contextualizing this research within broader perspectives. Thank you, Dr. Wrobel, for helping me develop a biocultural lens and for directing me towards and facilitating the use of micro-CT methods in this project.

I would like to express my sincere appreciation for the efforts of everyone involved in the initial excavations and subsequent curation of the human skeletal remains and archaeological material from Mis Island. Thank you to The British Museum, Sudan Archaeological Research Society, and Michigan State University for their roles in these processes and all who were part of the archaeology and research teams associated with Mis Island. I am particularly grateful for the work by Dr. Angela Soler and Dr. Carolyn Isaac and the impact their research had on my own. To Dr. Isaac, thank you also for your insights on this project and your kind mentorship since the beginning. I would also like to thank Lilli Antonelli and Savannah Sass for their assistance during the data collection process in the lab during the early phases of this research. My thanks also to alumni Dr. Emily Streetman and Dr. Jared Beatrice for their insights related to my research interests.

The micro-CT component of this dissertation would not have been possible with the assistance of Jeremy Hix of the MSU Radiology IQ Advanced Molecular Imaging Facility and the Institute for Quantitative Health Sciences and Engineering. Thank you so much, Jeremy, for all your help in scanning and your guidance with the software for analysis.

My many thanks for the support provided by the Department of Anthropology and College of Social Science. I would like to thank our current and previous Graduate Program Directors, Drs. Stacey Camp and Mindy Morgan, and department staff including Joan Reid, Roxanne Moran, Jocelyn Janicek, Kathy McGlynn, and Cathi Pierce. Thank you to everyone with the Division of Human Anatomy for supporting me and cheering me on to the finish line. My particular thanks to Dr. Nicole Geske, Dr. Lindsey Jenny, Dr. Melanie McCollum, Bill McMillan, Alex Pereida, Tim Currie-Dennis, Erin Lyon, and Josh Vincent.

I have had the great honor to meet and work with amazing fellow graduate students during my time at MSU. Dr. Mari Isa and Alex Goots are two of the most caring people I know, and I am forever grateful for their friendship. Memories of our adventures will always bring me joy. To Dr. Jen Vollner, Dr. Caitlin Vogelsberg, Dr. Emily Streetman, Dr. Amber Plemons, Dr. Kelly Kamnikar, Micayla Spiros, Rhian Dunn, Clara Devota, and Aubree Marshall, thank you so much for your camaraderie over the years.

Finally, I cannot thank my family and friends enough for everything, especially my parents and brother. It certainly “took a village”—thank you to everyone part of that village not named here.

TABLE OF CONTENTS

CHAPTER ONE: INTRODUCTION

Malaria has a pervasive presence around the world that has afflicted generations of people living in environments conducive to the mosquito, which transmits the disease-causing parasite. Within these contexts, there is a dynamic and interdependent interaction between human hosts, mosquito vectors, and malarial parasites as human activity within the environment can further influence risk and exposure to this disease. For people living in the Nile River Valley, malaria has historically had a significant effect on morbidity and mortality. In ancient Nubia, malaria is believed to have posed a high burden and risk during the medieval period due to an increase in human population and settlement along the Nile River facilitated by an intensification of *saqia* water-wheel irrigation agriculture.

Prior to and over the course of the medieval period (375–1500 CE), there was a significant population increase along the Middle Nile Valley, with a rapid growth of rural settlements in Northern Nubia and the Dongola Reach during the sixth century (Obłuski, 2020). This expansion is attributed to the heightened implementation of *saqia* water-wheel irrigation, which facilitated farming for extended harvesting seasons and enabled a population growth in areas that were previously less inhabited along the Nile (Malcom et al., 2007; Obłuski, 2020). However, the intensification of *saqia* irrigation during this period is believed to have created conditions posing a particularly high risk of malaria (Malcom et al., 2007). These shifts in human population and farming practice with an accompanying increase in cultivatable land are hypothesized to have created conditions favorable for an increase in mosquito populations and concomitantly, malaria. With such circumstances favorable for increased malarial risk, this irrigation technology may have had deleterious impact on public health (Judd, 2004).

This dissertation research investigates hypothesized malarial infection in Nubia during the medieval period and the potential impact of these events using paleopathological approaches and a biocultural framework. The dissertation focuses on the skeletal remains excavated from two medieval cemeteries at the Upper Nubian site of Mis Island, located near the Fourth Cataract of the Nile River. As part of the Merowe Dam Salvage Archaeology Project (MDASP), the Mis Island skeletal sample was excavated by the British Museum and the Sudan Archaeological Research Society and was curated at Michigan State University. To investigate the presence of malarial infection, this research used an approach developed by Smith-Guzmán (2015a) which entails examining skeletal remains for a series of five lesions as possible indicators of the disease. These lesions are cribra orbitalia, humeral cribra, femoral cribra, spinal porosity, and periosteal reaction. A diagnostic outcome algorithm was then used based on these lesions to infer how many and which individuals may have been infected with malaria. While some of these skeletal lesions have been the focus of research on their expression and co-occurrence, others have received less attention and the combination of all five has not been extensively examined since Smith-Guzmán's (2015a) study.

Within the field of bioarchaeology, there is a need to thoroughly understand the formation and expression of paleopathological lesions regarding the processes involved in their manifestation and variation among individuals (DeWitte and Stojanowski, 2015). Towards this, an evaluation of skeletal lesions encountered in archaeological material can benefit from an approach that involves systematically examining the morphology and distribution of lesions, and considering the biological processes associated with the anatomical site (Mays, 2018). To build on current perceptions of the skeletal lesions implicated in malarial infection, this dissertation therefore examines the lesions' relationship with the affected individual's age, as well as the association among these lesions, to contribute further insight into their development and patterns of expression. For one of these lesions—femoral cribra—there is a need to further understand variation in the lesion's external appearance and the bone processes underlying its expression.

Femoral cribra is a porous lesion on the anterior-inferior femoral neck that has been surrounded by a history of disagreement and ambiguity, which has extended into current understandings of the lesion (Göhring, 2021). In addition to uncertainties regarding its etiology, variation in its appearance has led to contrasting interpretations of its presence. With current understandings of femoral cribra as a pathological stress marker, associated insight into possible lesion "severity" and "activity" is needed. Such information aids in interpretating its presence, in that assessing whether the lesion might be active or healing can help in separating disease processes that were ongoing at the time of death from those that may have been inactive (Wood et al., 1992). To address these needs, this dissertation research involved visually examining femoral cribra lesions for several variables possibly representing lesion "severity" and "activity" and assessed their association with the age of the individual. Additionally, micro-computed tomography (micro-CT) methods were used to investigate the relationship between changes visible from femoral cribra's external surface and the types of bone processes occurring at the trabecular level.

The site of Mis Island

The site of Mis Island was situated upstream of the Nile's Fourth Cataract in modern day Sudan. Excavation of Mis Island, as well as multiple sites along the Fourth Cataract, began as part of a large salvage archaeological project initiated by the Sudan Archaeological Research Society (SARS) in response to the planned construction of the Merowe Dam. Now inundated by the dam, the site lies under the Merowe Reservoir. Mis Island was less than 2km across east to west and approximately 1km north to south. Before being flooded, the islands in this stretch of the Nile were described as having a desert landscape at their centers with oasis-like vegetation closer to the riverbanks (Welsh, 2013). The riverbanks of these islands at the Fourth Cataract were rocky with narrow areas of fertile soil (Näser, 2007). The Nile Valley adjacent to Mis Island and its neighboring islands was closely bordered by desert (Welsh, 2013).

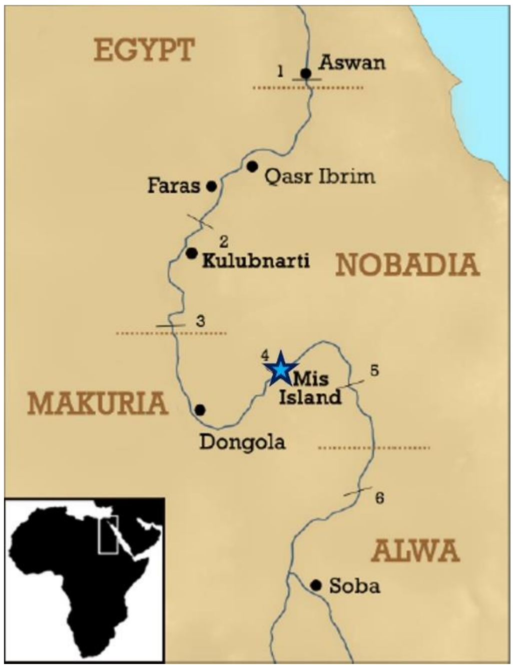

Figure 1.1: Map of medieval Nubia showing the location of Mis Island, adapted from Hurst (2013:28) (star added to mark location of Mis Island).

In the 1980s, the Sudan government renewed interest in a project first proposed in 1942 to build a dam at this region of the Nile (Ahmed, 2014a; Welsby, 2003). The National Corporation for Antiquities and Museums (NCAM) recognized that the engineering activities and concomitant flooding associated with this dam had the potential to affect numerous archaeological sites in the Fourth Cataract region (Ahmed, 2014a). In response to the anticipated inundation of archaeological sites, the NCAM recruited several international archaeological groups to be involved in the Merowe Dam Archaeological Salvage Project (MDASP) before completion of the dam in 2009 (Ahmed, 2014a; Welsby, 2003). Mis Island resided within the concession headed by the Sudan Archaeological Research Society (SARS) which involved approximately 40km of the Nile's left bank between Amri and Kirkbekan and the immediate islands (Ahmed, 2014a; Welsby, 2006). The SARS concession was headed by Project Director Derek Welsby and the Field Director for the area including Mis Island was Andrew Ginns (Ahmed, 2014a). First surveyed in 1999, a total of fifteen archaeological sites on Mis Island were identified, six of which were investigated further through excavations in the 2005–2006 and 2006–2007 field seasons by SARS and the British Museum (Ginns 2007, 2006). The primary sites excavated are as follows: a Late Christian church and associated cemetery referred to as 3-J-18 near the center of the island; cemetery 3-J-10 located 300m north of the church; cemetery 3-J-11 at the northern border of the island; cemetery 3-J-20 at the highest elevation on the east side of Mis; medieval settlement 3-J-19 located 50m east of the church and north of cemetery 3-J-20; and Kerma cemetery 3-J-22 50m south of cemetery 3-J-11 (Ginns 2007, 2006).

While archaeological findings demonstrate that Mis Island was inhabited in the Kerma and Meroitic periods and through the medieval phases, the majority of work on Mis Island concentrated on its medieval occupation dating from the mid-fifth to early fifteenth centuries CE (Ginns, 2006). Mis Island represented a small rural community situated in the territory of the medieval Nubian kingdom of Makuria (Welsby, 2002). Medieval settlement at Mis Island is observed by its primary sites of a late Christian church, a settlement, and several cemeteries. Also observed on Mis Island are Muslim burials associated with the end of the medieval period (Ginns, 2010a) which were not excavated to comply with religious observations (Soler, 2012). The Muslim cemetery remained in use by modern inhabitants until construction of the dam, demonstrating the continuous occupation of Mis Island (Ginns, 2010a).

Through multiple bioarchaeological research studies, the site of Mis Island has provided a unique window into medieval Nubian history and rural life. Previous paleopathological research on Mis Island includes examining the effects of stress and disease on the skeletal health of adults (Soler, 2012) and subadults (Hurst, 2013) excavated from two cemeteries: cemetery 3-J-10 (1100–1500 CE) and cemetery 3-J-11 (300–1400 CE). Among the adult individuals from these cemeteries, Soler (2012) found a high frequency of paleopathological lesions suggestive of stress that are not specific to a certain condition; however, the majority of these lesions demonstrated healed expressions. In examining these non-specific lesions in the subadult remains, Hurst (2013) observed a higher prevalence of stress indicators compared to the adult group and more active expression of the lesions in younger individuals. Soler and Hurst propose that the inhabitants of Mis Island during the medieval period experienced high levels of stress early in life but were also able to survive and recover from stress experienced in childhood and adulthood.

Research goals

This study focuses on the following research goals:

- To investigate the skeletal indication of malaria at Mis Island during the medieval period and how prevalent the disease may have been within the context of settlement patterns and irrigation technology.
- To examine potential temporal fluctuations in the disease during the medieval period potentially associated with changes in the Nile River's levels.
- To assess these individuals' experiences of malaria as they relate to possible exposure and endemicity of the disease.

- To consider the formation and consistency in the skeletal lesions' expression associated with hypothesized malarial infection.
- To explore patterns between variables observed on the external surface of femoral cribra potentially related to lesion "severity" and "activity" and if these are supported by the underlying trabecular microarchitecture.

Malarial risk and transmission are heavily influenced by human activity and interactions with their environment. This research intends to contribute to our understanding of the host-pathogen relationship within the context of events taking place in medieval Nubia. Investigating the dynamics of malaria in Nubia during the medieval period builds on the scholarship of health conditions for these communities and contributes insight into the potential influence of human activity on the endemicity of malaria during this time. With further understanding of the expression and formation of the skeletal lesions suggestive of malaria, this research also seeks to elucidate discussions regarding anemia, porous lesions, and changes in red bone marrow. A more coherent awareness of the biological processes underlying femoral cribra can be used in conjunction with other lines of evidence to construct appropriate interpretations from archaeological material. Recognizing differences in lesion expression possibly related to "severity" and "activity" can further aid in investigating disease pathogenesis and epidemiological patterns.

Organization of the dissertation research

Towards addressing these research objectives, this dissertation is organized into the following chapters. Chapter Two discusses bioarchaeological research on malaria and insights into the disease in the Nile River Valley, including the dynamic ecology of the Nile River and previous research on malaria in this setting. The archaeology of ancient Nubia is then discussed with a focus on the archaeological understandings and historical context of ancient Nubia spanning the Napatan to medieval periods (~800 BCE –1500 CE). Chapter Three presents research relevant to the paleopathology of anemia and the skeletal lesions implicated in malarial infection. After highlighting skeletal considerations in the pathophysiology of malaria, the trajectory of research on anemia in paleopathology is presented. Previous research examining the association between the skeletal lesions of interest and age of the individual, as well as the co-occurrence among the skeletal lesions, is also reviewed. Finally, previous work regarding the lesion femoral cribra is described including its proposed etiologies, variation in morphology on the lesion's surface, and its correlation with age of the individual.

Chapter Four details the research questions examined in this dissertation and the expected outcomes of each question with supporting information. Chapter Five describes the materials and methods associated with the dissertation and is organized by research questions that share common methods, subsamples, and statistical approaches. The skeletal remains that comprise the Mis Island sample are first discussed, followed by the data collection procedures, and finally the data analysis methods. In Chapter Six, the results of the data analyses are presented and organized by research question with descriptions regarding the patterns observed and the associated significance of the statistical tests. Finally, Chapter Seven provides a discussion that interprets and contextualizes the results of the data analyses. This chapter begins with a discussion on the estimated presence and prevalence of malaria at Mis Island during the medieval period, followed by interpretations of the investigation into the skeletal lesions implicated in hypothesized malaria, and finally a synthesis on the exploration of femoral cribra. Concluding thoughts, limitations of the study, and directions for future research are also presented at the end.

CHAPTER TWO: BIOARCHAEOLOGY OF MALARIA, MALARIA IN THE NILE RIVER VALLEY, & ARCHAEOLOGY OF ANCIENT NUBIA

This chapter begins with a review of researching malaria in bioarchaeology, including the use of a biocultural model and the current methodological approaches. The next section provides an overview of the ecological context of the Nile River as it relates to the malaria parasite's vector—mosquitoes—and discusses previous research examining malaria in the Nile River Valley. The final section presents archaeological insights and historical context of ancient Nubia spanning the Napatan to Medieval periods (~800 BCE–1500 CE). After providing a geographical and historical background, this section presents the major archaeological understandings progressing through the following time periods: Napatan Kingdom, Meroitic Empire, Post-Meroitic Period, and Medieval Period.

Bioarchaeology of malaria

Given the dynamic and interdependent interaction between human hosts, mosquito vectors, and malarial parasites in suitable environments, a biocultural approach is well-suited to investigations of malaria in past populations. A biocultural model enables exploration of the associations between social and cultural practices and their impact on human biology to generate inferences regarding archaeological questions and to better understand human-disease systems. In bioarchaeological research on malaria, this approach involves the incorporation of archaeological, epidemiological, historical, entomological, environmental, and when available, genetic insights and information related to the disease process of malaria (Marciniak et al., 2018; Smith-Guzmán et al., 2016). Such work thus examines how the presence of malaria and its multifaceted epidemiology is influenced by variables related to disease ecology and interactions between human hosts and their environment (Marciniak et al., 2018). A biocultural model to studying malaria in archaeological contexts involves examination of sociocultural, biological, and environmental variables operating at the macro- and micro-levels that interact to influence malarial infection at the archaeological site(s) of interest. Social and economic forces that could have influenced the dynamics of malaria in past communities include agriculture, population density, migration, trade, and construction activity (Marciniak et al., 2018). If such information is available, consideration of the presence and frequency of genetic conditions that provide some resistance to malaria and lessen infection severity (e.g., G6PD, thalassemia, sickle cell) should be included (Marciniak et al., 2018). However, in their study of malaria in Imperial Italy, Marciniak and colleagues (2018) note that the contemporary frequencies of resistance genes may not be directly representative of the past population they studied.

By drawing on these lines of evidence to study past malarial dynamics in a given spatial and temporal context, various research questions can be examined that range from more local to broad-scale foci. Within the setting of 1st–4th centuries central-southern Italy, Marciniak et al. (2018) reflect on comparing the presence of malaria between several sites that differ in environmental conditions, population structure and movement, and economic activity—discussing how such factors can impact experience of the disease within those communities. Bioarchaeological inquiry into malaria has also investigated the possibility of this disease as the source behind specific epidemics that significantly impacted past populations. Smith-Guzmán and colleagues (2016) explore the possibility of malaria as a disease behind the “Hittite plague” (1322 BCE) in a study of skeletal remains from Amarna, Egypt (1349–1332 BCE). This study also provides an example of considering epidemiological patterns of malaria (i.e., epidemic or endemic malaria).

With reference to climate change and its associated impacts on disease, Gowland and Western (2012) use a spatial epidemiological approach to explore the prevalence of skeletal indicators of poor health as signs of malaria in eastern England during the early to mid-Anglo-Saxon period—a time of climatic events that resulted in flooding of low-land areas and warmer temperatures in the region. The authors contextualize their study with historical records that describe endemic outbreaks consistent with malarial infection associated with the region's low-lying wetland areas. Gowland and Western map and compare the frequency of cribra orbitalia with the distribution of large populations of *Anopheline* mosquitos, lower altitude and marshy environments, and higher incidence of historic references to malaria across England. Gowland and Western conclude that the observed pattern of cribra orbitalia is most likely attributable to endemic malaria, in conjunction with coexisting diseases that can also contribute to severe malarial anemia. Another broad-scale study of malaria in the past, conducted by Smith-Guzmán (2015b), investigates the disease's prevalence and spread within the ancient Nile Valley region. The goal of this research was to analyze the spatiotemporal variation in reported cribra orbitalia rates from archaeological sites along the Nile Valley to infer the possible pervasiveness and distribution of malaria in the region, while also considering theoretical models of malaria's spread out of Africa.

While a correlation between cribra orbitalia and malaria has been presented, an analytical method developed by Smith-Guzmán (2015a) provides a more specific model for investigating the potential presence of malaria in past populations. Smith-Guzmán used an epidemiological approach to examine the prevalence of a series of paleopathological lesions in two modern skeletal samples. One of these samples was comprised of individuals from Uganda and adjacent East African countries where malaria is holoendemic and widespread in the population, and the other sample included individuals from the United States where malaria has been eradicated. In comparing these two samples, five lesions were observed more frequently in the sample endemic with malaria compared to the malaria-free sample. These five skeletal lesions are cribra orbitalia, humeral cribra, femoral cribra, spinal porosity, and periosteal reaction. Based on the patterns and associations of these lesions, Smith-Guzmán developed an algorithm of criteria that could indicate whether an individual may have been infected with malaria. Along with additional lines of evidence (e.g., archaeological, historical, ecological) in a study's context, the presence of these lesions has been interpreted as support for the possible presence of malaria within the sample (Buzon and Sanders, 2016; Smith-Guzmán et al., 2016).

In addition to gross skeletal examination, malarial detection methods in paleopathology include ancient DNA (aDNA) and immunological testing. Setzer (2014) describes gross examination of skeletal remains as associating skeletal indicators of anemia with ecological and historical information. While this approach provides insight into possible prevalence of infection, skeletal lesions are not specific to malaria as other disease processes could contribute to their formation. To test for malaria directly in archaeological remains, aDNA analysis is used and is considered the most definitive method for identifying malaria in archaeological remains.

Malaria in the Nile River Valley

Environmental conditions along most of the Nile River provide suitable habitats for the mosquito vector *Anopheles arabiensis*, the local populations of which are constrained to the marshy riverbanks and dependent on human population density (Malcolm et al., 2007). The annual flooding of the Nile offers particularly favorable breeding conditions for *An. arabiensis* mosquitoes as isolated pools are created from receding river levels (Scheidel, 2001). In a study of these mosquito vectors between the Third Cataract and Abu Hammed in the modern Northern

State of Sudan, Ageep and colleagues (2009) observed a seasonal pattern in mosquito population numbers that is associated with the fluctuations of the Nile River's levels. Most of the *An. arabiensis* presence in this region is focused along the main Nile River channel. As the river level rises, mosquito numbers decrease due to the disruption of breeding sites. However, as the river level falls again, stagnant pools of water are created which provide optimal breeding sites and a concomitant increase in population size. This ecological relationship creates a seasonal pattern observed by Ageep et al. during which larvae populations are lowest between July and October and quickly grow when the river recedes in November. While this cycle occurs along the river, the authors note how artificial habitats located away from the channel may not be affected by such fluctuations and thus, provide additional breeding sites that are more consistent.

Accounts from ancient Egypt describe a surge in mosquitoes following the Nile's inundation and reference an accompanying risk of illness that implicates malarial infection (Sabbatani et al., 2010; Scheidel, 2001). Multiple studies have detected the presence of malaria in ancient Egypt through ancient DNA analysis (Hawass et al., 2010; Lalremruata et al., 2013; Nerlich et al., 2008) and immunological techniques (Al-Khafif et al., 2018; Bianucci et al., 2008; Loufouma-Mbouaka et al., 2020; Miller et al., 1994; Rabino Massa et al., 2000). Similar work in ancient Nubia is represented by the detection of falciparum malaria in an individual from North Argin near the Second Cataract during the Ballana period (350–550 CE) (Miller et al, 1994). While these confirmatory tests provide evidence for the presence of malaria, paleopathological approaches examining skeletal lesions have provided insight into its prevalence and extent in the ancient Nile River region.

Smith-Guzmán's (2015a) method of estimating malaria from a series of skeletal lesions has been used in two studies from the Nile River Valley region. In a study of skeletal remains from Amarna, Egypt (1349–1332 BCE), Smith-Guzmán and colleagues (2016) explore the possibility of malaria as a disease behind the "Hittite plague" (1322 BCE). The prevalence of skeletal lesions in the sample indicates endemic malaria at Amarna during this time based on about half of the individuals showing signs of infection and a higher morbidity and mortality of subadults and reproductive-age females. This approach was also used in studying the skeletal remains excavated from Tombos (~1400–650 BCE), an Upper Nubian site located at the Third Cataract (Buzon and Sanders, 2016). Examining the skeletal lesions suggestive of malaria at Tombos revealed a relatively prevalent rate of infection with abundant spinal lesions. Whereas Amarna and Tombos represent urban centers within their respective contexts, this approach for exploring the prevalence of malaria has not been conducted on a rural settlement in the Nile River Valley, or at a medieval site when malarial burden is believed to have been elevated in Nubia.

Archaeology of Ancient Nubia

The geographical scope of Nubia covers the land in modern-day Egypt and Sudan between the First Cataract of the Nile River and the convergence of the White and Blue Nile Rivers. Coursing through this region is the Nile River with the Eastern and Western deserts on either side (Barbour, 1961). The Nile Valley encompasses the river and adjacent alluvial land, which typically does not exceed 2km in width (Barbour, 1961). A series of rocky cataracts positioned along the Nile River serve as points of reference when dividing the Nubian Nile Valley into regions. The main Nile maintains its flow throughout the year with water supply from the White Nile and rapidly floods during the summer from the Blue Nile (Barbour, 1961). Besides the Nile River, most of the waterways in Nubia do not hold water year-round (Barbour, 1961). Therefore, the Nile River Valley is vital to human settlement in this region. As demonstrated by Butzer's (1976) ecological approach to studying ancient Egypt, the Nile and its fluctuations in water supply had pervasive effects on inhabitants of the Valley regarding their settlement patterns, irrigation strategies, population capacities, and cultural institutions over time.

The earliest formal archaeological research on ancient Nubia commenced in the beginning of the twentieth century, shortly after Sudan became under the control of Britain and Egypt (Welsby, 2004). Throughout the history of ancient Nubian archaeology, much of the work has been driven by development and construction of dams on the Nile River and thus represent rescue operations. While these salvage excavations are a focus of the following discussion, it is important to recognize the contributions to our understandings of ancient Nubia from past and present archaeological research not associated with such efforts. The first wave of formal archaeological investigation into ancient Nubia was initiated by the construction and subsequent heightening of the Aswan Low Dam at the turn of the twentieth century. In response to imminent flooding, the Egyptian government formed the First Archaeological Survey of Lower Nubia in 1907 to uncover and document historical sites in danger of being lost south of the First Cataract (Reisner, 1910). This work, led by American archaeologist George A. Reisner, marked the first systematic archaeological research of ancient Nubia (Edwards, 2004). The Second Archaeological Survey of Nubia (1929–1934) expanded archaeological study further south towards the border of Sudan (Edwards, 2004). The first substantial archaeological excavation in Upper Nubia was led by John Garstang at Meroe around the same time as Reisner's survey (Edwards, 2004).

A second phase of formal archaeological research was initiated after 1959 in preparation for the construction of the Aswan High Dam. This work represented the first regional surveys of the Sudan and extended formal archaeological research to between the Second and Third

Cataracts (Edwards, 2004). The first published synthesis of contemporary archaeological work on Nubia was written by W.Y. Adams (1964, 1965, 1966), who incorporated the accumulation of findings into a broad reconstruction of ancient Nubia, largely through the lens of processual archaeology. The Aswan High Dam greatly impacted ancient Nubian archaeology as it permanently damaged areas along the northern Nubian Valley and directed subsequent attention towards more southern sites (Edwards, 2004).

In the early twenty-first century, a third series of rescue excavations were conducted as part of the Merowe Dam Archaeological Salvage Project (MDASP). This international research project was in response to the planned construction of the Meroe Dam at the Fourth Cataract and provided new insight from the middle Nile Valley. These three general periods of rescue archaeology have contributed to the foundation of archaeological work on ancient Nubia and played significant roles in shaping its course. However, the salvage nature of this work presents its own biases and complications with incomplete sampling and an inability to revisit sites with newer approaches.

The early archaeological investigations of ancient Nubia laid the foundation for future scholarship—for example, the chronology and pottery typologies developed by Reisner and the Harvard-Boston expedition have reached modern study. However, several issues and shortcomings of the initial body of work have had a lasting legacy and should be considered in discussions of ancient Nubia. The earliest group of scholars studying ancient Nubia had backgrounds in Egyptology and therefore, viewed Nubian culture through an Egyptological lens with Egyptocentric biases (Edwards, 2004; Welsby, 2004). Due to this partiality, analyses were constructed around an ancient Egyptian narrative and many ancient Nubian indigenous features were ascribed to Egyptian influence (Edwards, 2004). While Nubia is traditionally viewed as a reflection of Egypt, its role as Egypt's source of wealth should be recognized.

Due to this Egyptological approach dominant in early works, research focused on studying the interactions between Egypt and Nubia (Welsby, 2004). A lasting effect this tradition has held over Sudanese archaeology is that it has secluded the region from being incorporated into work in other areas of Africa (e.g., Chad Basin, Ethiopian plateau), where important ties may have existed (Edwards, 2004; Welsby, 2004). This northwardly emphasis with ancient Egypt, coupled with the initial Aswan Dam construction, also contributed to early studies concentrating on sites in Lower Nubia. The lack of research and insight from Upper Nubia in earlier works is often recognized, but was not comprehensively addressed until recently with an increase in southern excavations precipitated by dam construction. Initial investigations also tended to gravitate towards visually impressive monumental sites from certain time periods (Welsby, 2004). In placing greater attention on royal and elite archaeology, information about the non-elite populace is lacking in areas of ancient Nubia's history. Significant shifts in the archaeology of ancient Nubia have occurred since about a century after the first studies started in northern Nubia (Edwards, 2004). The following discussion presents the major archaeological understandings organized into time periods beginning with the Napatan Kingdom through the medieval period. This chronology does not extend more into the past to include a discussion of the Kerma and Late Kerma periods as they are outside the focus of the current research.

Napatan Kingdom (800–300 BCE)

The Kingdom of Kush is traditionally divided into two main phases—Napatan and Meroitic—separated by the relocation of the royal cemetery from Napata to Meroe around 300 BCE (Edwards, 2004). The Napatan Kingdom was centered in the Dongola Reach and extended from the upper valleys of the White and Blue Rivers to a northern frontier that fluctuated considerably over this period depending on their situation with Egypt (Welsby 1996). The lack of evidence pertaining to Napatan origins limits associated interpretations; however, by the eighth century BCE, Alara was committed to the cult of Amun which was fundamental in establishing the Napatan 25th Dynasty and legitimizing kingship.

In the early stages of the Kushite state formation, there was conflict in Egypt between the pharaoh and the temple of Amun (Welsby, 1996). Egypt was politically divided into different states by the eighth century BCE, independently ruled by regional kings (Edwards, 2004). These circumstances set the stage for the Kushite advancement into Egypt and the establishment of the 25th Dynasty Nubian pharaohs as rulers of both Nubia and Egypt. The reverence towards Amun shown by the early Napatan rulers was a strong catalyst in their taking control of Egypt (Welsby, 1996). While the motives of the 25th Dynasty were ideologically deterministic, the political aspirations of these rulers should also be acknowledged in their efforts to legitimize authority. The 25th Dynasty included six Nubian rulers who reigned between approximately 740–660 BCE (Edwards, 2004). After war broke out with the Assyrians and a period of aggression ensued, the Kushite rule in Egypt was eventually ended by the Assyrians.

Settlement during the Napatan period was focused along the Dongola Reach with centers around Tabo and Kawa (Edwards, 2004). Beyond a relatively substantial settlement around the Second Cataract, evidence of Napatan settlement in Lower Nubia is minimal (Edwards, 2004). The thinly scattered settlement pattern in Lower Nubia may reflect Napatan political and economic intentions to create enough of a connection between two foci—the Kushite centers further south and Egypt to the north (Edwards, 2004). By the 25th Dynasty, Napatan settlement is visible at Meroe, which would later become the Kushite capital (Edwards, 2004). With the revival of the Amun cult, Jebel Barkal expanded from continuous construction of Napatan temples and palaces by the Kushite kings (Edwards, 2004). In the Bayuda region and Western Desert, remnants of Napatan settlements may suggest some conflict between Kushite and non-Kushite people (Lohwasser, 2014). This theory of conflict is also indicated by historical records describing aggression between Kushites and the "Western Desert People".

The earliest royal Nubian pyramid burials were established el Kurru and Nuri, with five of the six 25th Dynasty pharaohs interred at el Kurru and Taharqo marking the beginning of the cemetery at Nuri (Edwards, 2004). The pyramid tombs of the Napatan pharaohs and their associated mortuary features demonstrate the significant ties the royal elite had to Egyptian politics and ideologies. Towards the end of the Napatan period after the death of Aspelta, the pyramids became increasingly untidy with poorly imitated hieroglyphs, representing a dissolving connection with Egyptian culture (Adams, 1964).

Knowledge of non-royal Napatan burials is broadly limited; however, some insight into mortuary ideologies over the Napatan period has been illuminated. A large cemetery at Sanam and two smaller ones at Meroe contained an array of mortuary customs, as some conveyed more Egyptian traditions and others displayed more indigenous pre-Napatan styles (Edwards, 2004). Pyramid burials similar to those at Nuri but on a smaller scale at these sites signify the presence of local elites. Non-elite Napatan burials uncovered around the Fourth Cataract also demonstrate a great degree of variation in mortuary characteristics and tomb superstructures, with most representing a continuation of traditions from previous time periods (Ahmed, 2014b). The variation in Egyptian and Nubian traditions visible in Napatan burials preclude the identification of a "typical Napatan" mortuary form (Edwards, 2004).

Meroitic Empire (300 BCE–350 CE)

In the last centuries of the first millennium BCE, a Kushite state emerged with a new center at Meroe between the Sixth and Fifth Cataracts. The beginning of the Meroitic period is marked by the royal cemetery relocating from Napata (el-Kurru and Nuri) to Meroe with the burial of King Arkamani (Edwards, 2004). This move may represent a symbolic re-focusing of power, as some inscriptions allude to dynastic upheaval around this transition (Edwards, 2004). While the totality of evidence suggests a degree of cultural continuity between the Napatan and Meroitic states, there were significant shifts in cultural traditions, including a greater presence of indigenous cults in state religion and the development of Meroitic as the official state language (Edwards, 2004). Many previous Napatan settlements were seemingly abandoned while new large Meroitic settlements appeared in central Sudan (Edwards, 2004). Around the beginning of the Meroitic period, major building projects were carried out at Meroe and dense urban sites with Amun temples were constructed nearby (Edwards, 2004).

A prestige-goods economy is presented as an important component of the Meroitic state and its sociopolitical structuring. The distribution of imported goods and their lack of utilitarian function reveal that they were reserved for the elite (Edwards, 1996; 2004). Therefore, Meroitic trade predicated on sociopolitical hierarchies and motivations rather than commercial needs. This prestige-goods economy seemed to operate on a larger scale as royals engaged in long-distance elite gift exchange with rulers of other territories in diplomatic contexts, as well as internally with local elite in maintaining power relations (Edwards, 1996). Evidence of long-distance elite gift exchange is suggested between the Meroitic kings and the Ptolemaic and Roman rulers (Edwards, 2004).

The southern and southeastern areas of the Meroitic kingdom are traditionally considered peripheries of the state; however, these groups likely played an active role in the Meroitic trade system and movement of prestige foreign goods. Meroitic presence has been observed in the Gezira region extending to the White and Blue Niles, suggesting some association with the state and role in the production of elite goods (e.g., gold) (Edwards, 1996; Lohwasser, 2014). Prestige goods from the south traveled to Meroe (e.g., gold, ivory, skins, ostrich feathers) and demonstrate trade from this region, perhaps via a retrieval system through Meroitic intermediaries in southern Gezira accessing goods with their neighbors to the south (Brass, 2015). Brass (2015) posits that the mobile pastoralist economy of the southern Gezira, as well as the southern Atbai, afforded them the mobility to interact with their borders in trade networks between the Meroitic kingdom along the Nile and across the east to the Red Sea. In the Eastern Desert, sites such as Tabot have revealed assemblages with Meroitic material culture but did not appear under Meroitic rule and were not Kushite sites (Lohwasser, 2014). These sites may represent the pathways of the Meroitic trading system with non-Kushite groups.

Differences between Upper and Lower Nubian settlement patterns and their agricultural infrastructure (Edwards, 1999), as well as their visible veneration of political and religious figures (Adams, 1974), suggest a lack of institutional uniformity across the Meroitic Kingdom despite shared allegiance to the state. The Upper Nubian Western Butana region to the east of the Blue Nile is suggested to have been the only area outside of the Meroitic heartlands (i.e., Shendi Reach) under direct control and power of the Meroitic royalty over subsistence production. This argument is made by Edwards (1999), who suggests that the numerous *hafirs* associated with the settlements in this region signify state control and management of subsistence activities, as their construction would entail significant oversight and inscriptions suggest they were state projects.

The profound presence of kingship and religious ideologies in Upper Nubia during this period is discussed by Adams (1974), who notes the vast majority of Meroitic royal monuments (i.e., temples, palaces, and royal burials) were located in the south. Within the southern provinces, portrayals of the rulers are numerous and highly associated with Egyptian kingship ideology as they depict the rulers connected to the most prominent gods among the southern pantheon—Amun and the local deity of Meroe Apedemak, who is not seen further north.

Contrary to traditional theories, Edwards (1999) argues that settlements in Lower Nubia were relatively small, significantly less populated, settled intermittently over the Meroitic phase, and designed more for storage than substantial domestic purposes. Previous models on the nature of Lower Nubian settlements suggested their primary purpose was agricultural production facilitated by s*aqia* (i.e., water wheel) irrigation. However, Edwards cites a reassessment of when the s*aqia* wheel could be dated, placing it at the early post-Meroitic instead of the Meroitic period. It should be noted though, that at the Meroitic settlement of Umm Muri adjacent to Mis Island, numerous fragments of *qadus* were found possibly indicating the use of *saqia* irrigation during this period (Ahmed, 2014b). Rather than agricultural production, Edwards (1999) suggests that the primary purpose of Meroitic settlement in Lower Nubia was to maintain communication and state trade between the Meroitic core and Egypt. Compared to Upper Nubia, Lower Nubia lacked royal monuments and references to the Meroitic rulers, both in general and in relation to deities (Adams, 1974). Adams (1974) suggests that this absence of royal depictions and demonstration of state strength indicate that political structuring of the Meroitic north was based more on secular institutions than ideologies of divine kingship.

Mortuary practices during the Meroitic phase are broadly variable. The royal tombs of the Meroitic rulers are located near Meroe and display Egyptian mortuary customs with pyramid superstructures and chapels (Adams, 1974). While some elite burials also display these features, “lesser” elite burials have been observed as brick mastabas with chapels or niches for offerings (Edwards, 2004). Burial forms were not universal and seemed largely reserved for higher status individuals, as indicated in non-elite cemeteries in the Meroitic heartland where most burials were not visibly marked (Edwards, 2004). Some mortuary forms seemed to have developed from Napatan traditions with east-west extended burials in chambers, multiple burials, and grave goods associated with socioeconomic status (Edwards, 2004).

In the transition to the Meroitic phase, the Napatan pottery traditions that were substantially influenced by Egyptian features were replaced by new distinctly Meroitic forms (Edwards, 2004). The sources of fabrics demonstrate a wide distribution of products and the decorations of wheel-made pottery are associated with symbols of the Meroitic state religion. By the late Meroitic stage, definite regional variation in ceramic culture is visible with Lower Nubian pottery displaying more decoration and assemblages including more imported vessels.

The disintegration of the Meroitic state likely corresponds to the dissolution of a central authority at Meroe and disruptions to the Meroitic economy, rather than traditional theories on the Kushite Kingdom’s collapse that present the end as some calamitous natural, military, or mass migration event (Edwards, 1996; Welsby, 1996). Some hypothesize that towards the late Meroitic phase, Egypt’s shift in trade routes to the Red Sea diminished the need for Kushite trade routes (Welsby, 1996). Additionally, as Roman Egypt became poorer and competition from the Axumites increased, sea transport may have made trade along the river less desirable (Welsby, 1996). While the Kushite state faced aggression from desert tribes before its dissolution, their lowered economic status in the later Meroitic may have restricted providing the resources necessary to ward off attacks (Welsby, 1996). Unrest in the late third century CE from the

Blemmyes' raids on Egypt likely disrupted Meroitic elite access to foreign luxury goods and thus, may have affected their prestige economy and central authority's capital (Edwards, 1996).

Post-Meroitic Period (350–500 CE)

Although the circumstances surrounding the Meroitic Empire's end are unclear, the subsequent dissolution of a central authority at Meroe gave way to the replacement of an imperial culture with several regional traditions (Edwards, 2004). These post-Meroitic regional groups would later emerge as the medieval kingdoms (Edwards, 2004). In the transition from the Meroitic to the post-Meroitic period, there are visible signs of discontinuity of the Meroitic state, including the abandonment of major monuments, the disappearance of the Meroitic language, and an absence of foreign goods in Upper Nubia (Edwards, 2004; Trigger, 1969). Traditional models of this transition between periods have been presented as a clear separation in the arrival of a new cultural group, particularly considering the replacement of ceramic assemblages and the loss of characteristic Meroitic wheel-made pottery (Edwards, 2004; Trigger, 1969). However, signs of continuity demonstrate a gradual and direct transition from Meroitic to post-Meroitic traditions with a maintained population (Edwards, 2004; el-Tayeb, 2010; Trigger, 1969).

The Third Cataract seemed to represent a tangible boundary between post-Meroitic Lower and Upper Nubian settlement, based on the regions' distinctive ceramic assemblages (Edwards, 1994). The center of post-Meroitic Lower Nubian settlement was focused around the south end of the Second Cataract and new settlement extended into areas that were largely unoccupied, such as the Batn el-Hajar (Edwards, 2004). The post-Meroitic settlements in Lower Nubia were the beginning of the Nobadian kingdom and displayed a distinctive culture with Romano-Egyptian influences and imported goods for elites (Edwards, 2004). While cemeteries in Lower Nubia represent both Meroitic and post-Meroitic periods, relatively few span the transition between both (Edwards, 2004). Presence of the Blemmyes at this time in Lower Nubia is suggested by handmade pottery associated with the east and Red Sea, as well as examples of cemeteries organized in a manner similar to those seen in the Red Sea Hills (Edwards, 2004).

In Upper Nubia, patterns of post-Meroitic settlement shifted from before as the new kingdom of Makuria was emerging (Edwards, 2004). The post-Meroitic period saw a scarcity of settlements in the Dongola Reach and minimal evidence of occupation at previous major Kushite centers (e.g., Jebel Barkal) (Edwards, 2004). A greater density of post-Meroitic settlement is observed downstream around Dongola, which would later become the capital of Makuria (Edwards, 2004). The presence of numerous post-Meroitic settlements in the Fourth Cataract region, which was void of any permanent settlement for most of the first millennium BC, suggests that there was a significant expansion into this area (Edwards, 2004). This post-Meroitic territorial extension is partly attributed to a widespread presence of the *saqia* wheel in the beginning of the period, which enabled increased cultivation and settlement, year-round crops, more dependable food supplies, and introduction of new crop species (Edwards, 2004). By the late Meroitic period at Qasr Ibrim, sorghum appeared in the region and subsequently developed durra features (Edwards, 2004). Additional new crops observed included different wheat forms, termis beans, peas, bulrush or pearl millet, and sesame (Edwards, 2004). This new technology and its effects are largely credited for the population growth in the late post-Meroitic/early medieval periods (Edwards, 2004).

The changes in ceramic assemblages during the post-Meroitic differed between Upper and Lower Nubia. Upper Nubian workshops for wheel-made pottery were abandoned with the decline of the Meroitic core and by the early post-Meroitic period, black and dark brown handmade wares were the most prevalent (el-Tayeb, 2010). Pottery uncovered in northern Nubia represents a different situation in the transition to the post-Meroitic period, as the end of the Meroitic Empire did not seem to significantly affect production. The manufacture of wheel-made pottery continued through the post-Meroitic to the end of the Christian period in the north and the presence of imported wheel-made pottery in Lower Nubian burials demonstrates their continued relationship with Upper Egypt (el-Tayeb, 2010). During the late third and fourth centuries, Romano-Egyptian wares were increasingly prevalent in the region; however, by the late fourth century, a more distinctly "Nubian" set of materials was developing (Edwards, 2004).

Mortuary practices shifted in the transition to the post-Meroitic period, during which time distinct regional variations are visible (el-Tayeb, 2010). The Meroitic custom of multiple individuals interred in the same grave disappeared in the post-Meroitic period, which may represent shifting beliefs of the afterlife (Edwards, 2004). Elite burials significantly changed from the Meroitic to post-Meroitic periods, as pyramid and mastaba superstructures were replaced by massive tumuli (Edwards, 2004). The largest and richest burials from post-Meroitic Lower Nubia are located at Qustul and Ballana; however, elite tumuli have also been observed in smaller settlements (e.g., Sesibi) (Edwards, 1994).

Interpretations of the royal burials at Qustul and Ballana have suggested that these post-Meroitic rulers in the north were Nubian and had some connection to the previous Meroitic state, perhaps considering themselves as a continuation of the Meroitic kings (Kirwan, 2002; Trigger, 1969). In the earliest tombs at Qustul, ties to Meroe are demonstrated in the prevalence of Meroitic culture and religious features (Kirwan, 2002). At Ballana, the royal silver crowns are nearly identical to those belonging to the Meroitic rulers (Trigger, 1969). Kirwan (2002) posits that following the end of Meroe, Nubians already integrated in Meroitic culture became the predominant power in the north and displayed themselves as the successors of the Meroitic royalty.

Christianization of Nubia

Over an extended and dynamic process, Christianity spread across Nubia and was adopted as state religion by the medieval period. At the time of Nubia's Christianization, two main denominations were present in the Byzantine Empire—the Melkites and Monophysites (Welsby, 2002). These two forms of Christianity were tied to differing political ideologies in Egypt, as Monophysites were Egyptian "nationalists" against Byzantine rule and Melkites supported Byzantine administration. Both denominations were introduced to Nubia, with Nobadia and Makuria seemingly adopting Monophysite and Melkite Christianity, respectively (Kirwan, 1984; Welsby, 2002). However, by the mid-to-late seventh century AD all three medieval Nubian kingdoms were regarded as Monophysite Christian (Welsby, 2002).

Across the three kingdoms, the royal families were presumably the primary focus of attention during the first Christian envoys (Kirwan, 1984). Religion was highly political within the Roman Empire's operations as a cohesive force to unite people under their influence (Welsby, 2002). Justinian and the emperors of his time were concerned about imminent Persian invasion into Egypt taking a route across the Red Sea and Sudanese Plain, as well as the attraction this might hold for Nubians (Kirwan, 2002). Therefore, introducing Byzantine Christianity into the Nubian kingdoms was seen as a means of integrating them into the Empire and securing the southern Egyptian border (Kirwan, 2002). However, these local rulers undoubtedly had their own motivations for adopting Christianity in their kingdoms and Christianization should not be viewed as an inevitable, passive event. Christianity significantly affected traditional sociopolitical institutions by essentially ending ideographic worship of the divine monarch (Żurawski, 2006) and the production of material goods associated with such veneration.

By incorporating the archaeological evidence from this Christianization process, the complexity and variation of Christianity's impact on Nubian societies is recognizable (Edwards, 2001). Archaeological indicators of the spread of Christianity include Christian symbolism on artifacts, production of artifacts associated with Christianity (e.g., ceramic assemblages), construction of churches, and Christian funerary practices (Edwards, 2001; Welsby, 2002). While the appearance of churches reflects more official and state-driven acts, burials displaying Christian mortuary customs are more indicative of personal beliefs and the adoption of Christianity by individuals (Welsby, 2002). Much of the scholarship on the Christianization of Nubia has been conducted through a lens of state worship and institutions which lacks recognition of private worship.

With the spread and adoption of Christianity as state religion, mortuary practices became more uniform across Nubia as they followed a unified ideological system (Welsby, 2002; Żurawski, 2006). This new religion offered a different set of eschatological views on death and the afterlife which required new practices and rituals surrounding funerary contexts (Żurawski, 2006). Over the adoption of Christianity, local funerary traditions gave way to a distinctive mortuary repertoire that embodied the Christian religious structure (Żurawski, 2006).

The typical Christian Nubian burial was predominantly oriented in an east-west direction, with the head on the western end and body in an extended position (Adams 1998; Welsby, 2002; Żurawski, 2006). Following Christian eschatological views on the transmigration of the soul rather than of a corporeal afterlife, Christian Nubians included minimal grave goods in burials, marking a profound divergence in funerary tradition (Adams, 1998; Welsby, 2002; Żurawski, 2006). Additionally, whereas pre-Christian mortuary rituals for elite individuals were intimately associated with striking monuments and grave goods, Christian ideologies deterred such practices as all people became equal at death and the rewards of the afterlife were possible for those who adhered to the Christian faith (Welsby, 2002; Żurawski, 2006). Visibly high-status tombs were therefore abandoned, although some burials within churches suggest interments for individuals of canonical status (Żurawski, 2006).

Although the belief in corporeal preservation of the deceased ended with Christianity, many burials included the mortuary practice of protecting the body and guarding it from direct exposure to the earth with slabs and bricks (Adams, 1998; Welsby, 2002; Żurawski, 2006). This practice may have connections to pre-Christian Nubian and Egyptian traditions and has been interpreted as a superstitious measure to protect the face and prevent evil spirits entering the body (Welsby, 2002). Shrouding of the decedents seems to be one of the most prevalent practices among Christian burials across Nubia during the entire medieval period (Adams 1998).

The use of superstructures in Nubian mortuary behavior has a deep history and while the presence of superstructures continued through Christianization, they took notably different forms from previous traditions (Adams, 1998). Over the course of Christianization, the tumulus superstructure was largely abandoned in areas where churches or monasteries were implemented; however, outside of these centers, the tumulus burial is observable for longer (Żurawski, 2006). Christian superstructures were predominantly two general types—mastabas and flat pavements (Adams, 1998; Welsby, 2002; Żurawski, 2006). The new manifestation of superstructures varied considerably in form and became a common aspect of Christian Nubian burials, particularly during the Early and Classic Medieval periods (Adams, 1998; Welsby, 2002; Żurawski, 2006). The cross as a religious symbol appeared in the medieval Nubian mortuary complex with

Christianization and was a principal component of funerary behavior (Welsby, 2002). In addition to cross-shaped superstructures, crosses were incorporated into mortuary customs as cross-shaped stelae and crosses made of terracotta or wood installed on top of tombs.

The arrival and subsequent adoption of Christianity in Nubia was a gradual process that began during the post-Meroitic period and continued through the medieval period in variable ways across Nubia. During this time, Christian cemeteries began where pre-Christian burials had ended, demonstrating the complexity of continuity and change over this process (Żurawski, 2006). This transition is also marked by burials that display a combination of pre-Christian and Christian mortuary features aligned with a transition in ideological views (Welsby, 2002). The replacement of pre-Christian temples with churches also reveals an extended process, as some were modified or built before the "official conversion", as well as centuries afterwards (Welsby, 2002). This evidence demonstrating the inconsistency within the Christianization process prompts a reconsideration of presenting medieval Nubia as "Christian Nubia" (Edwards, 2001).

Medieval Period (500–1500 CE)

The beginning of the medieval period in Nubia is traditionally marked by the "official conversion" and adoption of Christianity as state religion by the three Nubian kingdoms—Nobadia, Makuria, and Alodia (Alwa). The relationship between these Nubian polities and the Byzantine Empire were harmonious into the beginning of the seventh century (Welsby, 2002). However, Byzantine control in Egypt was interrupted by the Persian Empire in 619 CE (Welsby, 2002). As the Byzantine and Persian empires competed against each other, another power emerged in this struggle—the Arab Muslim Empire. In a vast campaign, Arab Muslim forces defeated the Byzantines and Persians around 673 CE and continued into Egypt (Welsby, 2002).

After taking Egypt, the Arab Muslim forces traveled west and south, taking over the Byzantine powers in Libya, Tunisia, and Algeria; however, were stopped at Nubia.

In 652 CE, a campaign into Nubia led by Abdallah b. Sa'id Abi Sahr advanced to Dongola and laid siege to the capital (Welsby, 2002). After fighting ensued between Muslim and Nubian forces, historical accounts describing what followed differ depending on the source's sympathies or affiliation (Spaulding, 1995; Welsby, 2002). However, they generally depict the Makurian king seeking peace with the Muslim Egyptian forces and both parties striking an agreement referred to as the *baqt* by external sources. (Spaulding, 1995; Welsby, 2002). In these *baqt* terms, both parties were allowed freedom of movement in the other country, although residency was restricted (Spaulding, 1995). Additionally, Nubia would send enslaved peoples to Egypt and repatriate Arab prisoners, and Egypt would give Nubia foodstuff and likely additional elite goods (Spaulding, 1995). For medieval Makuria, Spaulding (1995) suggests that the *baqt* was an expression of the Nubian royal gift exchange that extended into their past forms of diplomacy. From this perspective, the agreement was therefore an acknowledgement of the new Islamic rule in Egypt with which medieval Nubia would interact.

The Medieval Kingdoms

Located between the First and Third Cataracts, the medieval Kingdom of Nobadia grew from post-Meroitic settlement and established a capital at Faras (Edwards, 2014). In northern Nubia, numerous walled settlements date to early medieval construction and may represent an unstable northern frontier for Nobadia around this time (Edwards, 2014). Another early medieval settlement pattern is a scattering of small sites, particularly in the Batn el-Hajar and Third Cataract regions. These settlements may represent farming communities associated with the post-Meroitic establishment of unoccupied areas facilitated by *saqia* irrigation (Edwards, 2014). A shift in late medieval Nobadian settlement is seen with the abandonment of settlements in the Second Cataract region and sudden increase in occupation of the Batn el-Hajar and Third Cataract regions (Edwards, 2014). This regional abandonment may have been instigated by threats of Egyptian aggression in the north (Adams, 2001).

The Kingdom of Makuria was located from the Third Cataract to around the Fifth Cataract with a capital at Dongola (Adams, 1991). The first figures of authority in Makuria's early stages of formation may have been interred in the burial grounds at Tanqasi and ez-Zuma, located downstream of the Fourth Cataract (Godlewski, 2014). These burials demonstrate a significant departure in social differentiation with multi-chamber tombs, complex grave shafts, and large mounds. After a substantial population increase during the fourth and fifth centuries, the appearance of fortified sites in the fifth and sixth centuries indicates an urbanization process and perhaps economic organization by the early ruling elites (Godlewski, 2014). A series of defensive fortresses occupied the Fourth Cataract region, the largest of which were built at the beginning of the seventh century and then abandoned after a century, perhaps from external threats and/or combining of regional powers (Żurawski, 2014).

In the beginning of the medieval period, Nobadia and Makuria had an adverse relationship, perhaps related to the rival Christian denominations they had adopted (Adams, 1991). However, at some point the two kingdoms united under the single Makurian king (Adams, 1991). While subservient to the kings in Makuria, Nobadia had a regional administrative figure—the Eparch of Nobadia. The process and timing surrounding this union is unclear, but the alliance was likely in place by the *baqt* agreement and endured over six centuries. Although both kingdoms were joined under the king at Dongola, cultural, economic, and political differences existed between them, suggesting they did not become a uniform entity after merging (Adams, 1991).

In the mid-eleventh century, Makuria entered into an alliance with Alodia and the Kingdom of Dotawo was established as a new form of Makuria (Godlewski, 2014). The Kingdom of Dotawo was seemingly synonymous with Makuria; however, in the thirteenth century, kings of Makuria and kings of Dotawo existed (Adams, 1991). Adams suggests that the kings of Dotawo may have lived near Qasr Ibrim at this later date and acted as authoritative figures in Nobadia, superior to the Eparch (Adams, 1991). While the Eparch apparently dealt with trade and relations with Egypt, the king of Dotawo seemed to operate within the civil and legal sphere (Adams, 1991). The Kingdom of Dotawo brought the establishment of Old Nubian as the predominant language in the church, state administration, and community while traditional Greek and Coptic were used in monastic groups (Godlewski, 2014).

The Kingdom of Alodia (Alwa) is described as the most wealthy and powerful of the medieval Nubian kingdoms in historical accounts (Welsby, 2014). As the Kushite power center Meroe was diminishing, massive tumuli with elite grave goods appeared at el-Hobagi (~70km upstream) which likely represents the early Alodian power base (Welsby, 2014). The majority of Alodian material culture seemingly continued from earlier post-Meroitic traditions (Edwards, 2004). By the sixth century, the new settlement of Soba was occupied and may have already served as Alodia’s capital (Welsby, 2014). Soba was a large urban center and a religious and political focus, containing at least seventeen churches with two large churches located in the city center adjacent to a palatial structure (Edwards, 2004; Welsby, 2014). Many fortifications have been observed downstream and may signify a larger defense system. The kingdom’s borders were likely fluid and dependent upon their interactions with neighboring groups and the high mobility of peripheral groups (Welsby, 2014). However, the terms in the *baqt* agreement suggest that Alodia and Makuria were contiguous. Along the Atbara, the Dihiyyun were Alodian subjects and may represent a union between Alodia and Beja.

Medieval Nubian economy

Given the lack of *seluka* land naturally available for cultivation, the spread of *saqia* irrigation resulted in an agricultural revolution, in which arable land significantly increased (Welsby, 2002). Many of the crops grown in the region today were cultivated during the medieval period (Welsby, 2002). The staple grain in medieval Nubia was dhurra/sorghum. Dhurra was used to make beer (*mizr*) and grains including dhurra and wheat were used to make flat unleavened bread called *kirsa*. Other crops included millet, wheat, dates, olives, palm trees, bananas, citrus, and cotton (Welsby, 2002). Crops that had been previously cultivated in Egypt appeared and the introduction of new crop species likely made year-round production possible (Welsby, 2002).

The later sixth century saw a new type of pottery, some of which displayed clear Christian symbolism (Edwards, 2004). These “Early Christian” wares represented a series of “Christian” pottery that would last for almost 1,000 years (Edwards, 2004). Two major production centers for “Early Christian” wares were located at Faras and Dongola, as well as a third production center for the distinctive “Soba ware” (Edwards, 2004). Compared to the pottery manufactured at Old Dongola, wares from Soba primarily stayed within the capital’s reaches rather than exchanged over long distances (Welsby, 2014). In the ninth century, new “Classic Christian” styles appeared (Edwards, 2004). Production at Faras was abandoned in the late tenth/eleventh centuries and the Nobadian pottery demands were increasingly met by Egyptian imports (Edwards, 2004). A significant rise in the amount of imported pottery from Aswan and

Lower Egypt is observed at Meinarti during this time (Adams, 2001). At Dongola, "Post-Classic" wares appeared in the eleventh century but are not observed far beyond this region (Edwards, 2004). In the late medieval period, a highly variable "Terminal Christian" collection of wares appeared and is suggestive of more local production (Edwards, 2004). At the end of the medieval period, wheel-made pottery disappeared and was replaced by a range of handmade wares.

The medieval Nubian kingdoms engaged in trade networks with Egypt and eastern polities over the medieval period. In the beginning of the medieval period, Makuria enjoyed a trade partnership with Byzantine Egypt, as suggested by the extensive presence of amphorae from the end of the sixth century (Godlewski, 2014). In turn, Makuria provided Byzantine Egypt with the goods they had historically presented to Egypt. After the *baqt* agreement, evidence suggests that Nubian and Muslim royalty engaged in diplomatic exchange of elite goods, in which Nubia imported luxury foods, vinegar, wine, horses, and textiles and provided Muslim princes with ivory, animal skins, dates, ebony, emery, alum, and exotic live animals (Spaulding, 1995). While Nubian economic dealings were tightly controlled by the elite, Muslim merchants seeking to trade in medieval Nubia after the *baqt* created avenues for more private commerce that decreased the exclusivity of foreign items (Spaulding, 1995).

The northern zone of Nobadia became open to free trade as Muslim merchants could establish their commerce and even own land (Adams, 1991). The coexistence of Christian Nubians and a Muslim minority is demonstrated by the presence of Muslim tombstones from the tenth and eleventh centuries in Wadi Halfa's predominantly Christian cemeteries (Shinnie and Shinnie, 1965). Egyptian coinage discovered in Lower Nubia suggests its circulation in the Nobadian market and historical documents indicate that the Nubian cash economy was directly connected to Egypt (Adams, 1991; Ruffini, 2012). Acting as a kind of viceroy, the Eparch of

Nobadia was primarily responsible for overseeing trade and foreign relations with Nubia's Muslim neighbors, as well as upholding the terms of the *baqt* (Adams, 1991). Documents from Qasr Ibrim discuss how independent Muslim agents and the Eparch acted as trade intermediaries for the kings of Makuria and Alodia (Welsby, 2002).

At Soba East, a large Muslim community lived within the city and likely included a group of merchants (Welsby, 2002). Given Makuria's restrictions on the presence of Muslim traders, this may indicate a direct connection between Alodia and Egypt and/or Red Sea ports (Welsby, 2002). Texts describe routes between Alodia and the Red Sea and a relatively small amount of Islamic imports have been uncovered at Soba including rare "Islamic" glazed wares and fine glassware, as well as Chinese porcelain sherds from the twelfth and thirteenth centuries (Edwards, 2004; Welsby, 2002).

Collapse of the medieval Nubian Kingdoms

Beginning in the thirteenth century, a series of raids and campaigns was carried out between Makuria and Muslim Egypt (Welsby, 2002). After a succession of dynastic upheavals, the first Muslim Nubian ruler ascended to the Makurian throne in the early fourteenth century (Welsby, 2002). During his reign, the first evidence of a mosque at Dongola appeared and Egypt's imposed *jizya* ended. The Makurian centralized government weakened and perhaps spurred by aggression from the desert Arabs (likely the Beja), the royal court presumably departed Dongola and relocated to Nobadia in the mid-fourteenth century (Godlewski, 2014; Welsby, 2002). Evidence of increasing insecurity within the Makurian kingdom is represented by the presence castle-houses between Qasr Ibrim and the Third Cataract (1100–1500 CE), fortification of structures, appearance of fortresses, and relocation of settlements into more defensible and desolate areas (Welsby, 2002). The final manifestation of this polity, described as a continuation of the Dotawo Kingdom, was likely focused at Daw with one final bishopric at Qasr Ibrim and lasted until the end of the fifteenth century (Edwards, 2004; Godlewski, 2014).

Little is known regarding the decline and end of the Kingdom of Alodia. Some burials that possibly date to around its demise demonstrate neither Christian nor Muslim funerary rites and may represent decreased centralization (Welsby, 2014). In the late medieval period, an independent Kingdom of el-Abwab in the northern province of Alodia is described (Welsby, 2002) and may represent a fractured centralized Alodian authority. Alodia eventually fell to the Funj (Abdallab Arabs) from the south (Welsby, 2002). Accounts describe how Soba was already in ruins when the Funj entered Alodia and established their kingdom at Sinnar in 1504 CE (Edwards, 2004; Welsby, 2002).

CHAPTER THREE: PATHOPHYSIOLOGY OF MALARIA, PALEOPATHOLOGY OF ANEMIA, & SKELETAL LESIONS OF INTEREST

The first section in this chapter discusses the pathophysiology of malaria as it relates to possible effects on the skeleton, including the anemia involved in the disease. The paleopathology of anemia is then discussed, and a historical overview is provided regarding studying anemia in skeletal remains. The last section presents previous findings on the skeletal lesions studied in this dissertation, including their association with age of the individual and co-occurrence. Additionally, a review of femoral cribra is provided which discusses the proposed etiologies associated with the lesion and observations on variation in the lesion's appearance.

Pathophysiology of malaria

Malaria induces anemia in infected individuals through hemolytic anemia from extensive destruction of parasitized and non-parasitized red blood cells (White, 2018). Hemolytic anemia, which can be inherited or acquired, has been proposed as one of the possible anemias responsible for producing skeletal lesions, as it initiates increased erythropoiesis that leads to marrow hyperplasia (Walker et al., 2009). However, the hemolytic anemia of malaria is also accompanied by suppressed erythropoiesis and dyserythropoiesis (Lamikanra et al., 2007; White, 2018), rather than increased erythropoiesis. This inability to produce an adequate erythroid response may be due to the production of mediators that inhibit erythropoiesis, including proinflammatory cytokines, and perhaps the presence of hemozoin, a parasite byproduct of hemoglobin digestion (Lamikanra et al., 2007; White, 2018). In acute malaria, erythropoiesis is perturbed and reduced and the bone marrow "may be hypocellular, normocellular, or mildly hypercellular" (Bain et al., 2019:133; Wickramasinghe and Abdalla, 2000). In chronic malaria, however, total erythropoietic activity rises with increased marrow cellularity and erythroid hyperplasia (Wickramasinghe and

Abdalla, 2000). This suggests that chronic infection and severe anemia from malaria may be more likely to produce visible skeletal lesions than acute malarial infections.

In addition to anemia, malarial infection seems to cause an imbalance in osteoclast and osteoblast activity resulting in heightened bone resorption. This resorptive effect from malarial infection may be due to a surge in free heme (Moreau et al., 2012) and parasitic sequestering in the extravascular space of bone marrow (Farfour et al., 2012; Joice et al., 2014; Obaldia et al., 2018). In chronic cases, the prolonged buildup of parasitic products in marrow is suggested to ultimately result in increased osteoclast production and bone resorption (Lee et al., 2017). In two experimental studies involving mice infected with malaria, resorptive microarchitectural changes included reduced trabecular bone volume, increased trabecular spacing, and decreased trabecular numbers compared to control subjects (Lee et al., 2017; Moreau et al., 2012).

Malarial infection has a synergistic relationship with other pathologies which can result in comorbidities as host immune responses are lowered. In communities experiencing moderate to high transmission of malaria, conditions observed to manifest concurrently include bacterial, viral, and helminth infections, and malnutrition such as vitamins A and B12 deficiencies (White, 2018). Additionally, the prevalence of haemoglobinopathies that offer some protection against malaria, but also contribute to anemia, often parallel the incidence of malaria (White, 2018). Therefore, as these multiple conditions can affect individuals at risk or experiencing malarial infection, the resulting anemia can be “multifactorial” (White, 2018:7). In addition to this influence on morbidity, the combination of malarial infection with other infections or conditions can have profound effects on mortality (Carter and Mendis, 2002).

Paleopathology of anemia

In response to anemia, skeletal changes are considered to primarily result from the need to expand hematopoietic marrow to promote red blood cell production (Brickley, 2018). Due to a lack of healthy red blood cells, red bone marrow becomes overreactive to compensate for the disruption to hematopoiesis caused by blood loss, inhibited erythropoiesis, and/or increased hemolysis (Rivera and Lahr, 2017). This stress on the marrow tissue leads to expansion of hematopoietic centers (i.e., marrow hyperplasia), which in turn places pressure on the surrounding bone and initiates osteoblastic and osteoclastic activity (Rivera and Lahr, 2017). The resulting changes include expansion of the marrow space and openings from the marrow cavity to the external cortical surface (Wapler et al. 2004). Hyperplasia is also associated with interrupted remodeling of the external cortical bone that can produce porous lesions (Rivera and Lahr, 2017). Porous lesions of the cranium—porotic hyperostosis of the vault and cribra orbitalia of the orbital roof—have long been linked to anemia among possible etiologies. The types of anemia that could potentially be responsible for causing the lesions have been a source of debate, affecting interpretation of the lesions' presence in human skeletal remains.

Early paleopathological inquiry into the skeletal manifestation of anemia and interpreting its presence in archaeological remains is marked by J. Lawrence Angel's work. Among his publications on the subject is his 1966 article that first applied the term porotic hyperostosis to describe cranial porosities while discussing these lesions observed from prehistoric Eastern Mediterranean sites. Based on a history of endemic malaria, Angel links porotic hyperostosis to the hemolytic anemia involved in genetic conditions conferring some resistance to malaria—specifically, thalassemia and sickle cell anemia. However, he notes that thalassemia or sickle cell are unlikely causes of porotic hyperostosis in areas that lacked falciparum malaria. Subsequent researchers focused on the cause of these lesions in such regions where the hypothesis of thalassemia or sickle cell anemia did not fit due to relative low levels of these genetic variants in endemic populations (Hengen, 1971) and the presence of these cranial lesions in areas where malaria likely did not exist at the time (El-Najjar et al., 1976).

Following Angel's work, the iron deficiency anemia hypothesis was a primary etiological model and was attributed to various sources. Hengen (1971) suggests that the cribra orbitalia observed in crania from different time periods and geographic locations is most likely linked to iron deficiency anemia arising from insufficient iron intake, inadequate sanitation, and parasitic infections. El-Najjar and colleagues (1976) interpret patterns of porotic hyperostosis and cribra orbitalia prevalence from prehistoric and historic North American Southwest to iron deficiency anemia due to hypothesized differences in dietary iron. Stuart-Macadam (1992) later argues that iron deficiency anemia is not strongly associated with nutrition and diet. Instead, iron-deficiency anemia is presented as the result of an adaptive mechanism as the body reserves iron in response to pathogens. In this process, a chronic or high pathogen load can trigger a response by the immune system in which iron is relocated and stored in the liver in defense of invading pathogens whose growth is facilitated by iron. Therefore, the lack of iron in blood strengthens the host's defense against microbial invaders. Holland and O'Brien (1997) contend that this parasite model is too simplistic in its application of evolutionary processes that focus on short-term outcomes and ignore long-term costs. The authors suggest that this response is more of a maladaptation rather than successful adaptation and conclude that porotic hyperostosis and cribra orbitalia are likely the result of a combination of synergistic and interacting factors.

Among several arguments against the iron deficiency hypothesis, the most noted criticism is articulated by Walker and colleagues (2009). In their paper, Walker et al. insist that iron-deficiency anemia cannot cause marrow hypertrophy in these lesions because it inhibits red blood cell production, which requires iron to perpetuate. These researchers instead contend that megaloblastic anemia and hemolytic anemia are the likely etiologies of the cranial lesions because they result in premature red blood cell destruction, initiating a compensatory response from the body to produce more red blood cells. Walker and colleagues discuss how porotic hyperostosis and many cases of cribra orbitalia may likely be caused by megaloblastic anemia acquired by infants during nursing. This is due to low maternal vitamin B_{12} levels and unsanitary living conditions that contribute to additional nutrient deficiencies and gastrointestinal infections. While marrow hypertrophy from anemia is a likely common cause of cribra orbitalia, Walker et al. suggest another possible etiology—subperiosteal hematomas, which are associated with multiple diseases (e.g., scurvy).

This position countering iron deficiency anemia was in turn contradicted by Oxenham and Cavill (2010), who claim that Walker et al.'s (2009) assertions on the relationship between iron deficiency anemia and erythropoiesis are not supported by the clinical literature. In their discussion, Oxenham and Cavill (2010) contend that increased erythropoietic activity can increase from iron deficiency anemia (resulting from blood loss and/or a low-iron diet). The authors explain that in iron deficiency anemia, there is a lack of iron to supply the stimulated red marrow and there is insufficient iron for erythroblasts. A large portion of these cells is then unable to make enough hemoglobin in time to become mature red blood cells, and are thus destroyed in the marrow. Following this is a significant increase in erythropoiesis, albeit an ineffective response. The authors conclude that hemolytic, megaloblastic, and iron deficiency anemias are all possible etiologies for porotic hyperostosis and cribra orbitalia.

In further response to the dismissal of iron deficiency as a potential etiology, McIlvaine (2015) argues that excluding it altogether from paleopathological interpretations relating to porotic hyperostosis could be premature. McIlvaine's concern is that if iron deficiency does restrict erythropoiesis, hidden heterogeneity may result in skeletal samples. Vitamin B_{12} deficiency in megaloblastic anemia and iron deficiency anemia often co-occur given their shared causes. When these two deficiencies occur at the same time, iron deficiency may restrict marrow hypertrophy and thus prevent the expression of porotic hyperostosis and cribra orbitalia, despite the marrow being stimulated by B_{12} deficiency. Therefore, McIlvain argues that in excluding the iron deficiency anemia hypothesis, skeletal populations may demonstrate hidden heterogeneity as iron deficiency could mask the expression of vitamin B_{12} deficiency. In such cases, individuals who have multiple nutritional deficiencies and are thus the most nutritionally stressed would resemble the non-stressed individuals because neither sub-group would display evidence of porotic hyperostosis. Ultimately, McIlvaine supports the inclusion of multiple indicators of stress and a biocultural framework in bioarchaeological interpretations.

The following predominant model for interpreting anemia from the skeleton has centered on hemolytic and megaloblastic anemias and iron deficiency anemia, the latter often being noted as disputed. An observable absence of marrow expansion underlying these lesions has been interpreted as lack of support for a diagnosis of anemia, such as Wapler and colleagues' (2004) histological examination of cribra orbitalia lesions in a group of remains from ancient Nubia. Although, based on recent research, Rivera and Mirazón Lahr (2017) suggest other forms of anemia as sources of cribra orbitalia when the lesions demonstrate a lack of bone marrow expansion, including anemia of chronic disorder or disease that result in marrow hypoplasia rather than hyperplasia.

The causes behind these lesions, and the associated implications regarding their interpretation, is an area of contestation and further research. Most recently, Brickley (2018) argues for the implementation of a biological approach when analyzing lesions associated with anemia. This approach entails drawing on clinical literature and examining the relationship between the location of lesions across the skeleton and the age of the individual. Porous lesions resulting from anemia are thought to manifest only in regions of red or mixed marrow with potential for hyperplastic responses. As the distribution of hematopoietic marrow changes over time, lesions are therefore age-dependent, and age should be considered when forming possible diagnoses.

Lesions of interest: association with age and co-occurrence

Previous studies examining the relationship between the lesions of focus in this dissertation and age of the individual have found patterns regarding the cribrous lesions. In a modern skeletal sample from Uganda, where malaria is holoendemic, Smith-Guzmán (2015a) reports an association between age-at-death and humeral and femoral cribra with higher prevalences of the lesions in younger individuals. Additionally, while humeral and femoral cribra were significantly more frequent in younger individuals, Smith-Guzmán (2015a) notes that cribra orbitalia was observed across age groups. Schats (2021) also reports a significantly higher prevalence of humeral and femoral cribra, as well as cribra orbitalia, in subadults compared to adults in a skeletal sample from the medieval/early modern Netherlands (800–1600 CE). Furthermore, Schats (2021) notes a common pattern in the prevalence of cribra orbitalia, humeral cribra, and femoral cribra across age groups with the lesions' frequencies at their highest in the child age group (4–12 years) and decreasing with age. While adult individuals demonstrated a decrease in the chances of displaying humeral and femoral cribra with increasing age, Schats did not find a similar trend for cribra orbitalia. In assessing the hypothesized activity of the three cribrous lesions in subadult and adult remains from late medieval archaeological sites in NW Spain, Mangas-Carrasco and López-Costas (2021) observe more signs of healing from the lesion's surface with increasing age for cribra orbitalia, humeral cribra, and femoral cribra.

The co-occurrence between cribra orbitalia, humeral cribra, and femoral cribra has presented in varying patterns for all three lesions, although a relatively strong connection between humeral and femoral cribra has been observed. An association between cribra orbitalia, humeral cribra, and femoral cribra was described by Miquel-Feucht and colleagues (1999) as part of a "cribrous syndrome" upon noting similar external and internal appearances of the postcranial cribrous lesions compared to cribra orbitalia. In addition to observing cortical reduction and trabecular expansion in the lesions, the authors describe a correlation between the three lesions in a sample of subadult skeletal remains from Spain. Djuric and colleagues (2008) also describe a co-occurrence of the three lesions and report a frequency of their combined expression in 33.33% (5/15) of subadult (0–14 years) remains studied. Among the lesions investigated in a malaria-endemic skeletal sample, Smith-Guzmán (2015a) reports a significant association between humeral cribra and femoral cribra; however, cribra orbitalia was not correlated with the cribrous postcranial lesions in the study sample. Smith-Guzmán therefore suggests the potential for varying processes behind the expression of cribra orbitalia in the population. In examining the association between pairs of the three cribrous lesions, Schats (2021) also observes a significant association between humeral cribra and femoral cribra in subadult individuals. While more frequent in subadults, Schats reports that the co-occurrence of all three lesions was uncommon in the study sample. Schats concludes that the findings do not support a “cribrous syndrome”; however, a relatively small subadult sample size may not have captured the potential for this lesion pattern.

Femoral cribra

The earliest cited source describing femoral cribra is often attributed to Harrison Allen, who stated that “the neck is marked in front near the articular surface by a faint depression, which is often cribriform in appearance and may receive the name of the cervical fossa” (1882:190). Since then, such porous features observed in this area of the femoral neck have been referred to as various iterations of “cervical fossa of Allen” (Angel 1964; Finnegan, 1978; Kate, 1963; Meyer, 1924, 1934), but is also discussed under the names Empreinte (Odgers, 1931; Schofield, 1959), anterior cervical imprint (Kotsick, 1963), cribra femoris (Blondiaux et al., 2015; Molleson et al., 1998), and femoral cribra (Djuric et al., 2008; Djuric et al., 2010). Adding to this inconsistency are conflicting definitions and studies that conflate femoral cribra with other features, such as Poirier’s facet (e.g., Odgers, 1931), thus making it difficult to distinguish the findings between discrete features. The dynamic nature of the femoral neck with its propensity to display several features of interest led J. Lawrence Angel to refer to its anterior surface as the “reaction area,” which “in its most dramatic form is an eroded fossa, the cervical fossa of Allen” (1964:130). This lesion has been categorized as a postcranial nonmetric trait (Finnegan and Faust, 1974; Finnegan, 1978), but is among a subset of nonmetric traits whose “origin and development is either unknown or debated” (Mann et al., 2016:xii).

Furthermore, porous lesions observed at the same area of the femoral neck have been presented as disparate lesions based on variations in their appearance and labeled either Allen’s fossa or femoral cribra (Göhring, 2021). Göhring (2021) describes Allen’s fossa as a demarcated concave area of exposed trabeculae that is a nonmetric trait created by friction of the zona orbicularis, and femoral cribra as a more diffuse area of convex trabecular expansion that is considered pathological in nature. Others offer a more encompassing definition for femoral cribra that attributes these variations in appearance to different expressions of the lesion (Radi et al., 2013). In the current research, the lesion of interest is referred to as femoral cribra and defined as an area of cortical disruption or porosity perforating the cortical surface on the anterior-inferior femoral neck (Miquel-Feucht et al. 1999; Radi et al., 2013) with varying expressions that are investigated to better understand possible underlying processes.

Proposed etiologies

Various etiologies have been proposed for femoral cribra and its related monikers that are attributed to pathological origins or associated with biomechanical stress, either from general contact with soft-tissue structures or specific activities. These different etiological categories subsequently affect the interpretation of this lesion's presence in skeletal remains. The non-pathological explanations suggested to produce femoral cribra include prolonged acetabular contact while sleeping (Meyer, 1924, 1934), hyperflexion from a squatting posture (Schofield, 1959), contact with the rectus femoris tendon associated with an erect bipedal posture (Kate, 1963), and tightening of the zona orbicularis of the hip joint capsule (Odgers, 1931) which is included in recent discussions of porous lesions at the femoral neck. Göhring (2021) presents Allen's fossa as a nonmetric trait separate from femoral cribra that is caused by biomechanical factors including rubbing of the zona orbicularis on the femoral neck during activity. Göhring attributes the lesion femoral cribra, however, as indicative of pathology. Other recent examinations of porous lesions at the femoral neck cast doubt on interpretations of femoral cribra as a specific activity-related marker (Radi et al., 2013), and propose that the lack of anatomical insertion at this site renders propositions of biomechanical alteration or injury as dubious (Miquel-Feucht et al., 1999).

Current etiological understandings of femoral cribra describe it as a pathological stress marker. Femoral cribra has been likened to cribra orbitalia in morphology and is occasionally grouped together with both cribra orbitalia and humeral cribra in an assemblage of lesions referred to as “cribrous syndrome” (Miquel-Feucht et al., 1999). The presence of femoral cribra, in conjunction with other cribrous lesions, has been associated with hypothesized etiologies including magnesium deficiency from malnutrition and/or malabsorption (Djuric et al., 2008; Miquel-Feucht et al., 1999), tubercular granuloma within bone marrow (Blondiaux et al., 2015), anemia from pathogenic stress (Djuric et al., 2008; Djuric et al., 2010; Smith-Guzmán, 2015a), inherited anemia (Mendiela et al., 2014), and anemia from some combination of nutritional, infectious, or genetic origin (Paredes et al., 2015).

Previous microscopic observations of femoral cribra support anemia as a possible etiology. In a qualitative histological analysis on twelve subadult cases of femoral cribra, Djuric and colleagues observed “thinning and porosity of the cortical bone, enlargement of intertrabecular space, and growth of the trabeculae perpendicular to the bone surface” (2008:469). Based on their two-dimensional assessment, Djuric and colleagues (2008) propose that these characteristics could be due to marrow expansion and are thus consistent with an etiology of chronic anemia.

Variation in morphology

Variation in femoral cribra’s appearance has been observed in previous examinations of the lesion within skeletal samples. In these discussions, proposed classifications of this variation are based in terms of general size, location, and “severity” of the lesion. Miquel-Feucht and colleagues (1999) classify femoral cribra into three categories based on the location and extent of the lesion distributed over the femoral neck's anterior and inferior surface. Other classificatory systems describe varying degrees of femoral cribra's expression that allude to "severity" or "intensity". Odgers's categories of the lesion include "slight" or "marked erosions" (1931:355). Kotsick divides the range of variation into two types—a demarcated "ulcer-like excavation" or a diffuse, cortical discontinuity displaying a "moth-eaten appearance" (1963:395). More recently, Djuric et al. (2008) apply Nathan and Haas's (1966) classifications of cribra orbitalia to femoral cribra with varying intensities of "porotic, cribrotic, and trabecular"; however, they do not compare these different grades in their analyses. Mangas-Carrasco and López-Costas (2021) also follow Nathan and Haas's (1966) scoring system and analyzed the severity of femoral cribra in their study sample using a four-grade scale that ranges from small pores on the surface, which become increasingly connected, to exposure of trabecular structure. Radi and colleagues (2013) propose that the lesion can be described as either a cluster of pores on the cortical surface, or an area of cortical erosion that exposes trabeculae and may be depressed. The authors note that this latter expression of femoral cribra is consistent with Finnegan's (1978) definition of Allen's fossa, which Göhring (2021) suggests is a separate lesion unassociated with femoral cribra.

Another process in the pathogenesis of femoral cribra possibly contributing to differences in the lesion's appearance may be the amount of remodeling of the affected bone, or stage of "activity" at time of death. Mangas-Carrasco and López-Costas (2021) present stages of healing in their analysis of femoral cribra as active, mixed, or inactive that correspond to the relative visibility of the lesion's morphology on the bone's surface. For this system, active lesions are described as readily apparent, mixed lesions are recorded as less defined, and inactive lesions are observed as barely discernable. A raised, thickened border which sometimes surrounds the porous bone of femoral cribra has been linked to possible lesion "activity" with Angel (1964) and Finnegan (1978) likening it to an inflammatory response and perhaps "a partial healing process" (Angel, 1964:135). In presenting a description of Allen's fossa and distinguishing it from femoral cribra, Göhring states that Allen's fossa "does not show a bony ridge or rim," but does have a clear cortical margin that is proposed to be due the zona orbicularis eroding the cortical surface during activity (2021:4).

One factor that may affect the presence of femoral cribra and its differential appearance is the individual's age. Kotsick (1963:395) links variation in the lesion's expression to age, even referring to one form of femoral cribra that has a "worn cancellous appearance" as the "teenage imprint", which may represent an early stage of the lesion. In examining the prevalence of femoral cribra among age groups in skeletal samples, previous studies report higher frequency of this lesion in subadults and younger adults compared to older age groups (Miquel-Feucht et al., 1999; Radi et al., 2013; Schats, 2021; Smith- Guzmán, 2015a). Additionally, Mangas-Carrasco and López-Costas (2021) report more active-looking lesions in subadult individuals and more lesions that appear healed in adult individuals within their skeletal sample from medieval northwest Spain (12th–15th centuries). This age-related pattern, as well as the location of femoral cribra in the region of epiphyseal union, has led some to suggest that it manifests earlier on during growth (Lewis, 2018; Smith- Guzmán, 2015a). Porous lesions resulting from anemia are thought to manifest only in regions of red or mixed marrow with potential for hyperplastic responses and thus, are age-dependent (Brickley, 2018). In the proximal femur, hematopoietic marrow is retained past twenty-five years of age (Kricun, 1985). This retention, coupled with red marrow's heightened reactivity in subadults, could contribute to a hyperplastic change in response to a pathological stimulus (Lewis, 2018). Considering anemia as a possible etiology of femoral cribra, the lesion could develop from the need for increased erythropoiesis and concomitant marrow hyperplasia (Smith- Guzmán, 2015a). The lesion may also manifest later in cases of chronic anemia, especially hemolytic anemia, as non-converted red marrow can become hyperplastic and result in expansion (Kricun, 1985).

CHAPTER FOUR: RESEARCH QUESTIONS & EXPECTATIONS

This dissertation investigates hypothesized malarial infection in Nubia during the medieval period and the potential impact of these events using paleopathological approaches and a biocultural framework. This research focuses on the skeletal remains excavated from the site of Mis Island, located near the Fourth Cataract of the Nile River, which is believed to have practiced *saqia* agriculture during the medieval period based on excavated archaeological material. This research investigates the potential extent of the disease at Mis Island using Smith-Guzmán's (2015a) approach for inferring malarial infection from the skeleton, which entails examining skeletal remains for a series of five lesions associated with the disease and using a diagnostic outcome algorithm to infer how many and which individuals may have been infected with malaria.

The prevalence of hypothesized malaria is explored between the sites' cemeteries and across age and sex cohorts. Cemeteries 3-J-10 and 3-J-11 represent discrete burial areas on Mis Island and differ in time of use. While cemetery 3-J-10 was active during the late medieval period (1100–1500 CE), cemetery 3-J-11 spanned pre-medieval to late medieval years (300–1400 CE). By comparing the prevalence of posited malarial infection between these cemeteries, this research examines potential temporal fluctuations in this disease. The prevalence of hypothesized malaria is compared between age and sex groups to generate inferences about relative exposure and the endemicity of malaria in this area during the medieval period. Investigating the dynamics of malaria in medieval Nubia builds on the scholarship of health conditions for populations living in the Nile River Valley at the time and contributes insight into the potential influence of posited agricultural and populational trends on malarial risk during the medieval period.

Given the context of hypothesized prevalence of malaria, this dissertation explores the manifestation of the skeletal lesions implicated in the disease to contribute insights into this suite of lesions and discussions about their etiology. This research examines the lesions' relationship with the affected individuals' age and the association among these lesions to contribute further understanding into their formation and patterns of expression. For one of these lesions—femoral cribra—there is a need to further understand variation in the lesion's external appearance, the bone processes underlying its expression, and the role an individual's age may have in the lesion's manifestation. The research therefore visually examines femoral cribra lesions for several variables possibly representing lesion "activity" and "severity" and assesses their association with the age of the individual. By examining the variation in femoral cribra's appearance across age groups, this analysis aims to assess lesion formation and progression in conjunction with age-related variables and possible healing activity. This assessment also seeks to better understand potential patterns in femoral cribra's appearance that may be related to different stages of "activity" and "severity".

To investigate the relationship between changes visible from femoral cribra's external surface and the types of bone processes possibly occurring at the trabecular structural level, this research used micro-computed tomography (micro-CT) methods to acquire three-dimensional scans from a subsample of femora and derive a series of variables that reflect trabecular bone microarchitecture from the region underlying the lesion. This analysis follows a framework based on Morgan's (2014) micro-CT research on cranial porous lesions, and investigates the trabecular microarchitecture associated with femoral cribra to explore the types of bone processes involved in its formation, while considering proposed etiologies suggested to cause this lesion. Part of this analysis seeks to evaluate the relationship between external, macroscopic signs of unremodeled or remodeling femoral cribra and the internal, microscopic changes occurring at the trabecular level that would inform descriptions of lesion "activity" (i.e., whether a lesion may be "active" or "healing"). Another facet of this analysis explores morphology of the lesion potentially corresponding to "severity" by assessing whether cortical alteration on the surface differs with internal trabecular variables.

This chapter outlines the research questions of the dissertation research and discusses the expected outcomes for each question. The overarching aims of this research are to 1) investigate the prevalence and patterns of hypothesized malaria at Mis Island during the medieval period while considering the interactions between human activities, ecological contexts, and biological aspects of malaria, 2) explore the manifestation of the skeletal lesions of interest regarding their presence across age groups and co-occurrence, and 3) investigate femoral cribra's formation and progression based on its macroscopic and microscopic expression and relationship with age.

Research Question 1: *Is there skeletal indication of malarial infection at Mis Island during the medieval period and if so, how prevalent may malaria have been?*

Expectation 1: *Skeletal indication of malarial infection is expected to be present in the Mis Island sample and the estimated prevalence of hypothesized malaria is anticipated to be relatively high.*

The arable land at Mis Island would have likely provided a conducive environment for mosquito vector populations. Additionally, the inferred presence of *saqia* agriculture practices at Mis Island would have provided further sites for mosquito breeding, potentially supporting some degree of continuous malarial transmission. Indication of *saqia* irrigation at Mis Island during the medieval period is supported by remnants of the *qadus* jar uncovered at the medieval settlement 3-J-19 on Mis Island (Thomas, 2008). Although the *qadus* is not exclusive to *saqia* irrigation, its primary use is in the cattle-driven water wheels part of this technique. With an increase in irrigated areas and water sources to support mosquito breeding, this farming practice may have resulted in a larger and/or more supported mosquito population and concomitant higher risk of malaria.

While there were many urban centers in Makuria, uncovered settlements demonstrate a steady distribution of villages along the Nile throughout the medieval period (Obłuski, 2020). In the Fourth Cataract, remains of medieval sites indicate a settlement pattern of numerous and scattered small communities (Obłuski, 2020), several of which are observed in the vicinity of Mis Island. Additionally, the Fourth Cataract region saw the establishment of multiple fortified sites and churches during the medieval period, which were involved in the region's organization over several phases (Żurawski, 2014). Therefore, while Mis Island was in a region of seemingly dispersed population density, the settlement practices were not so isolated as to restrict malarial transmission. Rather, the settlement pattern surrounding Mis Island in the Fourth Cataract region during the medieval period may have been associated with a regional population of appropriate size and proximity to sustain malarial transmission and be susceptible to inter-communal spread.

Research Question 2: *Are there differences in the frequency of hypothesized malaria between individuals from cemeteries 3-J-10 and 3-J-11?*

Expectation 2: *The hypothesized presence of malaria is expected to be relatively similar between these two cemeteries, with potential for a higher frequency of infection in cemetery 3-J-11.*

While Soler (2012) observed a similar overall prevalence of stress among adults from cemeteries 3-J-10 and 3-J-11, Hurst (2013) found significantly higher incidence of cribra orbitalia in subadults from 3-J-11 compared to 3-J-10. The current research may find a similar pattern in greater prevalence of skeletal lesions suggestive of malaria among the cemetery 3-J-11 subadult individuals. Additionally, there were periods before the late medieval phase during which the Nile River was at significantly lower levels than normal (Edwards, 2004). An ecological relationship between the seasonal shifts in the Nile River's levels and *An. arabiensis* populations has been observed in the Northern State of Sudan in which mosquito numbers decrease during the river's flooding as the high waters wash away breeding sites along the river (Ageep et al., 2009; Dukeen and Omer, 1986). However, once the river's flood water diminishes, mosquito populations increase as the receding water creates stagnant pools that provide optimal breeding sites (Ageep et al., 2009; Dukeen and Omer, 1986). Based on this seasonal pattern between the mosquito vector's environment and population status, abnormally low levels of the Nile could potentially provide sustained water sources for breeding rather than high water levels disrupting mosquito breeding sites. As such, mosquito vector populations and malarial transmission may have continued with mosquito populations possibly further supported by the use of artificial breeding sites including those associated with irrigation.

Research Question 3: *Are there differences in the frequency of hypothesized malaria between sex and age cohorts at Mis Island?*

Expectation 3: *Indication of malarial infection is expected to be present in all sex and age cohorts with higher frequencies in younger age groups.*

A relatively similar prevalence of estimated malarial infection between males and females is expected with the hypothesis that there was not a considerable difference in exposure to mosquito vectors. Variation in exposure to mosquito vectors could result from differences in habitual activities, such as higher involvement in agricultural work which can influence risk of infection via close proximity to mosquito breeding grounds (Naidoo et al. 2011). However, any differences in activities between males and females that may have been present at Mis Island during the medieval period are not expected to have placed a differential burden of exposure to water sources that could have supported mosquito vector breeding and affected malarial spread.

This research question also considers the degree of endemicity at Mis Island during the medieval period which depends on at-risk groups, immunity, and periodicity of contact (Carter and Mendis, 2002). Endemic malaria involves some permanency of transmission, although this may be further classified as stable or unstable. Stable endemic malaria transmission is associated with environmental conditions that are favorable for continuous mosquito life cycles and the presence of malaria throughout the year (Carter and Mendis, 2002). Due to a regularity of exposure to malaria, some degree of protective immunity may be acquired by individuals in these regions. Areas experiencing unstable endemic malaria transmission are associated with a generally persistent presence of malaria, but the rate of infection is irregular following shifts in the epidemiological environment (Carter and Mendis, 2002). A period of interrupted contact between mosquito vectors and human hosts can result in decreased acquired immunity depending on the duration. During epidemics of malaria, there is a significant increase in transmission and all age groups in the population lack immunity (Carter and Mendis, 2002). Therefore, epidemic malaria may be more likely to result in higher mortality before skeletal indications manifest compared to endemic malaria, which may be more likely to involve some level of protection and chronic anemia (Smith-Guzmán et al., 2016).

This analysis is expected to find indication of endemic malaria with signs of infection in all age groups, with a higher frequency in younger individuals as they are at greatest risk of infection (Carter and Mendis, 2002). Mis Island is situated in a region that has been categorized as having an unstable endemic malarial risk (Snow et al., 2008), which is likely associated in part with the relationship between the Nile River's flooding and the mosquito's ecological niche. Mosquito populations along the Nile in northern Sudan tend to decrease during the flood season and increase as the river recedes, leaving stagnant pools of water used by mosquitoes as breeding sites (Dukeen and Omer, 1986). The increase in mosquito vector population can then lead to heightened risk of exposure for human hosts inhabiting the area. In line with the elevated frequencies of hypothesized malaria expected across age groups in this investigation, high prevalence of estimated malarial infection in older age groups may be anticipated as indications of possible lapses in acquired immunity.

Research Question 4a: *Are the skeletal lesions suggestive of malaria significantly associated with age?*

Expectation 4a: *The lesions are expected to be associated with age and present more frequently in younger individuals, particularly with respect to cribra orbitalia, humeral cribra, femoral cribra, and spinal porosity.*

The five lesions of interest—cribra orbitalia, humeral cribra, femoral cribra, spinal porosity, and periosteal reaction—and their association with the individuals' age are examined to evaluate age-related patterns in expression and to further consider their onset and chronicity. With anemia as a posited cause, this analysis examines the relationship between distribution of these lesions and changes in red marrow with age. Porous lesions resulting from anemia are thought to manifest only in regions of red or mixed marrow with potential for hyperplastic responses and are thus age dependent (Brickley, 2018). Therefore, these lesions are expected to be more prevalent in younger individuals.

Such a pattern for cribra orbitalia, humeral cribra, and femoral cribra were observed by Schats (2021) in an investigation of these three lesions among skeletal remains excavated in the

Netherlands from the medieval/early modern period (800–1600 CE). In studying these remains, which were part of a research project studying the presence of malaria, Schats observed that cribra orbitalia, humeral cribra, and femoral cribra were significantly more prevalent in subadults compared to adults. Schats also found that as age increased, the chances of displaying humeral cribra and femoral cribra significantly decreased; however, this trend was not true for cribra orbitalia.

Research Question 4b: *Are there significant associations among the paleopathological lesions suggestive of malaria?*

Expectation 4b: *Porous lesions are expected to frequently co-occur and demonstrate significant associations, particularly in younger individuals.*

Investigating the degree of association between these lesions further considers their formation with regard to the pathogenesis of malaria and the consistency in their patterns of expression. The pattern of correlation among lesions observed in this research is predicted to parallel that found by Smith-Guzmán (2015a) based on a shared hypothesized etiology of malaria, particularly with significant associations between humeral cribra and femoral cribra. While cribra orbitalia, humeral cribra, and femoral cribra are likely to frequently co-occur, cribra orbitalia may not be significantly associated with the other cribrous lesions as it has been associated with multiple etiologies (Wapler et al., 2004).

A relatively frequent co-occurrence, although not statistically significant, between cribra orbitalia, humeral cribra, and femoral cribra was observed by Gomes and colleagues (2022) in a sample of subadult remains from Portugal dating to the 19th to 20th centuries. While Schats (2021) found that these three cribrous lesions were uncommon to co-occur in the same individual within a skeletal sample from the Netherlands (800–1600 CE), their concurrent expression was seen more in subadult individuals than adults. Furthermore, for the subadult individuals Schats found femoral cribra frequently associated with cribra orbitalia and humeral cribra, and a statistically significant moderate association between humeral cribra and femoral cribra. Schats did not observe significant associations between pairs of the three cribrous lesions, although the subadult sample size was small suggesting that potential associations among the lesions of focus in the current research may be age-related.

Research Question 5a: *Are the macroscopic variables observed on the external surface of femoral cribra associated with age?*

Expectation 5a: *Femoral cribra in subadult remains is expected to be larger and appear unremodeled compared to femoral cribra in adult remains, which is anticipated to be of more varied size and demonstrate signs of remodeling and potentially a raised cortical edge around the perimeter.*

This pattern is anticipated based on femoral cribra's hypothesized etiology including anemia and the potential differences in extent of lesion remodeling from surviving health insults with age. A pattern of larger and more active-looking femoral cribra is anticipated in subadult ages when marrow is more reactive and cortical bone is thinner, thus potentially resulting in more severe lesions in response to stress (Lewis, 2018). Additionally, femoral cribra is expected to appear more active and severe in younger individuals compared to older individuals who survived prior pathological insult and might demonstrate remodeling lesions at different stages of healing.

Mangas-Carrasco and López-Costas (2021) found a clear pattern in the activity of femoral cribra with age-at-death in skeletal remains excavated from archaeological sites in NW Spain dating to the late medieval period (12th–15th centuries). In examining the lesions' surface for signs of remodeling and scoring them as active, mixed, or inactive, the authors observed more active femoral cribra lesions in subadult individuals and more healing/healed lesions in adult individuals. Mangas-Carrasco and López-Costas also investigated potential severity of femoral crbira across age groups. While they did not include measurements of the lesion in their analyses, they used a 4-grade scale that progresses from small pores that increasingly become larger and exhibit trabeculae as the most severe score. The authors did not find significant differences in severity of femoral cribra by age; however, the study subsample was small.

Research Question 5b: *Are there patterns between macroscopic variables observed on the external surface of femoral cribra potentially related to lesion "activity" and "severity"?*

Expectation 5b: *The presence of a raised cortical border around the lesion is expected to be associated with signs of remodeling and size of femoral cribra is expected to be associated with extent of cortical bone reduction.*

The presence of a raised cortical border surrounding the cribrous area of the lesion (a "cortical window") is expected to be associated with signs of remodeling, as it was suggested as indication of possible "healing" processes by Angel (1964). Lesion size is anticipated to vary with scores proposed by Radi and colleagues (2013) describing the extent to which the cortical surface has been affected. Femoral cribra presented as a cluster of pores on the cortical surface (Radi et al. Score 1) is anticipated to be associated with smaller lesions while femoral cribra displaying cortical erosion and exposed trabeculae (Radi et al. Score 2) are expected to be larger. This prediction is based on a hypothesis that femoral cribra progresses from smaller lesions with relatively less cortical modification to comparatively larger lesions in which the cortical surface has been further reduced.

Research Question 6a: *Are there differences in trabecular microarchitecture at the anterior-inferior femoral neck between unaffected individuals and affected individuals displaying femoral cribra with varying degrees of skeletal remodeling (i.e., "activity")?*

Expectation 6a: *Compared to unaffected individuals, affected individuals with lesions thought to be active are anticipated to show lower values for BV/TV, higher values for BS/BV and Tb.Sp., and either lower or higher values for Tb.Th. and Tb.N. Comparisons between unaffected individuals and affected individuals with lesions thought to be healing are expected to follow a similar patten, although not as distinct as comparing unaffected individuals and affected individuals with active lesions. In comparing lesions hypothesized to be active with those that appear to be healing, those lesions that demonstrate signs of remodeling on the surface are expected to exhibit higher values for BV/TV and Tb.Th., lower values for BS/BV and Tb.Sp., and either lower or higher values for Tb.N.*

The expected patterns of trabecular measurement differences for these comparisons are based on the types of bone processes (i.e., resorptive, formative, or mixed) hypothesized to be involved in the appearance of femoral cribra and possible signs of its activity from the surface. Compared to unaffected femora, the trabecular variables of femora with femoral cribra are anticipated to follow expected differences indicative of resorptive or mixed processes. These processes are hypothesized to be associated with the presence of the lesion and a proposed etiology of anemic conditions (Djuric et al., 2008). However, such differences are predicted to be more pronounced in comparing unaffected individuals and affected individuals with active lesions than in comparing unaffected individuals and affected individuals with healing lesions. This outcome is anticipated based on the thought that remodeling lesions would exhibit trabecular microarchitecture more similar to bone without the lesion. Finally, affected individuals displaying skeletal remodeling are expected to present microarchitectural differences indicative of formative processes compared to those without indication of remodeling from the surface, therefore supporting potential interpretations of "healing" lesion activity.

Research Question 6b: *Are there differences in trabecular microarchitecture at the anterior-inferior femoral neck between unaffected individuals and affected individuals displaying varying extents of femoral cribra (i.e., "severity")?*

Expectation 6b: *Compared to unaffected individuals, affected individuals with lesions thought to be active and displaying varying degrees of cortical modification are anticipated to show lower values for BV/TV, higher values for BS/BV and Tb.Sp., and either lower or higher values for Tb.Th. and Tb.N. These differences are expected to be more pronounced in comparing unaffected femora and affected femora with more severe looking lesions than in comparing unaffected femora and affected femora with less severe looking lesions. In comparing affected individuals with lesions that appear less severe and more severe based on extent of cortical surface disruption, lesions that appear more severe are anticipated to demonstrate lower values for BV/TV, higher values for BS/BV and Tb.Sp. and either lower or higher values for Tb.Th. and Tb.N.*

The expected patterns of trabecular measurement differences for this set of comparisons are based on the types of bone processes (i.e., resorptive, formative, or mixed) hypothesized to be involved in the appearance of femoral cribra and possible signs of its severity from the surface. Compared to unaffected femora, the trabecular variables of the selected femora with femoral cribra are anticipated to follow expected differences indicative of osteoclastic activity and/or mixed cellular activity that would suggest a skeletal response to anemia, which is hypothesized to be associated with the lesion (Djuric et al., 2008). However, such differences are predicted to be more pronounced in comparing unaffected individuals and affected individuals with more severe looking lesions than in comparing unaffected individuals and affected individuals with less severe looking lesions. Finally, in comparing affected femora that appear less severe and more severe, lesions that appear more severe are expected to present microstructural differences suggestive of increased osteoclastic change or marrow hyperplasia.

CHAPTER FIVE: MATERIALS & METHODS

This chapter describes the skeletal sample studied in this dissertation and the data collection and analysis methods used to address the research questions. The first section details the demographic composition of the Mis Island skeletal sample of focus in this research. The second section describes the methods involved in investigating the presence of malaria at Mis Island during the medieval period and in examining the associated suite of skeletal lesions implicated in the disease. Finally, the methods used in exploring the external appearance of femoral cribra and its internal trabecular microarchitecture are discussed.

All statistical analyses were performed in R Studio using Version 4.2.2 (Posit team, 2022) and statistical significance was set at $p \leq 0.05$. Pearson chi-square tests were used to evaluate significance of associations between categorical variables except when one or more of the expected cell frequencies was less than five, in which case Fisher's exact test was used instead. To assess the effect size of statistically significant outcomes, phi coefficients (φ) were calculated in instances of 2x2 contingency tables and Cramer's V statistics were used when contingency tables were larger. These measures were interpreted as follows: values 0 to 0.10 indicating a small effect, values between 0.11 and 0.30 suggesting a moderate effect, and values greater than 0.31 signifying a large effect (Wagner and Gillespie, 2019).

The Mis Island skeletal sample

The research sample studied in this dissertation comprises the human skeletal remains excavated from cemeteries 3-J-10 and 3-J-11 at the site of Mis Island. Cemetery 3-J-10 was situated in an area of alluvial deposits and was surrounded by rock outcrops (Ginns, 2010a, 2006). This cemetery was potentially where the last Christian burials on Mis Island were interred and was in use in the Late Medieval Period between approximately 1100 CE and 1500 CE, which includes the time period of Nubia converting to Islam (Ginns, 2006). On the southwest side of the cemetery, there is a "visible transition of belief" demonstrated by a shift in grave monument type with the early Muslim burials positioned near the Christian burials (Ginns, 2006:17). An estimated 262 box-grave monuments were believed to be present at this site and by the end of the excavations, a total of 126 sets of human skeletal remains were recovered from across the cemetery (Ginns, 2010a). All of the burials were aligned east to west and there were two main burial styles observed in the cemetery—standard box-type monuments with or without rocks or mud-bricks covering the head (Ginns 2010a, 2007).

Cemetery 3-J-11 was located closer to the river near the northern edge of the island in a terrain of alluvial formation and pebble deposits (Ginns 2010b). Representing the largest burial site on Mis Island, this cemetery spanned 300 CE – 1400 CE and thus was in use from the Meroitic Period through the Late Medieval Period (Ginns, 2006; Soler, 2012). A total of 288 sets of human remains were excavated from across cemetery 3-J-11 which was about half of the individuals likely interred at this site (Ginns, 2010b). The stone box-type monuments varied in size and style between graves and based on the variations in burial practices, this cemetery contained three primary phases (Ginns, 2010b, 2007, 2006). In most cases at cemetery 3-J-11, burials were oriented east to west to varying degrees (Ginns, 2010b).

The human skeletal remains excavated from cemeteries 3-J-10 and 3-J-11 were previously curated by the Department of Anthropology at Michigan State University on behalf of the British Museum. During this time, Soler (2012) and Hurst (2013) analyzed the adult and subadult remains, respectively, and estimated age-at-death and biological sex as appropriate. These demographic data reported by Soler (2012) for adult individuals and Hurst (2013) for subadult individuals were used in the current research to group the Mis Island individuals into age and sex cohorts for analyses. Soler (2012) estimated adult age-at-death with methods involving the pubic symphysis, auricular surface of the ilium, sternal rib ends, and cranial suture closure. Soler also estimated the biological sex of adult individuals using features of the pelvis and cranium and mandible. To estimate age-at-death for subadult individuals, Hurst (2013) used methods involving dental development stage, dental eruption, epiphyseal union, and long bone length. Hurst (2013) estimated biological sex for adolescent individuals if appropriate and possible.

Individuals whose age-at-death could be estimated had been placed into standard age groups by Soler (2012) and Hurst (2013). Table 5.1 lists the subadult and adult age groups and associated age ranges used in the current research which are based on Hurst's (2013) adjustments to the *Standards for Data Collection from Human Skeletal Remains* (Buikstra and Ubelaker, 1994) and Human Bioarchaeological Database (Redfern, 2010) categories. These systems were used in the current research to group individuals into age cohorts as appropriate for each research question. Individuals whose biological sex could be estimated had previously been assessed as male, probable male, female, probable female, or a category of unknown sex. To increase subsample sizes in the current study, probable males were grouped into the male category and probable females were combined with the female group.

Table 5.1: Subadult and adult age groups with associated age ranges based on Hurst's (2013) revised *Standards* and Human Bioarchaeological Database categories.

Revised *Standards* (Buikstra & Ubelaker, 1994)	**Revised Human Bioarchaeological Database (HBD) (Redfern, 2010)**
Infant (<3 years)	Infant (<3 years)
Child (3–11 years)	Child (3–7 years)
Adolescent (12–19 years)	Juvenile (8–16 years)
Young Adult (20–34 years)	Adolescent (17–19 years)
Middle Adult (35–49 years)	
Older Adult (≥50 years)	
Unknown Age Adult (≥20 years)	

Of the total number of individuals from Mis Island (n = 402), 370 individuals were associated with at least one skeletal element to assess the presence of at least one of the five lesions of focus for this research. These individuals therefore represent the full sample for this dissertation, the demographic composition of which is displayed in Table 5.2. Of the total 370 individuals included in the study, 121 individuals were from cemetery 3-J-10 and 249 individuals were from cemetery 3-J-11. Skeletal remains with age-at-death estimates of less than two-years-old and associated with an age range including an estimate of less than twelve months were excluded from current analyses, as the presence of the lesions could not be reliably assessed. Otherwise, individuals from all age groups were included in the research sample. As shown in Table 5.2, the study sample included relatively equal proportions of male and female individuals from both cemeteries.

Table 5.2: Mis Island research sample separated by cemetery, age-at-death, and biological sex.

	3-J-10				3-J-11				**Total**
Age Group (*Standards*)	Male	Female	Unknown	**Total**	Male	Female	Unknown	**Total**	
Infant	–	–	19	**19**	–	–	31	**31**	**50**
Child	–	–	23	**23**	–	–	68	**68**	**91**
Adolescent			5	**5**	3	2	16	**21**	**26**
Young Adult	12	4	–	**16**	14	20	2	**36**	**52**
Middle Adult	23	15	1	**39**	30	26	1	**57**	**96**
Older Adult	2	11	–	**13**	12	21	–	**33**	**46**
Unknown Age Adult	1	5	–	**6**	–	1	2	**3**	**9**
Total	**38**	**35**	**48**	**121**	**59**	**70**	**120**	**249**	**370**

Investigating malaria at Mis Island and the associated series of skeletal lesions (Research Questions 1, 2, 3, 4a & 4b)

Data collection

To investigate malaria at Mis Island, this research used a method developed by Smith-Guzmán (2015a), who proposed a suite of five skeletal lesions as indicators of malaria. These skeletal lesions are cribra orbitalia, humeral cribra, femoral cribra, spinal porosity, and periosteal reaction. The first four of these lesions are manifested as porous lesions that completely perforate cortical bone on the orbital plate of the frontal bone, the humeral and femoral necks, and the lateral and anterior surfaces of the vertebral bodies. Periosteal reaction is observed as the deposition of new bone on the outer cortex of long bone shafts as the result of an inflammatory response of the periosteum due to infection or trauma. The presence of these lesions was evaluated based on Smith-Guzmán's descriptions and scored as 1=present, 0=absent, or unscorable. Lesions that could be expressed bilaterally were scored as present when they appeared on the right, left, or both skeletal elements.

The diagnostic outcome algorithm generated by Smith-Guzmán (2015a:630) was used to infer whether an individual may have been infected with malaria, thus providing insight into potential prevalence and patterns of malaria across the sample. The algorithm entails looking at whether an individual displays a certain combination of lesions, as follows: if an individual displays femoral cribra, humeral cribra, or cribra orbitalia and also presents with spinal porosity or periosteal reaction, then the individual is associated with a "positive diagnosis" score; however, if an individual does not demonstrate one of these combinations of lesions, the individual is scored as "negative diagnosis" and interpreted as not associated with potential malarial infection. For each individual with the necessary skeletal elements present, this algorithm was used to score which individuals met the criteria for a "positive" or "negative" diagnosis of malaria.

Criteria for "Positive Diagnosis" (Smith-Guzmán (2015a:630)) = (Cribra orbitalia or humeral cribra or femoral cribra are present) *and* (Spinal porosity or periosteal reaction are present)

Data analysis

In investigating hypothesized malarial infection at Mis Island during the medieval period for Research Question 1, frequency data for the five skeletal lesions were compiled and compared with those provided by Smith-Guzmán (2015a) taken from two modern samples—one endemic for malaria and one that is non-endemic (i.e., malaria-free). Frequencies of each lesion were calculated by dividing the number of individuals exhibiting a given lesion in relation to the total number of skeletal elements observable for that lesion. This comparison was carried out to evaluate whether the prevalence of lesions observed in the Mis Island sample were more similar to a population associated with a high prevalence of malaria or one considered to not have been affected by malaria.

After performing Smith-Guzmán's (2015a) algorithm for each individual to infer a possible "positive diagnosis" or "negative diagnosis" of malaria, the frequency of individuals scored as "positive diagnosis" was calculated in relation to the total number of individuals with the appropriate skeletal completeness. For individuals with observable lesions that did not result in a "positive diagnosis" but were missing lesions that could have produced a positive result, no score was given. Because this could introduce bias in assessing the frequencies of estimated malaria, a conservative overall prevalence was calculated based only on individuals scorable for all five lesions (Buzon and Sanders, 2016; Smith, 2015). The regular and conservative estimates for the prevalence of malaria at Mis Island during the medieval period were compared to published frequencies that had used the same method from the sites of Tombos in Upper Nubia (Buzon and Sanders, 2016) and the South Tombs Cemetery at Amarna, Egypt (Smith-Guzmán et al., 2016). The site of Tombos is located at the Third Cataract of the Nile River and was inhabited between the mid-18th Dynasty of the Egyptian New Kingdom and the Napatan Period (~1400–650 BCE) (Buzon and Sanders, 2016). The skeletal remains excavated from the South Tombs Cemetery in Amarna, Egypt date to the Amarna Period (1349–1332 BCE) (Smith-Guzmán et al., 2016). Of the total Mis Island subsample that was sufficiently preserved for the algorithm to be performed, the results were then parsed according to intra-site comparisons.

For Research Question 2, the prevalence of individuals with hypothesized malarial infection and the associated five skeletal lesions were compared between cemetery 3-J-10 and cemetery 3-J-11. Hypothesized malaria was compared between both cemeteries overall and by age group (e.g., young adults from 3-J-10 vs. young adults from 3-J-11) using chi-square or Fisher's exact tests as appropriate. Each lesion was also compared between cemeteries with chi-square tests and significant results were further assessed by calculating associated phi coefficients. Potential differences in indications of malaria between cemeteries were then evaluated between males from cemetery 3-J-10 and males from cemetery 3-J-11, and between females from cemetery 3-J-10 and females from cemetery 3-J-11. For these analyses, only individual remains that could be assessed for biological sex estimation were included. Chi-square tests were used to examine hypothesized malaria infection and each skeletal lesion between males and females from both cemeteries with subsequent calculation of phi coefficients for statistically significant outcomes.

The prevalence of hypothesized malaria between age and sex cohorts was examined in Research Question 3. Hypothesized presence of malaria was compared between males and females separated by age groups using chi-square and Fisher's exact tests. The prevalence of each lesion between males and females was also compared with chi-square tests and phi coefficients for statistically significant results. Chi-square test and Cramer's V statistic were utilized to investigate the inferred malarial status across age groups. Further examination between age of the individual and the skeletal lesions was not included at this stage as that relationship was a focus for the subsequent research question.

The relationship between age and the skeletal lesions suggestive of malaria was examined in Research Question 4a using chi-square tests and Cramer's V statistics. To better visualize the relationship between these variables, a multiple correspondence analysis (MCA) was performed and presented in a biplot. The test was conducted with the presence and absence of the five skeletal lesions and the *Standards* age groups of infant, child, adolescent, young adult, middle adult, and older adult. The association among the five lesions was then investigated with chi-square and Fisher's exact tests and phi coefficients to address Research Question 4b. These analyses were performed on all individuals and then separated by subadult individuals (infant, child, and adolescent age groups) and adult individuals (young, middle, and older adults and adults of unknown age). The co-occurrence specifically between cribra orbtialia, humeral cribra, and femoral cribra was also examined to contribute to previous discussions of their correlation as part of a "cribrous syndrome", originally defined by Miquel-Feucht and colleagues (1999). The prevalence of all three lesions together and as pairs were assessed across the entire sample, and separately among subadult and adult individuals. These findings were discussed in relation to observations made in other studies.

Exploring the expression of femoral cribra (Research Questions 5a & 5b and 6a & 6b)

External features of femoral cribra—Data collection

The investigation on femoral cribra's external expression potentially associated with "severity" and "activity", and the pattern of these variables across age groups, was conducted on all proximal femora displaying the lesion in the Mis Island cemetery 3-J-10 and 3-J-11 groups. For this research component, individuals in the "Unknown Age Adult (≥20 years)" age group were not included in the subsample as this age-at-death estimate was not narrow enough for more nuanced interpretation of the results. Additionally, individuals whose age-at-death estimates were less than two-years-old and associated with age ranges involving an estimate of less than twelve months were excluded from the subsample, as the femoral neck was not morphologically distinct enough to assess the presence or absence of femoral cribra.

A series of macroscopic observations were collected from the external surface of each femoral cribra lesion to investigate variation in these feature's relationship with age and their potential association with lesion "activity" and "severity". As many variables that could be observed were collected for each femoral cribra lesion but were considered not recordable if the lesion was too damaged or incomplete. To evaluate possible changes related to "activity", each femoral cribra lesion was visually examined for indication of unremodeled and remodeling bone. Following Mensforth and colleagues' (1978) descriptions for porotic hyperostosis, "active" femoral cribra may be presented as sharp-edged lesions, whereas femoral cribra that has experienced some degree of remodeling, or "healing", may display smooth-edged bone in the affected area. Observations noting these sharp- vs. smooth-edged differences were made for each case, with those presenting exclusively sharp-edged margins recorded as possible "active" lesions and those exhibiting rounded bony margins within the lesion recorded as possible “healing” lesions. Additionally, the presence or absence of a raised, thickened border which sometimes surrounds the porous area was evaluated (i.e., a “cortical window”). This border was considered present when there was a distinct margin immediately adjacent and encircling the lesion’s pores or trabeculae (Figure 5.1).

Figure 5.1: Example of bilateral “cortical windows” encircling femoral cribra (Cemetery 3-J-10, Skeleton 1005).

To assess possible differences in “severity”, femoral cribra was scored using Radi and colleagues’ (2013) categories that reflect the degree of cortical disruption. If femoral cribra was present on a femur, the lesion’s appearance was assessed according to this system and scored as either 1) a cluster of pores on the cortical surface, or 2) an area of cortical erosion exposing trabeculae that may be depressed. This scoring system was selected for the current study given the relatively unambiguous distinction between the two scores, as well as previous findings of low intraobserver and interobserver error (Radi et al., 2013). In addition to these scores, several measurements were taken using a tape measure to investigate variation in lesion size. These measurements included the perimeter of the lesion and lengths of the lesion parallel and perpendicular to the femoral neck.

External features of femoral cribra—Data analysis

Analyses of the variation in femoral cribra's external surface were conducted separately for left and right femora as both skeletal elements were not present for every individual. Individuals were separated and compared according to the *Standards* age group categories (Table 5.1), except in analyses involving measurements of the lesion. For analyses that examined the three measurements of femoral cribra, the subadult age ranges used in the Human Bioarchaeological Database (Table 5.1) were used as these involve narrower age ranges that could better account for growth of the femoral neck with increasing age.

Towards addressing Research Question 5a, Fisher's exact test and Cramer's V statistic were used to examine the relationship between age groups and femoral cribra's Radi et al. Score, estimated activity, and presence of a cortical window. Multiple correspondence analysis (MCA) was used to explore the relationship between age group, Radi et al. Score, estimated activity, and status of a cortical window. Scatter plots were used to investigate variation in size, represented as perimeter of the lesion, and estimated activity of the lesion across age groups. In examining Research Question 5b, Fisher's exact tests were used to assess the association between hypothesized lesion activity and the presence of a cortical window for left and right femora, and phi coefficients were used to evaluate the strength of these associations. Lesion size was compared between Radi et al. Scores 1 and 2 by calculating the mean and standard deviation of each score for the three femoral cribra measurements taken perpendicular to the femoral neck, parallel to the femoral neck, and around the lesion's perimeter. These calculations were conducted separately by age group using the subadult age ranges of the Human Bioarchaeological Database. Boxplots were also used to compare these three measurements between lesions with Radi et al. Scores 1 and 2 within each age group.

Internal features of femoral cribra—Data collection

A total of 27 femora were examined with micro-CT methods to explore trabecular microarchitecture (Table 5.3). The maximum length of a femur to fit in the sample sled was 405mm, which was one criterion for including proximal femora in the study sample. Preference was given towards femora belonging to individuals whose skeletal remains were excavated from cemetery 3-J-11 at Mis Island; however, femora were selected from the cemetery 3-J-10 subsample if needed. For individuals presenting bilateral expressions of femoral cribra, the left femur was selected for the sample and the right femur was included if the left was either absent or unsuitable for micro-CT analysis. While asymmetrical expressions of femoral cribra is a subject to evaluate in future research, the current study focused on the lesion's variation across individuals. Additionally, previous work by Radi and colleagues (2013) did not find significant differences in the frequency and appearance of femoral cribra between sides. To gain a better understanding of femoral cribra's variation and development, subadult and adult individuals from different age cohorts were included. In addition to age group, adult individuals were separated by sex for comparison.

Table 5.3: Number of femora per cohort examined using micro-CT methods, separated by affected/unaffected status, cemetery, and side (YA: Young Adult, MA: Middle Adult).

Cohort	Affected				Unaffected				**Total**
	3-J-11		3-J-10		3-J-11		3-J-10		
	Left	Right	Left	Right	Left	Right	Left	Right	
Subadult 2–3 yrs	1	–	1	–	2	–	–	–	**4**
Subadult 3–5 yrs	3	–	–	–	–	2	–	–	**5**
Subadult 4–7 yrs	2	–	1	–	–	1	–	–	**4**
Subadult 10–15 yrs	1	–	1	–	–	–	–	–	**2**
YA Female 20–34 yrs	1	–	–	1	–	1	–	–	**3**
YA Male 20–34 yrs	1	1	–	–	–	–	1	–	**3**
MA Female 35–49 yrs	1	–	–	1	–	1	1	–	**4**
MA Male 35–49 yrs	1	–	–	–	1	–	–	–	**2**
Total	**17**				**10**				**27**

The selected sample included proximal femora with and without femoral cribra to compare trabecular microarchitecture between affected and unaffected individuals. The subsample of femora with femoral cribra displayed varying expressions of the lesion based on macroscopic observations investigated for their potential association with "activity" and "severity". These characteristics primarily included the appearance of sharp- vs. smooth-edged lesion margins and the extent of porosity/exposed trabeculae. The subsample of femora without femoral cribra demonstrated either no visible signs of porosity or, in the case of subadult individuals, displayed porosity associated with remodeling during growth. This normal porosity seen on the surface of subadult metaphyses is due to resorption under the periosteum, revealing haversian canals in the cortical bone (Ortner, 2003). Although this porosity at juvenile metaphyses can overlap and be confused with pathological change (Buikstra and Ubelaker, 1994; Ortner, 2003), this study sought to distinguish pathological porosity as perforations through the cortex and exposure of trabecular bone (Brickley and Ives, 2006) displayed on the anteroinferior femoral neck. The subsample without femoral cribra was selected to parallel the age and sex composition of the subsample with femoral cribra to allow for more controlled comparisons.

Micro-CT scan and data acquisition was conducted with the facilities at the MSU Institute for Quantitative Health Science & Engineering (IQ) and with the aid of Jeremy Hix of the MSU IQ Imaging Core Facility. The Quantum GX2 micro-CT imaging system manufactured by PerkinElmer was used for scanning and the Bone Phantom QRM-MicroCT-HA-D10 was used for calibrating hydroxyapatite density. Image acquisition settings included: 90kV, 88µA, voxel size 120µm, FOV acquisition of 70 and recon of 60, and scan time of approximately 14 minutes. After the micro-CT images were acquired, the Analyze 14.0 (AnalyzeDirect, Overland Park, KS) software application Bone Microarchitecture Analysis (BMA) was used for processing micro-CT scans, collecting quantitative data on trabecular microarchitecture, and visually assessing cortical and trabecular differences.

Generating volumes of interest (VOIs)

Before obtaining quantitative measurements from the micro-CT scans, a volume of interest (VOI) was selected from each scanned specimen. The measurements were then calculated from the trabecular bone captured within the VOI's boundaries. The approach for VOI selection must be carefully considered, as the dimension, size, and location of a VOI will impact the interpretation of the results. A VOI that is inappropriately small or large relative to the region of interest can introduce unintended biases into the study by under- or over-sampling trabecular microarchitecture (Fajardo and Müller 2001; Lazenby et al. 2011). Improperly fitted VOIs across a study sample can thus increase the potential of Type I and Type II errors (Lazenby et al., 2011; Morgan, 2014). This consideration also applies to comparing individuals of varying body size, as a uniform VOI across the sample can over- or under-sample (Fajardo and Müller, 2001, Lazenby et al., 2011). Some researchers, therefore, suggest scaling VOIs for each case rather than establishing a fixed sized VOI to decrease the potential for error (Lazenby et al., 2011). Previous research suggests that manually-adapted VOIs produce more pertinent and comprehensive results compared to fixed geometric VOIs (Djuric et al., 2013; Marchand et al., 2010). In a micro-CT study on porous lesions of the orbit and cranial vault, Morgan (2014) tested the reliability and reproducibility of uniform 2D and 3D VOIs and custom sized 3D VOIs in cranial bones. Compared to 2D and 3D standard fixed size VOIs, custom sized 3D VOIs with varied dimensions depending on each individual specimen were considered the most appropriate method for quantifying bone microarchitecture.

The location of the sampled bone must also be considered, as trabecular architecture can change over relatively short distances (Whitehouse and Dyson 1974; Whitehouse, 1975). Therefore, anatomical and biomechanically relevant variables specific to the location should be taken into account when determining a VOI. For example, the proximal femur is a biomechanically complex structure with varying trabecular groups and morphological features across its anatomical regions. The trabeculae underlying the medial femoral neck, where femoral cribra manifests, belong to the principal compressive group (Whitehouse and Dyson, 1974). This vertical system extends from the medial proximal diaphysis to the articular surface of the head and is characterized by dense trabeculae (Whitehouse and Dyson, 1974).

In the current research, custom sized 3D VOIs were established for each specimen which resulted in approximately cube-shaped subregions. For femora displaying femoral cribra, the VOIs were generated to encompass the visibly affected surface and the trabeculae underneath. For femora without the lesion, the VOIs were created to mirror the size and location of the VOIs of their affected counterparts. Scans were rotated as needed to ensure proper VOI selection in affected and unaffected femora. Using the Transform application, the VOI dimensions were adjusted within *x*, *y*, and *z* planes to encompass the region of focus. A 3D rendering of the scanned specimen was used to visualize the medial-lateral and superior-inferior boundaries of the VOI from the bone's surface. After these edges were established, the depth of the VOI was adjusted to one quarter of the anterior-posterior distance from the surface. This depth was chosen to isolate and emphasize the trabeculae directly underlying the area of interest while also attempting to avoid potential biomechanical influences of the femoral neck's trabecular structure.

Prior to establishing this protocol of VOI selection, the researcher assessed the scanned trabecular regions to confirm its suitability and considered biases in varying the morphology and location of the subregions (Kivell et al., 2011). To limit potential confounding effects in comparing data from VOIs at different areas on the anteromedial femoral neck, subregions of the unaffected femora were made specific for comparing to each of the affected femora in a cohort group that displayed lesions in slightly different locations. Therefore, for some comparisons multiple VOIs were created from one unaffected femur to be compared with its affected counterparts depending on whether lesions varied in location. Additionally, data from affected femora with lesions at slightly different areas on the femoral neck were only compared to other affected femora in their cohort group if they were similar in location or if the VOIs could be adjusted appropriately for comparison.

Image thresholding and segmentation

After isolating the VOI from a scanned femur, the process of segmentation was conducted to identify objects within that subregion. Image segmentation involves establishing threshold values for voxels of varying gray levels that accurately associate with the given object in that volume of interest (e.g., bone tissue vs. space occupied by air). The Segment module allows automatic and manual approaches to distinguish bone from non-bone objects and to isolate cortical bone from trabecular bone (AnalyzeDirect, Overland Park, KS). The outcome of this procedure was an object map with the following features defined and separated from which quantitative measurements were automatically calculated: air surrounding the specimen, cortex, intra-trabecular space, and trabecular bone.

To better segment cortex from trabecular bone in the VOIs with similar grayscale values, this research used the Walls tool with the Spline option to define curved boundaries interpolated across each slice of the subregion separating cortical and trabecular bone. After a Wall was established across the subregion, the objects were separated through threshold segmentation. This process entails assigning a range of voxels in the volume to a certain object such that all voxels falling between the threshold's minimum and maximum values are ascribed to that object. In this research, thresholds were derived using the Segment module which calculated the volume histogram and provided the option to produce up to eight threshold values. These automatically calculated threshold values were used in segmenting bone from air in the subregion and the most appropriate threshold option was determined through visual assessment. The threshold range that distinguished bone was assigned for the cortex and trabecular bone objects, which were then separated using the Object Separator tool in conjunction with the pre-defined Wall drawn between them. Intra-trabecular space and the air surrounding the bone were then assigned to threshold values less than those assigned to bone. These two objects were also then separated using the Object Separator tool which was made more effective with the already established Wall.

Data acquisition

After establishing the VOIs, quantitative measures were automatically calculated for the trabecular bone within each femora's VOI using the BMA (Bone Microarchitecture Analysis) application. Data for the five variables described as follows were derived from each VOI (AnalyzeDirect, Overland Park, KS; Hildebrand et al., 1999; Morgan, 2014):

- **Bone volume density** (BV/TV, %): the ratio of trabecular bone volume (BV) to the total volume of interest (TV)
- **Specific bone surface** (BS/BV, mm^2/mm^3): the ratio of the bone surface area (BS) to the volume of trabecular bone (BV)
- **Trabecular thickness** (Tb.Th., mm): the mean thickness of trabeculae within a volume of interest
- **Trabecular number** (Tb.N., 1/mm): the average number of trabeculae per unit length and reported as a 2D variable for each axial slice
- **Trabecular spacing** (Tb.Sp., mm): the mean distance between trabeculae within a volume of interest

Standard deviation values were calculated for trabecular thickness, number, and spacing. As a two-dimensional measurement, trabecular number was originally reported for each axial slice in a given VOI. In order to arrive at a single value representative of Tb.N. for the entire VOI, the mean across slices was calculated.

Internal features of femoral cribra—Data analysis

These variables were understood in the following terms (Morgan, 2014). Bone volume density and specific bone surface were examined to evaluate how the amount of bone was affected by an underlying cause. Trabecular thickness represented the relative amount of bone and differences resulting from trabecular resorption or formation. Trabecular number reflected the general structure and organization of the trabecular bone with differences indicating bone resorption or formation. Trabecular spacing corresponded to organization and amount of marrow space with changes suggesting trabecular resorption or formation.

For Research Questions 6a and 6b the data for the five quantitative, microarchitectural measures were compared among individuals within their respective demographic cohorts. The first set of comparisons (Research Question 6a) were between unaffected individuals and affected individuals displaying femoral cribra hypothesized to reflect either “active” or “healing” lesions based on macroscopic signs of skeletal remodeling on the surface. All affected lesions included in this stage of analysis shared a Radi et al. 2 Score. Lesions that appeared “active” and “healing” were also compared with each other within their respective cohorts. The second set of comparisons (Research Question 6b) were between unaffected individuals and affected individuals with “active” femoral cribra of varying expressions possibly reflecting lesion “severity”, which was described as either “less severe” or “more severe” based on indications from the surface. A subgroup of lesions inferred to be “less severe” or “more severe” were then compared with each other in the same cohort. Comparisons were conducted between pairs of individuals from the same cohort with equivalent VOIs and were made across the five variables. For each comparison pair, the measures for one individual were evaluated to be either greater than or less than the other individual for each variable. This process was done across pairs and tabulated to investigate potential patterns. Differences in the variables were interpreted in terms of inferred types of bone processes as presented by Morgan (2014) and contextualized as potential insight into the pathogenesis of femoral cribra. The anticipated changes to the trabecular microarchitectural variables for these processes described by Morgan (2014:149) are as follows:

- **Resorptive processes** (osteoclastic activity): decrease in BV/TV and Tb.Th., increase in BS/BV and Tb.Sp., and either decrease or increase in Tb.N.
- **Formative processes** (osteoblastic activity): increase in BV/TV and Tb.Th., decrease in BS/BV and Tb.Sp., and either decrease or increase in Tb.N.
- **Mixed processes** (mixed cellular activity): decrease in BV/TV, increase in BS/BV and Tb.Sp., and either decrease or increase in Tb.Th. and Tb.N.

CHAPTER SIX: RESULTS

Research Question 1

Research Question 1: *Is there skeletal indication of malarial infection at Mis Island during the medieval period and if so, how prevalent may malaria have been?*

The frequencies of each lesion in the Mis Island sample were calculated (Table 6.1) and compared to those reported by Smith-Guzmán (2015a) for malaria-endemic and malaria-free samples (Table 6.2 and Figure 6.1). Within the Mis Island sample, femoral cribra was the most prevalent of the five lesions (77%), followed by cribra orbitalia and periosteal reaction (both 59%), spinal porosity (52%), and humeral cribra (37%). When compared to Smith-Guzmán's (2015a) endemic and non-endemic samples, the Mis Island sample demonstrated higher frequencies of femoral cribra and humeral cribra. The frequencies of cribra orbitalia and periosteal reaction in the Mis Island sample were similar to those of the malaria-endemic sample, although slightly higher in the Mis Island sample. The prevalence of spinal porosity in the Mis Island sample was intermediate between the endemic and non-endemic samples.

Table 6.1: Prevalence of lesions observed in the total Mis Island sample.

Lesion	Present	Absent	Total	Prevalence (%)
Cribra orbitalia	173	119	292	59%
Humeral cribra	94	161	255	37%
Femoral cribra	226	66	292	77%
Spinal porosity	164	152	316	52%
Periosteal reaction	198	136	334	59%

Table 6.2: Frequencies of lesions in the Mis Island sample compared to Smith-Guzmán's (2015a) endemic and non-endemic samples.

Lesion	Mis Island	Endemic	Non-endemic
Cribra orbitalia	59%	57%	2%
Humeral cribra	37%	24%	5%
Femoral cribra	77%	39%	0%
Spinal porosity	52%	89%	18%
Periosteal reaction	59%	52%	17%

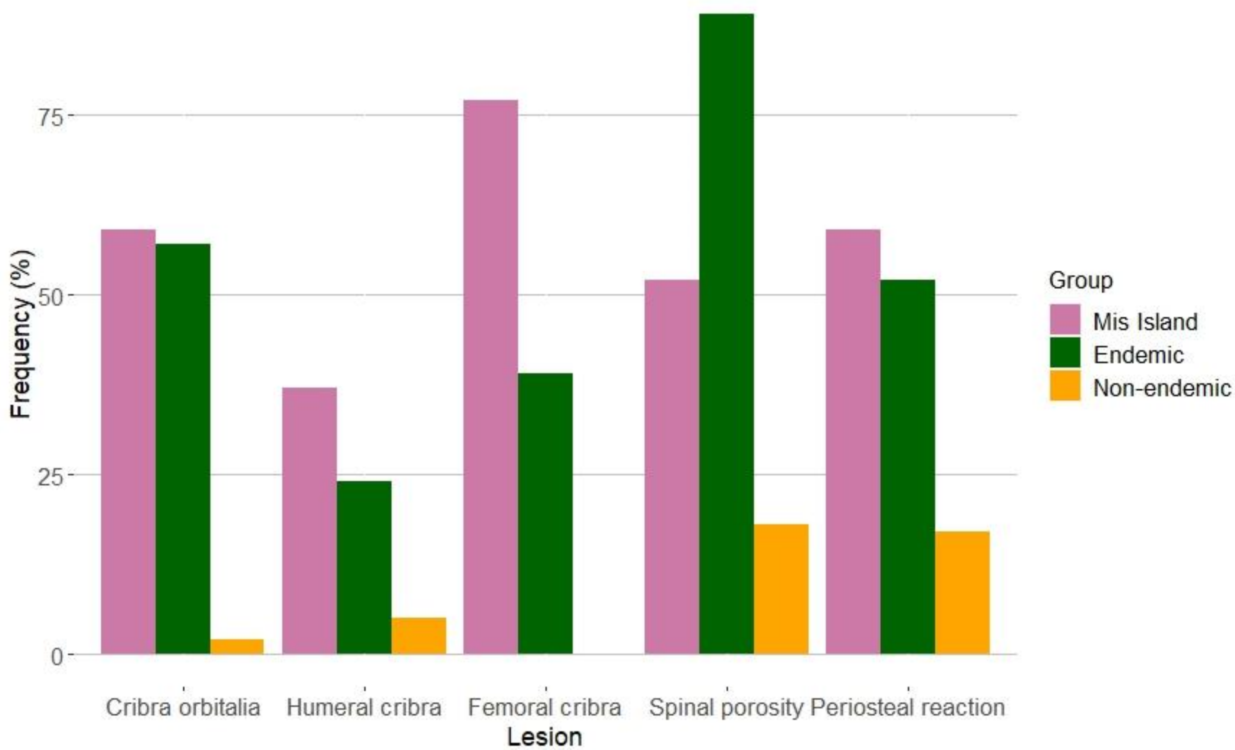

Figure 6.1: Grouped bar plot of lesion prevalence in the Mis Island sample and Smith-Guzmán's (2015a) endemic and non-endemic samples.

Of the total sample (n = 370), 296 individuals could be assessed for the potential presence of malaria using a subset of the lesions in the algorithm presented by Smith-Guzmán (2015a). The demographic data of this subsample are presented in Table 6.3. Within this subsample, 223 individuals (75%) met the algorithmic criteria for a "positive diagnosis" and thus demonstrated signs of possible infection (Table 6.4). Two hundred individuals were scorable for all five lesions and 155 met the "positive diagnosis" criteria (Table 6.4). Therefore, a conservative estimate of 78% displayed indications of hypothesized malarial infection. When separated by cemetery, 71% and 77% of individuals from cemeteries 3-J-10 and 3-J-11 met the criteria for a "positive diagnosis", respectively. When only the individuals scorable for all five lesions were included for the algorithm from each cemetery, conservative estimates of 80% and 76% indicated signs of possible infection in cemeteries 3-J-10 and 3-J-11, respectively.

Table 6.3: Individuals with the appropriate skeletal elements present to estimate either a "positive or negative diagnosis" for malaria using Smith-Guzmán's (2015a) algorithm (M: Male, F: Female, U: Unknown).

	3-J-10				3-J-11				**Total**
	M	F	U	**Total**	M	F	U	**Total**	
Infant (<3 yrs)	–	–	19	**19**	–	–	23	**23**	**42**
Child (3–11 yrs)	–	–	19	**19**	–	–	60	**60**	**79**
Adolescent (12–19 yrs)	0	0	5	**5**	2	2	16	**20**	**25**
Young Adult (20–34 yrs)	9	4	–	**13**	13	17	1	**31**	**44**
Middle Adult (35–49 yrs)	15	11	1	**27**	22	22	1	**45**	**72**
Older Adult (≥50 yrs)	1	8	–	**9**	6	17	–	**23**	**32**
Unknown Age Adult (≥20 yrs)	–	1	–	**1**	–		1	**1**	**2**
Total	**25**	**24**	**44**	**93**	**43**	**58**	**102**	**203**	**296**

Table 6.4: Prevalence of "positive diagnoses" and "negative diagnoses" for Mis Island cemeteries 3-J-10 and 3-J-11 following a regular estimate approach and a conservative estimate approach.

		"Positive Diagnosis"	"Negative Diagnosis"	Total	Frequency of "Positive Diagnosis"
Regular estimate	3-J-10	66	27	93	71%
	3-J-11	157	46	203	77%
	Total	**223**	**73**	**296**	**75%**
Conservative estimate	3-J-10	48	12	60	80%
	3-J-11	107	33	140	76%
	Total	**155**	**45**	**200**	**78%**

The frequencies of hypothesized malarial infection for the total Mis Island sample were compared to those reported from studies on the Upper Nubian site Tombos (Buzon and Sanders, 2016) and the South Tombs Cemetery in Amarna, Egypt (Smith-Guzmán et al., 2016) which used

Smith-Guzmán's method to estimate the potential prevalence of malaria (Table 6.5). Of the total number of individuals analyzed from Tombos dating between the New Kingdom and Napatan periods (~1400–650 BCE, n = 60), 37% individuals met the algorithmic criteria for a "positive diagnosis". Of the individuals analyzed from the South Tombs Cemetery dating to the Amarna Period (1349–1332 BCE, n = 417 although it is unclear if all individuals were included), an estimated 50% of individuals displayed indication of potential infection. Both the regular and conservative estimates for the prevalence of hypothesized malaria at Mis Island (~300–1500 CE)—75% and 78%, respectively—were higher than those found in the skeletal remains analyzed from Tombos and the South Tombs cemetery.

Of the estimates reported from the other sites, the closest frequency to those from Mis Island was the estimate based only on complete skeletal remains (i.e., a conservative estimate) from Tombos dating to the Third Intermediate and Napatan Periods (Table 6.5). The conservative estimate from this subsample was 56% (10/18) and was associated with a regular estimate of 48% (11/23) (Buzon and Sanders, 2016). The next closest frequency was that reported from the South Tombs Cemetery which was an estimate of 50% (Smith-Guzmán et al., 2016). The estimated prevalence of malaria in the Tombos New Kingdom subsample was the most dissimilar compared to Mis Island and was reported at 30% (11/37) and conservatively at 35% (7/20) (Buzon and Sanders, 2016).

Table 6.5: Regular and conservative estimates for the prevalence of malaria at Mis Island, Tombos (Buzon and Sanders, 2016), and the South Tombs Cemetery (Smith-Guzmán et al., 2016).

Site	Estimated Prevalence of Malaria: Regular estimate	Estimated Prevalence of Malaria: Conservative estimate
Mis Island, Fourth Cataract, Upper Nubia (Medieval Period)	75%	78%
Tombos, Third Cataract, Upper Nubia (*All time periods*: New Kingdom – Napatan Periods)	37%	
Tombos, Third Cataract, Upper Nubia (Third Intermediate & Napatan Periods)	48%	56%
Tombos, Third Cataract, Upper Nubia (New Kingdom Period)	30%	35%
South Tombs Cemetery, Amarna, Egypt (Amarna Period)	50%	

Research Question 2

Research Question 2: *Are there differences in the frequency of hypothesized malaria between individuals from cemeteries 3-J-10 and 3-J-11?*

The prevalence of hypothesized malaria was first compared between all individuals from cemeteries 3-J-10 and 3-J-11. A chi-square test between both cemeteries revealed no significant difference in the prevalence of inferred malarial infection (Table 6.6). Furthermore, a similar frequency of “positive diagnoses” for malaria was found between both cemeteries, as 71% of individuals from cemetery 3-J-10 and 77% of individuals from cemetery 3-J-11 displayed signs of possible infection (Table 6.6). When separated by age, Fisher’s exact and chi-square tests yielded no significant differences between cemeteries 3-J-10 and 3-J-11 for each age cohort (Table 6.6). The frequencies of “positive diagnoses” for malaria were also similar between the same age groups from both cemeteries (Table 6.6).

Table 6.6: Prevalence of "positive diagnoses" (P.D.) and "negative diagnoses" (N.D.) between cemeteries 3-J-10 and 3-J-11, separated by age group, as well as p-values from Fisher's exact (FET) tests and chi-square tests (df = 1).

	3-J-10				**3-J-11**				**3-J-10 vs. 3-J-11**
	P.D.	N.D.	Total	P.D.%	P.D.	N.D.	Total	P.D.%	
Infant (<3 yrs)	14	5	19	74%	17	6	23	74%	FET $p = 1.00$
Child (3–11 yrs)	16	3	19	84%	48	12	60	80%	FET $p = 1.00$
Adolescent (12–19 yrs)	5	0	5	100%	19	1	20	95%	FET $p = 1.00$
Young Adult (20–34 yrs)	11	2	13	85%	28	3	31	90%	FET $p = 0.62$
Middle Adult (35–49 yrs)	15	12	27	56%	30	15	45	67%	$\chi^2 = 0.48$ $p = 0.49$
Older Adult (≥50 yrs)	4	5	9	44%	14	9	23	61%	FET $p = 0.45$
Total	**65**	**27**	**92**	**71%**	**156**	**46**	**202**	**77%**	$\chi^2 = 1.46$ $p = 0.23$

In comparing the prevalence of each lesion between individuals from cemeteries 3-J-10 and 3-J-11, significant differences were found between the cemeteries for cribra orbitalia and spinal porosity (Table 6.7). Cribra orbitalia was observed at a higher frequency among individuals from cemetery 3-J-11 (64%) than individuals from cemetery 3-J-10 (49%), which was a pattern found across all age groups (Table 6.8). Spinal porosity was also more prevalent among individuals from cemetery 3-J-11 (59%) than individuals from cemetery 3-J-10 (37%); however, only the adult age groups from cemetery 3-J-11 demonstrated higher frequencies in spinal porosity compared to individuals from cemetery 3-J-10 (Table 6.11). Although these comparisons yielded statistically significant results, the associated phi coefficients suggest that the effects are relatively small for cribra orbitalia and small-medium for spinal porosity (Table 6.8 and Table 6. 11, respectively). The results for humeral cribra, femoral cribra, and periosteal reaction reflected no significant differences in the prevalence of these lesions between individuals from cemetery 3-J-10 and individuals from cemetery 3-J-11 (Table 6.7). In comparing their prevalence between cemeteries, these three lesions were observed at similar frequencies in cemetery 3-J-10 and 3-J-11 (Tables 6.9, 6.10, and 6.12).

Table 6.7: Results of chi-square tests (df = 1) between cemeteries 3-J-10 and 3-J-11 for each lesion and phi coefficients for significant results (bolded p-values).

Cribra orbitalia	$\chi^2 = 6.13$ **p = 0.013** $\varphi = -0.15$
Humeral cribra	$\chi^2 = 0.24$ p = 0.62
Femoral cribra	$\chi^2 = 0.018$ p = 0.89
Spinal porosity	$\chi^2 = 12.18$ **p = 0.00048** $\varphi = -0.2$
Periosteal reaction	$\chi^2 = 0.70$ p = 0.40

Table 6.8: Prevalence of cribra orbitalia (CO) in cemeteries 3-J-10 and 3-J-11, separated by age.

	3-J-10				3-J-11			
	CO Present	CO Absent	Total	%	CO Present	CO Absent	Total	%
Infant	14	5	19	74%	16	2	18	89%
Child	14	4	18	78%	39	8	47	83%
Adolescent	1	3	4	25%	17	1	18	94%
Young Adult	6	8	14	43%	19	14	33	58%
Middle Adult	6	21	27	22%	20	32	52	38%
Older Adult	4	6	10	40%	15	13	28	54%
Total	**45**	**47**	**92**	**49%**	**126**	**70**	**196**	**64%**

Table 6.9: Prevalence of humeral cribra (HC) in cemeteries 3-J-10 and 3-J-11, separated by age.

	3-J-10				3-J-11			
	HC Present	HC Absent	Total	%	HC Present	HC Absent	Total	%
Infant	9	9	18	50%	6	18	24	25%
Child	11	10	21	52%	37	22	59	63%
Adolescent	2	2	4	50%	9	6	15	60%
Young Adult	3	6	9	33%	12	11	23	52%
Middle Adult	1	20	21	5%	2	36	38	5%
Older Adult	1	4	5	20%	1	17	18	6%
Total	**27**	**51**	**78**	**35%**	**67**	**110**	**177**	**38%**

Table 6.10: Prevalence of femoral cribra (FC) in cemeteries 3-J-10 and 3-J-11, separated by age.

	3-J-10				3-J-11			
	FC Present	FC Absent	Total	%	FC Present	FC Absent	Total	%
Infant	13	6	19	68%	16	9	25	64%
Child	16	6	22	73%	60	6	66	91%
Adolescent	5	0	5	100%	17	0	17	100%
Young Adult	12	2	14	86%	25	7	32	78%
Middle Adult	18	6	24	75%	27	11	38	71%
Older Adult	5	1	6	83%	9	12	21	43%
Total	**69**	**21**	**90**	**77%**	**154**	**45**	**199**	**77%**

Table 6.11: Prevalence of spinal porosity (SP) in cemeteries 3-J-10 and 3-J-11, separated by age.

	3-J-10				3-J-11			
	SP Present	SP Absent	Total	%	SP Present	SP Absent	Total	%
Infant	6	12	18	33%	9	17	26	35%
Child	13	8	21	62%	33	27	60	55%
Adolescent	5	0	5	100%	18	1	19	95%
Young Adult	9	4	13	69%	29	4	33	88%
Middle Adult	4	29	33	12%	28	21	49	57%
Older Adult	0	9	9	0%	10	20	30	33%
Total	**37**	**62**	**99**	**37%**	**127**	**90**	**217**	**59%**

Table 6.12: Prevalence of periosteal reaction (PR) in cemeteries 3-J-10 and 3-J-11, separated by age.

	3-J-10				3-J-11			
	PR Present	PR Absent	Total	%	PR Present	PR Absent	Total	%
Infant	14	5	19	74%	18	10	28	64%
Child	12	10	22	55%	28	36	64	44%
Adolescent	2	3	5	40%	10	9	19	53%
Young Adult	9	4	13	69%	20	12	32	63%
Middle Adult	24	11	35	69%	31	18	49	63%
Older Adult	5	7	12	42%	21	10	31	68%
Total	**66**	**40**	**106**	**62%**	**128**	**95**	**223**	**57%**

To examine possible differences of hypothesized malaria between males and females from cemeteries 3-J-10 and 3-J-11, only individuals whose remains could be estimated for biological sex were included (n = 49 for 3-J-10, n = 101 for 3-J-11). A chi-square test between males from cemetery 3-J-10 and males from cemetery 3-J-11 yielded no significant difference for inferred malaria (Table 6.13). Additionally, similar frequencies of “positive diagnoses” were found in both subgroups (Table 6.13). While a Fisher’s exact test between female individuals from 3-J-10 and 3-J-11 did not result in a significant difference, the p-value approached statistical significance (Table 6.13). In comparing the frequencies of “positive diagnoses” for malaria between females from both cemeteries, a higher frequency of 79% was found among female individuals from 3-J-11 compared to the frequency of 58% observed among females from 3-J-10 (Table 6.13). The outcome of a chi-square test between both males and females from 3-J-10 and males and females from 3-J-11 did not result in a significant difference (Table 6.13).

Table 6.13: Prevalence of “positive diagnoses” (P.D.) and “negative diagnoses” (N.D.) between cemeteries, separated by sex, and results of chi-square (df = 1) and Fisher’s exact tests.

	3-J-10				3-J-11				3-J-10 vs. 3-J-11
	P.D.	N.D.	Total	P.D.%	P.D.	N.D.	Total	P.D.%	
Male	16	9	25	64%	28	15	43	65%	$\chi^2 = 0.0086$ $p = 0.93$
Female	14	10	24	58%	46	12	58	79%	FET $p = 0.061$ $\varphi = -0.22$
Total	30	19	49	61%	74	27	101	73%	$\chi^2 = 2.25$ $p = 0.13$

The prevalence of the five lesions between males from cemeteries 3-J-10 and 3-J-11, and between females from both cemeteries, was assessed using chi-square or Fisher’s exact tests as appropriate. Of the five lesions, spinal porosity was found to be significantly different between males from cemetery 3-J-10 and males from 3-J-11, and between females from cemetery 3-J-10 and 3-J-11 (Table 6.17). In examining the frequency of spinal porosity in each group, males from cemetery 3-J-11 displayed a higher prevalence of the lesion (68%) than males from cemetery 3-J-10 (29%), and a higher frequency of the lesion was observed among females from cemetery 3-J-11 (55%) than females from cemetery 3-J-10 (19%) (Table 6.17). A significantly higher prevalence of spinal porosity among individuals from cemetery 3-J-11 than cemetery 3-J-10 was also found when males and females were combined within their respective cemeteries and compared (Table 6.17). The associated phi coefficients for these comparisons indicate moderate-strong effects (Table 6.17).

No significant differences were found in comparing males from cemetery 3-J-10 and males from 3-J-11, and between females from cemetery 3-J-10 and 3-J-11 for cribra orbitalia, humeral cribra, femoral cribra, and periosteal reaction (Tables 6.14, 6.15, 6.16, and 6.18, respectively). When males and females from cemetery 3-J-10 and males and females from cemetery 3-J-11 were compared, a significantly higher prevalence of cribra orbitalia was found among individuals from cemetery 3-J-11 compared to individuals from cemetery 3-J-10 (Table 6.14). However, the phi coefficient associated with this result suggests a weak relationship.

Table 6.14: Prevalence of cribra orbitalia (CO) between cemeteries 3-J-10 and 3-J-11, separated by sex, and results of chi-square tests (df = 1). Phi coefficient (φ) provided for significant outcome (bolded p-value).

	3-J-10				3-J-11				3-J-10 vs. 3-J-11
	CO Present	CO Absent	Total	%	CO Present	CO Absent	Total	%	
Male	8	20	28	29%	22	31	53	42%	$\chi^2 = 1.32$ p = 0.25
Female	9	16	25	36%	33	28	61	54%	$\chi^2 = 2.32$ p = 0.13
Total	17	36	53	32%	55	59	114	48%	$\chi^2 = 3.86$ p = **0.050** $\varphi = -0.15$

Table 6.15: Prevalence of humeral cribra (HC) between cemeteries 3-J-10 and 3-J-11, separated by sex, and results of Fisher's exact and chi-square tests (df = 1).

	3-J-10				3-J-11				3-J-10 vs. 3-J-11
	HC Present	HC Absent	Total	%	HC Present	HC Absent	Total	%	
Male	4	17	21	19%	7	28	35	20%	FET p = 1
Female	1	13	14	7%	9	37	46	20%	FET p = 0.43
Total	5	30	35	14%	16	65	81	20%	$\chi^2 = 0.49$ p = 0.48

Table 6.16: Prevalence of femoral cribra (FC) between cemeteries 3-J-10 and 3-J-11 separated by sex and results of Fisher's exact and chi-square tests (df = 1).

	3-J-10				3-J-11				3-J-10 vs. 3-J-11
	FC Present	FC Absent	Total	%	FC Present	FC Absent	Total	%	
Male	18	6	24	75%	20	16	36	56%	$\chi^2 = 2.34$ p = 0.13
Female	18	3	21	86%	44	14	58	76%	FET p = 0.54
Total	36	9	45	80%	64	30	94	68%	$\chi^2 = 2.14$ p = 0.14

Table 6.17: Prevalence of spinal porosity (SP) between cemeteries 3-J-10 and 3-J-11 separated by sex and results of chi-square tests (df = 1). Phi coefficients (φ) provided for significant outcomes (bolded p-values).

	3-J-10				3-J-11				3-J-10 vs. 3-J-11
	SP Present	SP Absent	Total	%	SP Present	SP Absent	Total	%	
Male	8	20	28	29%	36	17	53	68%	$\chi^2 = 11.44$ **p = 0.00072** $\varphi = -0.38$
Female	5	21	26	19%	34	28	62	55%	$\chi^2 = 9.41$ **p = 0.0022** $\varphi = -0.33$
Total	13	41	54	24%	70	45	115	61%	$\chi^2 = 19.91$ p = **8.13e-06** $\varphi = -0.34$

Table 6.18: Prevalence of periosteal reaction (PR) between cemeteries 3-J-10 and 3-J-11 separated by sex and results of chi-square tests (df = 1).

	3-J-10				3-J-11				3-J-10 vs. 3-J-11
	PR Present	PR Absent	Total	%	PR Present	PR Absent	Total	%	
Male	22	10	32	69%	35	18	53	66%	$\chi^2 = 0.066$ p = 0.80
Female	18	13	31	58%	39	23	62	63%	$\chi^2 = 0.20$ p = 0.65
Total	40	23	63	63%	74	41	115	64%	$\chi^2 = 0.013$ p = 0.91

Research Question 3

Research Question 3: *Are there differences in the frequency of hypothesized malaria between sex and age cohorts at Mis Island?*

As there were no significant differences between males from cemeteries 3-J-10 and 3-J-11, and no significant differences between females from both cemeteries, males and females from the two cemeteries were combined for subsequent analyses. A chi-square test between males and females at Mis Island for the hypothesized presence of malaria yielded no significant difference (Table 6.19). Comparisons between males and females separated by age group also did not result in significant differences (Table 6.19). While the frequencies of "positive diagnoses" tended to be higher among females overall and across age groups, the frequencies between both males and females were relatively similar except for the older adult age group which involved a small subsample for males.

Table 6.19: Prevalence of "positive diagnoses" (P.D.) and "negative diagnoses" (N.D.) between males and females, separated by age group, and results of Fisher's exact (FET) and chi-square tests (df = 1).

	Male				Female				M vs. F
Age Group	P.D.	N.D.	Total	P.D.%	P.D.	N.D.	Total	P.D.%	
Adolescent (12–19 yrs)	2	0	2	100%	2	0	2	100%	FET $p = 1$
Young Adult (20–34 yrs)	19	3	22	86%	19	2	21	90%	FET $p = 1$
Middle Adult (35–49 yrs)	21	16	37	57%	22	11	33	67%	$\chi^2 = 0.72$ $p = 0.40$
Older Adult (≥50 yrs)	2	5	7	29%	16	9	25	64%	FET $p = 0.19$
Unknown Age Adult (≥20 yrs)	0	0	–	–	1	0	–	–	–
Total	44	24	68	65%	60	22	82	73%	$\chi^2 = 1.25$ $p = 0.26$

In comparing the prevalence of the five lesions between males and females, chi-square tests yielded no significant differences except for femoral cribra (Table 6.20). The overall prevalence of femoral cribra observed among female individuals (78%) was greater than that found among male individuals (63%), which was a pattern also observed across the adult age groups (Table 6.23). However, the phi coefficient associated with this result suggests a relatively weak relationship between males and females for femoral cribra (Table 6.20). The frequencies of cribra orbitalia, humeral cribra, spinal porosity, and periosteal reaction were relatively similar between males and females (Tables 6.21, 6.22, 6.24, and 6.25).

Table 6.20: Results of chi-square tests (df = 1) between males and females for each lesion and phi coefficients for significant results (bolded p-values).

Cribra orbitalia	$\chi^2 = 2.3682$ p = 0.1238
Humeral cribra	$\chi^2 = 0.17305$ p = 0.6774
Femoral cribra	$\chi^2 = 3.8763$ **p = 0.04897** $\varphi = -0.17$
Spinal porosity	$\chi^2 = 1.6886$ p = 0.1938
Periosteal reaction	$\chi^2 = 0.64175$ p = 0.4231

Table 6.21: Prevalence of cribra orbitalia (CO) between males and females separated by age.

	Male				Female			
	CO Present	CO Absent	Total	%	CO Present	CO Absent	Total	%
Adolescent	2	0	2	100%	2	0	2	100%
Young Adult	11	13	24	46%	12	9	21	57%
Middle Adult	13	30	43	30%	12	23	35	34%
Older Adult	4	7	11	36%	15	12	27	56%
Unknown Age Adult	0	1	1	0%	1	0	1	100%
Total	30	51	81	37%	42	44	86	49%

Table 6.22: Prevalence of humeral cribra (HC) between males and females separated by age.

	Male				Female			
	HC Present	HC Absent	Total	%	HC Present	HC Absent	Total	%
Adolescent	1	0	1	100%	0	1	1	0%
Young Adult	8	10	18	44%	7	7	14	50%
Middle Adult	1	31	32	3%	2	25	27	7%
Older Adult	1	4	5	20%	1	17	18	6%
Unknown Age Adult	0	0	0	0%	0	0	0	0%
Total	11	45	56	20%	10	50	60	17%

Table 6.23: Prevalence of femoral cribra (FC) between males and females separated by age.

	Male				Female			
	FC Present	FC Absent	Total	%	FC Present	FC Absent	Total	%
Adolescent	1	0	1	100%	2	0	2	100%
Young Adult	17	6	23	74%	20	3	23	87%
Middle Adult	19	10	29	66%	25	7	32	78%
Older Adult	1	6	7	14%	13	7	20	65%
Unknown Age Adult	0	0	0	0%	2	0	2	100%
Total	38	22	60	63%	62	17	79	78%

Table 6.24: Prevalence of spinal porosity (SP) between males and females separated by age.

	Male				Female			
	SP Present	SP Absent	Total	%	SP Present	SP Absent	Total	%
Adolescent	3	0	3	100%	2	0	2	100%
Young Adult	18	5	23	78%	19	3	22	86%
Middle Adult	17	26	43	40%	14	23	37	38%
Older Adult	6	6	12	50%	4	23	27	15%
Unknown Age Adult	0	0	0	0%	0	0	0	0%
Total	44	37	81	54%	39	49	88	44%

Table 6.25: Prevalence of periosteal reaction (PR) between males and females separated by age.

	Male				Female			
	PR Present	PR Absent	Total	%	PR Present	PR Absent	Total	%
Adolescent	1	1	2	50%	1	1	2	50%
Young Adult	17	7	24	71%	12	9	21	57%
Middle Adult	31	15	46	67%	23	13	36	64%
Older Adult	8	5	13	62%	18	12	30	60%
Unknown Age Adult	0	0	0	0%	3	1	4	75%
Total	57	28	85	67%	57	36	93	61%

A significant association was found between estimated prevalence of malaria and age group using a chi-square test χ^2 (5, n = 294) = 23.903, p-value = 0.00023, with a relatively moderate strength of association (V = 0.29). The highest frequency of "positive diagnoses" for malaria was observed in the adolescent age group (96%), followed by the young adult (89%) and child (81%) cohorts, and the infant age group (74%). The middle adult and older adult cohorts presented the lowest frequencies of hypothesized malarial infection (63% and 56%, respectively); however, these prevalences were more than half of the individuals in each group. Based on these results, a general pattern was observed in the prevalence of inferred malaria that increased with age to the adolescent cohort, followed by a high prevalence in the young adult group, and decreased with age in the middle and older adult groups.

Table 6.26: Prevalence of "positive diagnoses" (P.D.) and "negative diagnoses" (N.D.) between age groups.

Age	P.D.	N.D.	Total	P.D.%
Infant (<3 years)	31	11	42	74%
Child (3–11 years)	64	15	79	81%
Adolescent (12–19 years)	24	1	25	96%
Young Adult (20–34 years)	39	5	44	89%
Middle Adult (35–49 years)	45	27	72	63%
Older Adult (≥50 years)	18	14	32	56%
Total	221	73	294	75%

Research Question 4a & 4b

Research Question 4a: *Are the skeletal lesions suggestive of malaria significantly associated with age?*

The results presented in this section focus on the relationship between the skeletal lesions suggestive of malaria and age of the individual. The prevalence of cribra orbitalia, humeral cribra, femoral cribra, spinal porosity, and periosteal reaction by age group is shown Table 6.27, as well as the results of chi-square tests and Cramer's V statistics. In testing the association between each lesion and age group, significant associations were indicated for cribra orbitalia, humeral cribra, femoral cribra, and spinal porosity. Additionally, the related Cramer's V measures suggest that the associations between each of these four lesions and age are relatively strong. In examining the prevalence of the four lesions across age groups (Table 6.27 and Figure 6.2), humeral cribra and spinal porosity demonstrated their highest frequencies in the child, adolescent, and young adult age groups and lower frequencies for the infant, middle adult, and older adult age groups. Femoral cribra also presented at higher frequencies in the child and adolescent age groups, followed by young and middle adult groups, and exhibited its lowest frequencies in the infant and older adult groups. Cribra orbitalia showed similarly higher frequencies in the infant, child, and adolescent age groups, followed by young adult and older adult groups, and its lowest frequency in the middle adult age group. No significant association was found between periosteal reaction and age of the individual. The prevalence of periosteal reaction across age groups demonstrated a pattern generally opposite of that observed for the other lesions, with higher frequencies in the infant and adult age groups and lower frequencies in the child and adolescent age groups.

Table 6.27: Lesion prevalence by age group and results of chi-square tests (df = 5) and Cramer's V statistic (bolded p-values represent statistically significant results).

	CO			HC			FC			SP			PR		
Age Group	Affect.	n	%	Affect.	n	%	Affect.	n	%	Affect.	n	%	Affect.	n	%
Infant	30	37	81%	15	42	36%	29	44	66%	15	44	34%	32	47	68%
Child	53	65	82%	48	80	60%	76	88	86%	46	81	57%	40	86	47%
Adol.	18	22	82%	11	19	58%	37	37	100%	23	24	96%	12	24	50%
YA	25	47	53%	15	32	47%	22	31	71%	38	46	83%	29	45	64%
MA	26	79	33%	3	59	5%	45	62	73%	32	82	39%	55	84	65%
OA	19	38	50%	2	23	9%	14	27	52%	10	39	26%	26	43	60%
Total	171	288	—	94	255	—	255	289	—	164	316	—	194	329	—
Chi-square	$\chi^2 = 50.12$ **p = 1.31e-09**			$\chi^2 = 56.85$ **p = 5.42e-11**			$\chi^2 = 29.57$ **p = 1.79e-05**			$\chi^2 = 58.52$ **p = 2.46e-11**			$\chi^2 = 10.00$ p = 0.075		
Cramer's V	V = 0.42			V = 0.47			V = 0.32			V = 0.43			V = 0.17		

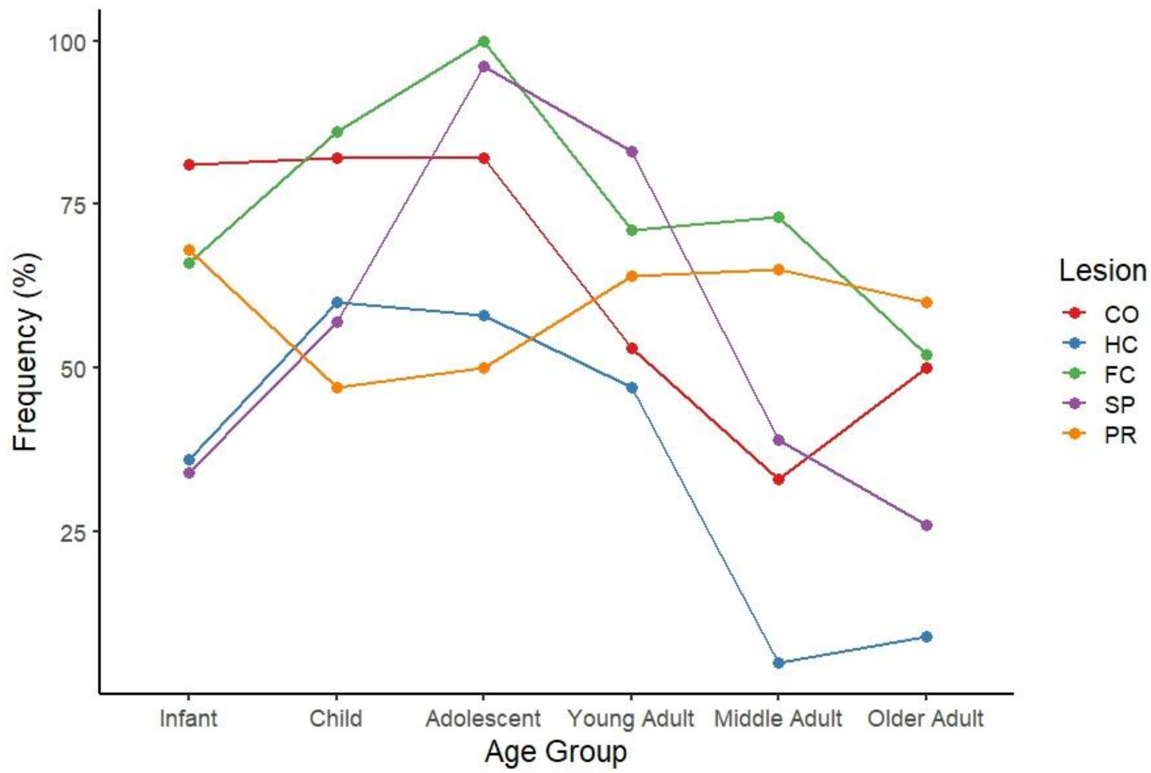

Figure 6.2: Plot of lesion frequency by age group for cribra orbitalia (CO), humeral cribra (HC), femoral cribra (FC), spinal porosity (SP), and periosteal reaction (PR).

The results of the multiple correspondence analysis involving the presence and absence of lesions and age groups are presented in the biplot below (Figure 6.3), which accounts for a total of 26.79% of variation. The first and second dimensions presented have eigenvalues of 0.367 and 0.302, respectively, and are representative of 14.7% and 12.1% of variation, respectively. The presence of humeral cribra, spinal porosity, femoral cribra, and cribra orbitalia, as well as the absence of periosteal reaction, clustered closer to the child, adolescent, and young adult age groups. Conversely, the presence of periosteal reaction and absence of humeral cribra, spinal porosity, femoral cribra, and cribra orbitalia clustered closer to the infant, middle adult, and older adult age groups. Regarding the relationship among the lesions, the presence of humeral cribra, spinal porosity, femoral cribra, and cribra orbitalia clustered closer together, whereas the presence of periosteal reaction was separated from these lesions by the second axis.

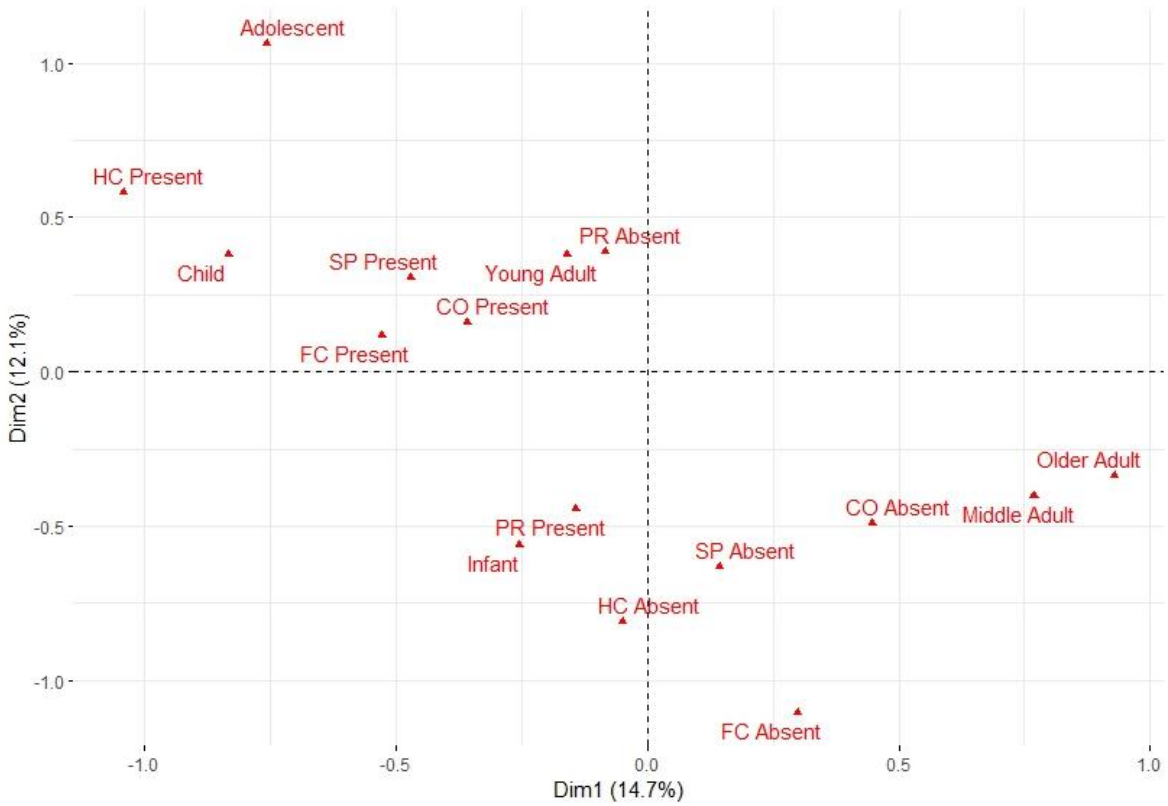

Figure 6.3: Multiple correspondence analysis biplot for age groups and the presence/absence of cribra orbitalia, humeral cribra, femoral cribra, spinal porosity, and periosteal reaction.

Research Question 4b: *Are there significant associations among the paleopathological lesions suggestive of malaria?*

The results of this section present findings on the relationship among the skeletal lesions suggestive of malaria. Table 6.28 displays the outcomes of testing the association between pairs of lesions for all individuals, regardless of age, with the appropriate skeletal elements present. Significant associations were found between the following pairs: cribra orbitalia and humeral cribra, cribra orbitalia and femoral cribra, humeral cribra and femoral cribra, humeral cribra and spinal porosity, femoral cribra and spinal porosity, and humeral cribra and periosteal reaction. All significant associations were positive except between humeral cribra and periosteal reaction which were inversely related. The association between humeral cribra and femoral cribra was relatively strong, and the association between humeral cribra and cribra orbitalia was generally moderate. The relationship between femoral cribra and cribra orbitalia, humeral cribra and spinal porosity, femoral cribra and spinal porosity, and humeral cribra and periosteal reaction were relatively weaker and reflected a small to medium level of association.

Table 6.28: Association between pairs of lesions for all individuals with the appropriate skeletal elements present; the upper values are the results of chi-square tests (df = 1) and the phi coefficients, and the lower values are the subsample sizes.

	CO	HC	FC	SP	PR
CO	–	$\chi^2 = 11.18$ **p = 0.00083** $\varphi = 0.23$	$\chi^2 = 5.88$ **p = 0.015** $\varphi = 0.16$	$\chi^2 = 3.15$ p = 0.076 $\varphi = 0.11$	$\chi^2 = 0.88$ p = 0.35 $\varphi = 0.06$
HC	n = 209	–	$\chi^2 = 24.47$ **p = 7.53e-07** $\varphi = 0.32$	$\chi^2 = 8.67$ **p = 0.0032** $\varphi = 0.19$	$\chi^2 = 5.07$ **p = 0.024** $\varphi = -0.14$
FC	n = 234	n = 236	–	$\chi^2 = 6.77$ **p = 0.0093** $\varphi = 0.16$	$\chi^2 = 2.79$ p = 0.095 $\varphi = -0.10$
SP	n = 258	n = 241	n = 266	–	$\chi^2 = 1.29$ p = 0.26 $\varphi = -0.07$
PR	n = 268	n = 244	n = 274	n = 295	–

The co-occurrence between pairs of lesions was then examined separately in subadult and adult subsamples. In assessing these relationships in the subadult age groups, the following pairs were significantly associated (Table 6.29): cribra orbitalia and femoral cribra, humeral cribra and femoral cribra, humeral cribra and spinal porosity, femoral cribra and spinal porosity, femoral cribra and periosteal reaction, and spinal porosity and periosteal reaction. These significant associations were all positive except the associations between femoral cribra and periosteal reaction, and spinal porosity and periosteal reaction which were inversely related. Relatively large measures of association were found between humeral cribra and femoral cribra, and between femoral cribra and spinal porosity. The relationship between femoral cribra and cribra orbitalia, humeral cribra and spinal porosity, femoral cribra and periosteal reaction, and spinal porosity and periosteal reaction displayed generally medium levels of association. When the lesions' co-occurrence was examined among adult individuals only, no significant associations between the pairs of lesions were found (Table 6.30).

Table 6.29: Association between pairs of lesions for subadult individuals with the appropriate skeletal elements present; the upper values are the results of the Fisher's exact tests (FET) and chi-square tests (df = 1) and the phi coefficients, and the lower values are the subsample sizes.

	CO	HC	FC	SP	PR
CO	–	FET p = 0.33 φ = 0.11	FET **p = 0.035** φ = 0.21	FET p = 0.46 φ = 0.07	FET p = 0.81 φ = 0.02
HC	n = 104	–	χ^2 = 24.35 **p = 8.05e-07** φ = 0.42	χ^2 = 4.93 **p = 0.026** φ = 0.19	χ^2 = 3.19 p = 0.074 φ = -0.15
FC	n = 114	n = 137	–	χ^2 = 13.67 **p = 0.00022** φ = 0.31	χ^2 = 4.99 **p = 0.026** φ = -0.18
SP	n = 114	n = 132	n = 140	–	χ^2 = 4.10 **p = 0.043** φ = -0.17
PR	n = 117	n = 136	n = 148	n = 144	–

Table 6.30: Association between pairs of lesions for adult individuals with the appropriate skeletal elements present; the upper values are the results of the Fisher's exact tests (FET) and chi-square tests (df = 1) and the phi coefficients, and the lower values are the subsample sizes.

	CO	HC	FC	SP	PR
CO	–	FET p = 0.44 φ = 0.09	χ^2 = 0.60 p = 0.44 φ = 0.07	χ^2 = 1.44 p = 0.23 φ = 0.10	χ^2 = 3.68 p = 0.055 φ = 0.16
HC	n = 105	–	FET p = 0.26 φ = 0.14	FET p = 0.069 φ = 0.19	FET p = 1 φ = -0.02
FC	n = 120	n = 99	–	χ^2 = 0.012 p = 0.91 φ = 0.01	χ^2 = 0.043 p = 0.84 φ = 0.02
SP	n = 144	n = 109	n = 126	–	χ^2 = 0.57 p = 0.45 φ = 0.06
PR	n = 151	n = 108	n = 126	n = 151	–

Table 6.31 displays the co-occurrence between the three cribrous lesions that have been considered part of a "cribrous syndrome" (Miquel-Feucht et al., 1999) in all individuals, as well as separated by subadults and adults. The combined presence of cribra orbitalia, humeral cribra, and femoral cribra was observed in 27% of all individuals with the skeletal elements present to assess the three lesions. When this co-occurrence was examined among subadults and adults separately, subadult individuals demonstrated a substantially higher frequency (44%) compared to adult individuals (8%). The prevalence of pairings between the three cribrous lesions revealed a similar pattern, in which pairs of lesions co-occurred at much higher frequencies in the subadult individuals than the adult individuals. Of the three pairings, the most commonly observed co-occurrence in both subadults and adults was cribra orbitalia and femoral cribra, followed by humeral cribra and femoral cribra, and lastly cribra orbitalia and humeral cribra.

Table 6.31: Co-occurrence between cribra orbitalia (CO), humeral cribra (HC), and femoral cribra (FC) among all individuals, and separated by subadult and adult individuals.

Combination of cribrous lesions	All Individuals	Subadults	Adults
CO + HC	26% (54/209)	43% (45/104)	9% (9/105)
CO + FC	49% (115/234)	68% (78/114)	31% (37/120)
HC + FC	36% (86/236)	51% (70/137)	16% (16/99)
CO + HC + FC	27% (51/192)	44% (44/101)	8% (7/91)

Research Question 5a & 5b

Research Question 5a: *Are the macroscopic variables observed on the external surface of femoral cribra associated with age?*

The results of this section examine the relationship between the age of the individual and variables reflecting the variation in appearance of femoral cribra from the lesion surface. As shown in Table 6.32, significant associations were found between age and the lesion variables Radi et al. score, estimated activity, and presence of a "cortical window" for both left and right femora. Furthermore, all associations for both left and right femora were relatively strong, particularly those between age and estimated activity and age and the presence of a cortical window.

Table 6.32: Results of Fisher's exact tests and Cramer's V statistics in examining the association between age and Radi et al. score, estimated activity, and cortical window (note: p-values between age and estimated activity are simulated based on 2,000 replicates).

Comparison	Left femora	Right femora
Age and Radi et al. Score	n = 203 **p = 0.0010** V = 0.33	n = 175 **p = 0.00025** V = 0.40
Age and Estimated Activity	n = 168 **p = 0.00050** V = 0.55	n = 168 **p = 0.00050** V = 0.54
Age and Cortical Window	n = 182 **p = 3.74e-08** V = 0.53	n = 159 **p = 1.637e-08** V = 0.53

Tables 6.33 and 6.34 display the prevalence of Radi et al. scores for femoral cribra across age groups for left and right femora, respectively. In examining the relationship between age and Radi et al. scores, the majority of femora in all age groups demonstrated a Score 2 for both left and right femora. This majority reached 77–100% for all age groups except the infant cohort, in which a Score 2 accounted for 58% and 57% of the observed left and right femoral cribra. The infant age group consequently demonstrated the most cases of Radi et al. Score 1 which was observed in 42% and 43% of left and right femora within the age cohort.

Table 6.33: Prevalence of femoral cribra lesions evaluated as Radi et al. Scores 1 and 2 separated by age group for left femora.

	Age group	n	Number of Radi et al. Score 1	Number of Radi et al. Score 2	% of Radi et al. Score 1	% of Radi et al. Score 2
Left femora	Infant (<3 yrs)	26	11	15	**42%**	**58%**
	Child (3–11 yrs)	73	10	63	**14%**	**86%**
	Adolescent (12–19 yrs)	21	0	21	**0%**	**100%**
	Young Adult (20–34 yrs)	31	7	24	**23%**	**77%**
	Middle Adult (35–49 yrs)	41	3	38	**7%**	**93%**
	Older Adult (≥50 yrs)	11	1	10	**9%**	**91%**

Table 6.34: Prevalence of femoral cribra lesions evaluated as Radi et al. Scores 1 and 2 separated by age group for right femora.

	Age group	n	Number of Radi et al. Score 1	Number of Radi et al. Score 2	% of Radi et al. Score 1	% of Radi et al. Score 2
Right femora	Infant (<3 yrs)	21	9	12	**43%**	**57%**
	Child (3–11 yrs)	67	2	65	**3%**	**97%**
	Adolescent (12–19 yrs)	22	1	21	**5%**	**95%**
	Young Adult (20–34 yrs)	24	3	21	**13%**	**88%**
	Middle Adult (35–49 yrs)	30	3	27	**10%**	**90%**
	Older Adult (≥50 yrs)	11	1	10	**9%**	**91%**

As shown in Tables 6.35 and 6.36, lesions estimated to be active or healing demonstrated a consistent trend with the age of the individual. Overall, for both left and right femora, the frequency of lesions believed to be active decreased with age, whereas the frequency of lesions that demonstrated signs of possible healing increased with age. In the infant, child, and adolescent age groups, the majority of femoral cribra lesions were assessed as active. In the young, middle, and older adult groups, the majority of femoral cribra lesions displayed signs of healing.

Table 6.35: Prevalence of femoral cribra lesions scored as active and healing separated by age group for left femora.

	Age group	n	Number of estimated active	Number of estimated healing	% of estimated active	% of estimated healing
Left femora	Infant (<3 yrs)	26	21	5	**81%**	**19%**
	Child (3–11 yrs)	71	60	11	**85%**	**15%**
	Adolescent (12–19 yrs)	21	14	7	**67%**	**33%**
	Young Adult (20–34 yrs)	29	11	18	**38%**	**62%**
	Middle Adult (35–49 yrs)	36	7	29	**19%**	**81%**
	Older Adult (≥50 yrs)	9	2	7	**22%**	**78%**

Table 6.36: Prevalence of femoral cribra lesions scored as active and healing separated by age group for right femora.

	Age group	n	Number of estimated active	Number of estimated healing	% of estimated active	% of estimated healing
Right femora	Infant (<3 yrs)	21	18	3	**86%**	**14%**
	Child (3–11 yrs)	66	56	10	**85%**	**15%**
	Adolescent (12–19 yrs)	22	17	5	**77%**	**23%**
	Young Adult (20–34 yrs)	22	10	12	**45%**	**55%**
	Middle Adult (35–49 yrs)	28	8	20	**29%**	**71%**
	Older Adult (≥50 yrs)	9	1	8	**11%**	**89%**

The presence of a cortical window demonstrated a distinct pattern between subadult and adult age groups (Tables 6.37 and 6.38). This feature was virtually absent in the infant, child, and adolescent cohorts, with only one femur displaying a cortical window from those groups. In the young, middle, and older adult age groups however, cortical windows were present and increased in frequency with age. The only age group in which cortical windows were observed in more than half of the affected femora was in the older adult cohort, although the subsample for this age group was small.

Table 6.37: Prevalence of femoral cribra lesions with and without a cortical window separated by age group for left femora.

	Age group	n	Window present	Window absent	% of window present	% of window absent
Left femora	Infant (<3 yrs)	26	0	26	**0%**	**100%**
	Child (3–11 yrs)	71	1	70	**1%**	**99%**
	Adolescent (12–19 yrs)	21	0	21	**0%**	**100%**
	Young Adult (20–34 yrs)	28	4	24	**14%**	**86%**
	Middle Adult (35–49 yrs)	29	8	21	**28%**	**72%**
	Older Adult (≥50 yrs)	7	5	2	**71%**	**29%**

Table 6.38: Prevalence of femoral cribra lesions with and without a cortical window separated by age group for right femora.

	Age group	n	Window present	Window absent	% of window present	% of window absent
Right femora	Infant (<3 yrs)	21	0	21	**0%**	**100%**
	Child (3–11 yrs)	66	0	66	**0%**	**100%**
	Adolescent (12–19 yrs)	22	0	22	**0%**	**100%**
	Young Adult (20–34 yrs)	19	5	14	**26%**	**74%**
	Middle Adult (35–49 yrs)	24	7	17	**29%**	**71%**
	Older Adult (≥50 yrs)	7	4	3	**57%**	**43%**

The results of the multiple correspondence analysis (MCA) involving age of the individual, estimated lesion activity, presence/absence of a cortical window, and Radi et al. Score for left femora and right femora with femoral cribra are presented in Figures 6.4 and 6.5, respectively. The MCA for affected left femora accounts for a total of 33.59% of variation. The first and second dimensions presented have eigenvalues of 0.542 and 0.382 and are representative of 19.7% and 13.9% of variation, respectively. The MCA for affected right femora accounts for a total of 35.25% of variation. The first and second dimensions presented have eigenvalues of 0.561 and 0.408 and are representative of 20.4% and 14.8% of variation, respectively. In the biplots for both left and right femora, Radi et al. Score 2 is centered near the origin, which reflects the relative ubiquity of this variable's expression in the sample and indicates that it is not a differentiating feature. Radi et al. Score 1 tended to cluster closer to the subadult age groups, particularly for left femora, and further away from adult age groups. Additionally, Radi et al. Score 1 was more distant from the lesion variables of estimated healing and presence of a cortical window. Active lesions and the absence of a cortical window clustered together and were closest to the infant, child, and adolescent age groups and further away from the adult cohorts. Conversely, lesions demonstrating signs of healing and the presence of a cortical window clustered closest to the middle and older adult groups, with the young adult cohort near these variables for right femora.

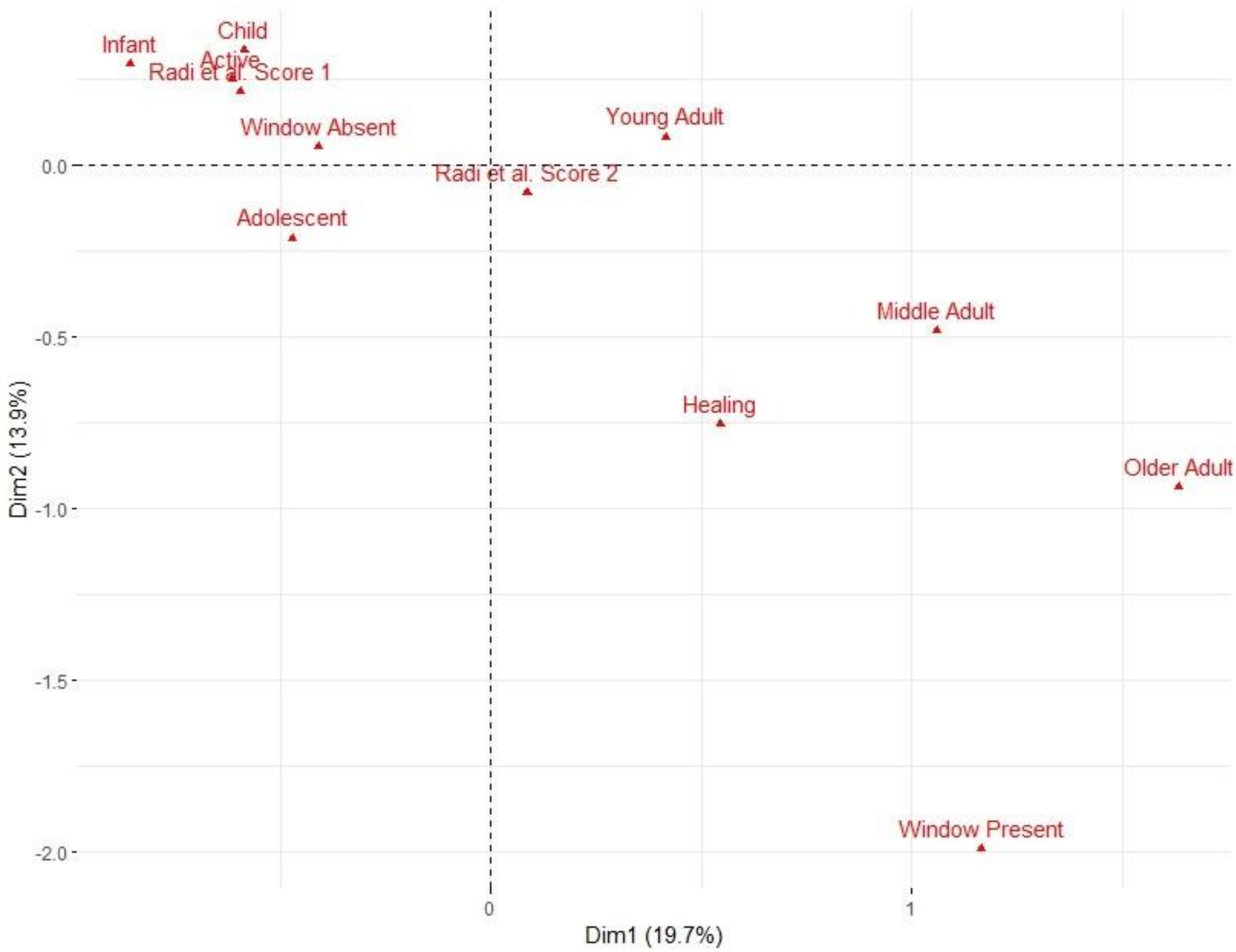

Figure 6.4: MCA biplot for age group and the hypothesized activity, presence/absence of a cortical window, and Radi et al. Score for left femora with femoral cribra.

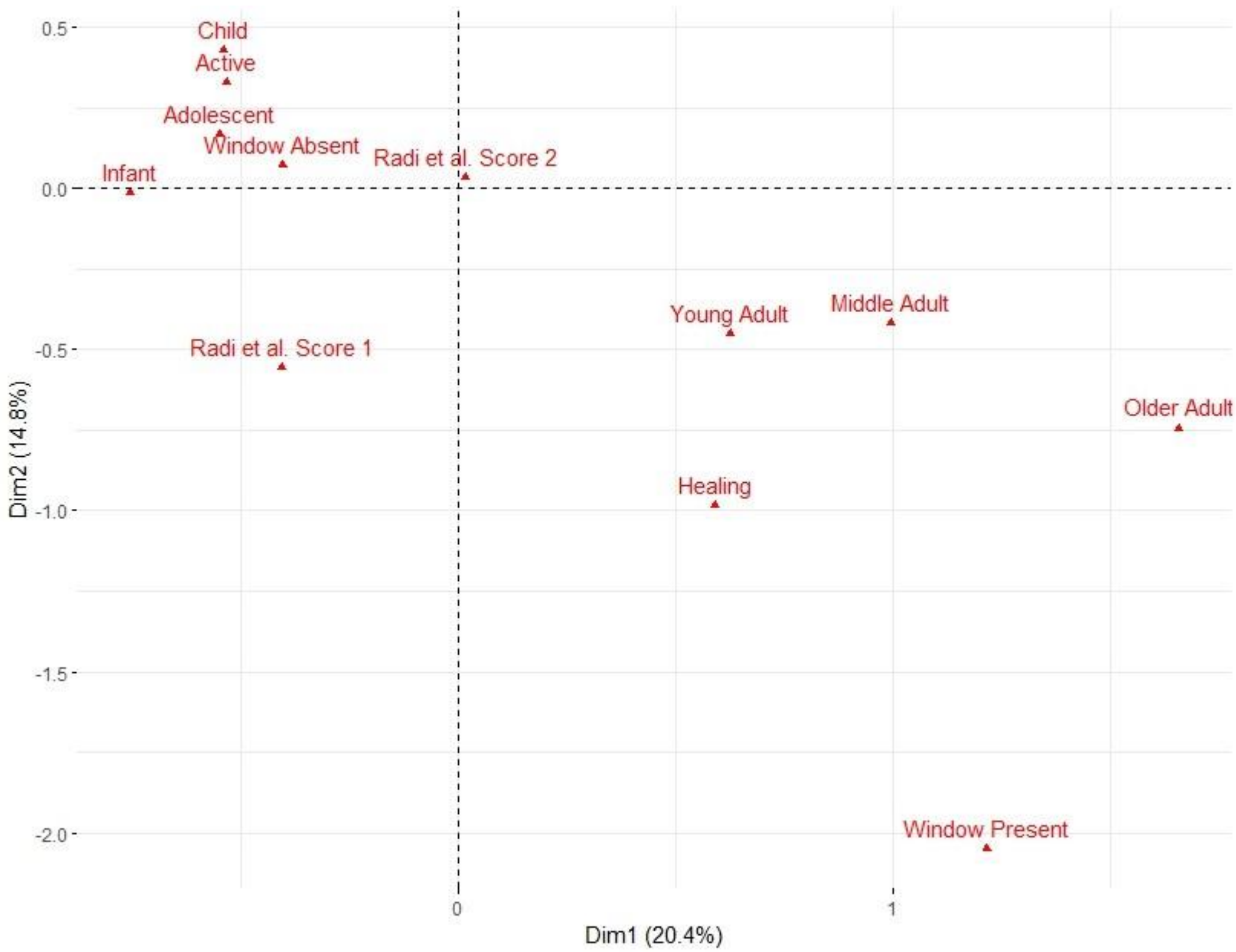

Figure 6.5: MCA biplot for age group and the hypothesized activity, presence/absence of a cortical window, and Radi et al. Score for right femora with femoral cribra.

Figures 6.6 and 6.7 display the measurements of lesion perimeter for femoral cribra estimated to be active and healing within each age group for left and right femora. As reflected in the previous analyses, the frequency of healing lesions generally increased with age. The adolescent age group demonstrated clustering of relatively larger lesions compared to other age groups. Additionally, the juvenile and adolescent cohorts had the largest lesion perimeters at the lowest ends of their ranges compared to the other age groups. In general, the range of lesion size was greater in the adult groups compared to the subadult age cohorts. Within each age group, there is overlap in the perimeter of femoral cribra between lesions estimated to be active and healing. However, in the adult age groups, the smallest lesions appear to be healing and in the subadult age groups the smallest lesions include both active and healing lesions with an overall greater proportion of active lesions.

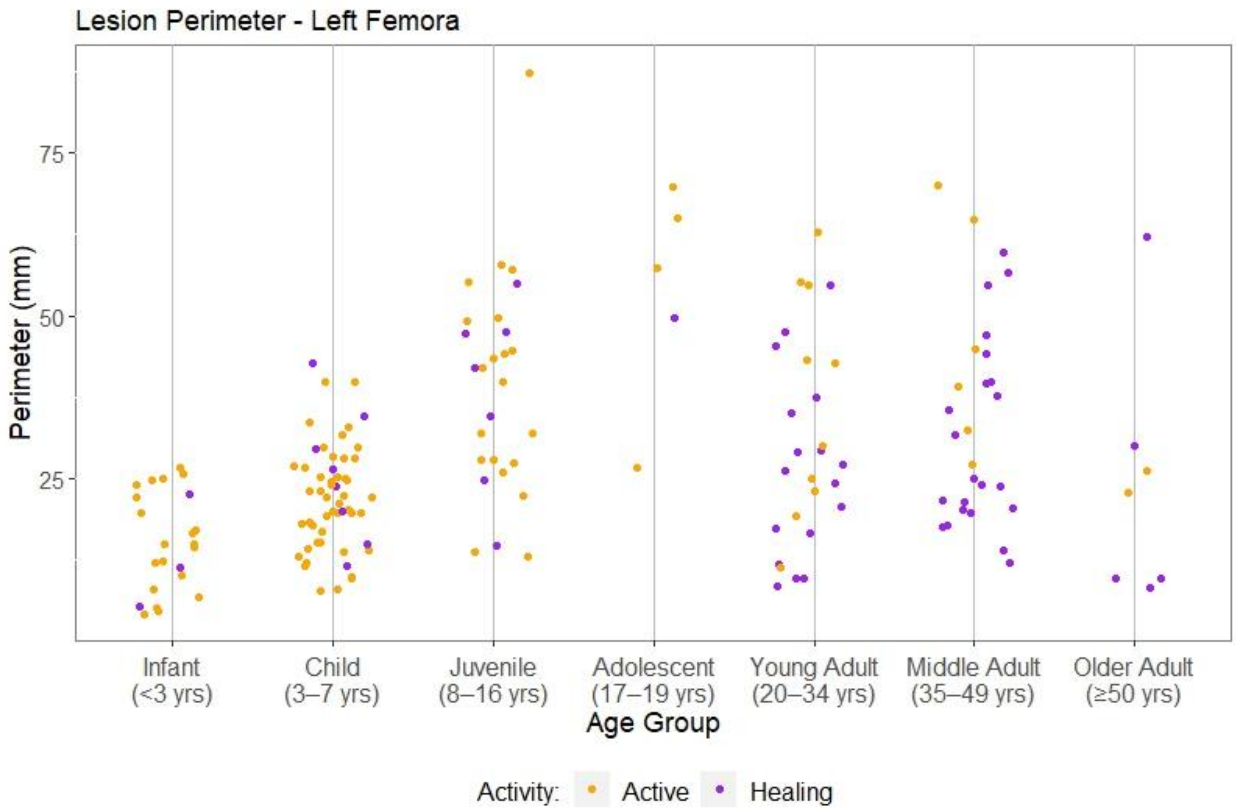

Figure 6.6: Scatter plot of lesion perimeter between lesions hypothesized to be active or healing for left femora, separated by age group.

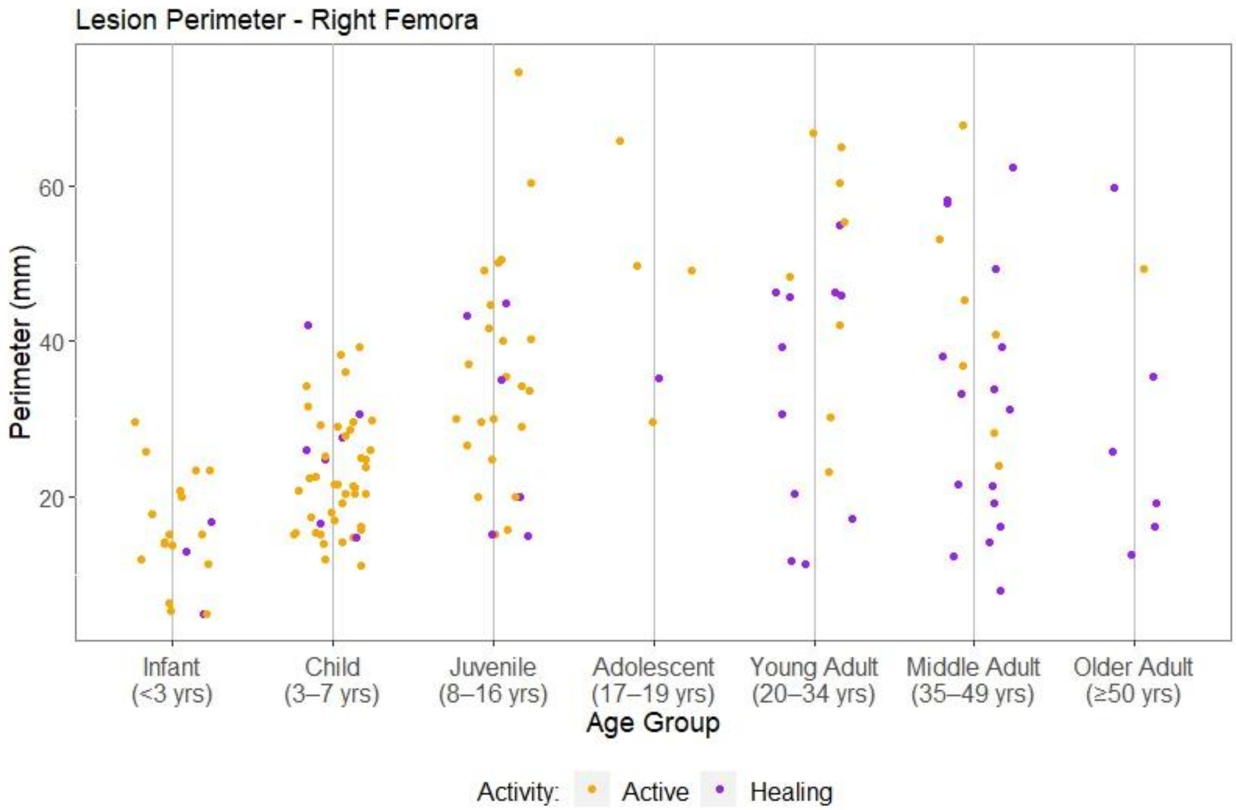

Figure 6.7: Scatter plot of lesion perimeter between lesions hypothesized to be active or healing for right femora, separated by age group.

Research Question 5b: *Are there patterns between macroscopic variables observed on the external surface of femoral cribra potentially related to lesion "severity" and "activity"?*

The association between the presence of a cortical window and whether a femoral cribra lesion displayed signs of remodeling was examined to explore a possible connection regarding hypothesized lesion activity. Fisher's exact tests between estimated activity of the lesion and the presence of a cortical window demonstrated a significant association for both left and right femora ($p = 0.00041$ and $p = 2.88e\text{-}06$, respectively). Phi coefficients indicate that both associations are medium to strong with the right side having a stronger association ($\varphi = 0.28$ for left femora and $\varphi = 0.39$ for right femora). Table 6.39 demonstrates relatively similar patterns between both variables for left and right femora, with the right femora having fewer cases of lesions displaying both signs of remodeling and an absent cortical window.

Table 6.39: Contingency tables between estimated activity and the presence of a cortical window for left and right femora.

		Window Absent	Window Present
Left	Active	109	4
	Healing	53	14
Right	Active	105	2
	Healing	38	14

The relationship between femoral cribra's Radi et al. Score and measurements of lesion length perpendicular to the femoral neck, length parallel to the femoral neck, and perimeter was evaluated in explore these variables' possible connection to lesion severity. Across age groups, lesions with a Radi et al. Score 2 tended to demonstrate greater lengths perpendicular to the femoral neck compared to those with a Radi et al. Score 1 for both left and right femora (Table 6.40 and Figures 6.8 and 6.9). Lesions displaying a Radi et al. Score 2 also demonstrated a greater range of measurements perpendicular to the femoral neck.

Table 6.40: Summary statistics of lesion length perpendicular to the femoral neck between lesions categorized as Radi et al. Scores 1 and 2 for left and right femora separated by age group.

	Perpendicular to Neck Measurements (mm)			
	Left Femora		Right Femora	
Age group	Score 1 Mean ± SD	Score 2 Mean ± SD	Score 1 Mean ± SD	Score 2 Mean ± SD
Infant (<3 yrs)	2.89 (±1.69) n = 9	7.79 (±2.64) n = 14	3.63 (±1.85) n = 8	7.75 (±2.05) n = 12
Child (3–7 yrs)	4.63 (±2.67) n = 8	6.12 (±1.98) n = 46	5 (±0.00) n = 1	8.32 (±3.70) n = 47
Juvenile (8–16 yrs)	4 (±0.00) n = 1	14.58 (±6.06) n = 26	7 (±1.41) n = 2	12.04 (±5.85) n = 28
Adolescent (17–19 yrs)	— n = 0	20.80 (±6.38) n = 5	— n = 0	18.83 (±4.96) n = 6
Young Adult (20–34 yrs)	5.67 (±3.50) n = 6	11.91 (±6.32) n = 22	6 (±3.61) n = 3	15.63 (±6.48) n = 16
Middle Adult (35–49 yrs)	6.67 (±2.08) n = 3	14.67 (±6.74) n = 27	6 (±2.65) n = 3	14.16 (±6.04) n = 22
Older Adult (≥50 yrs)	4 (±0.00) n = 1	11 (±7.62) n = 7	5 (±0.00) n = 1	11.63 (±7.19) n = 8

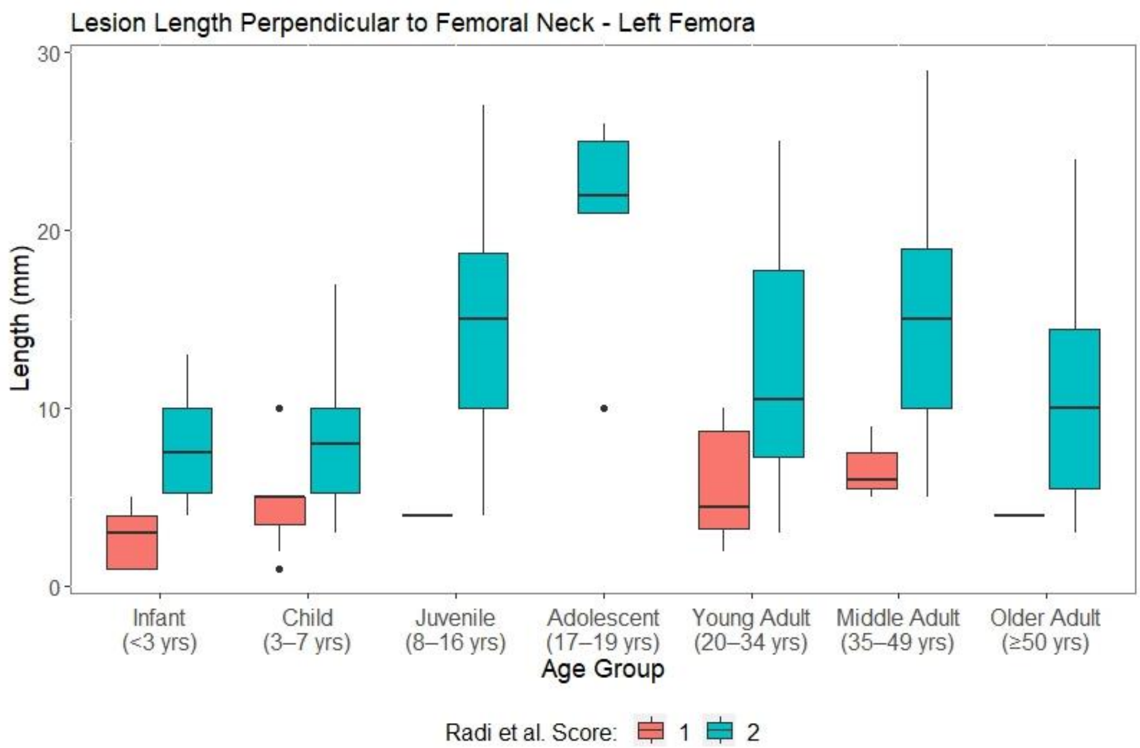

Figure 6.8: Boxplot of lesion length perpendicular to the femoral neck between lesions categorized as Radi et al. Score 1 or 2 for left femora, separated by age group.

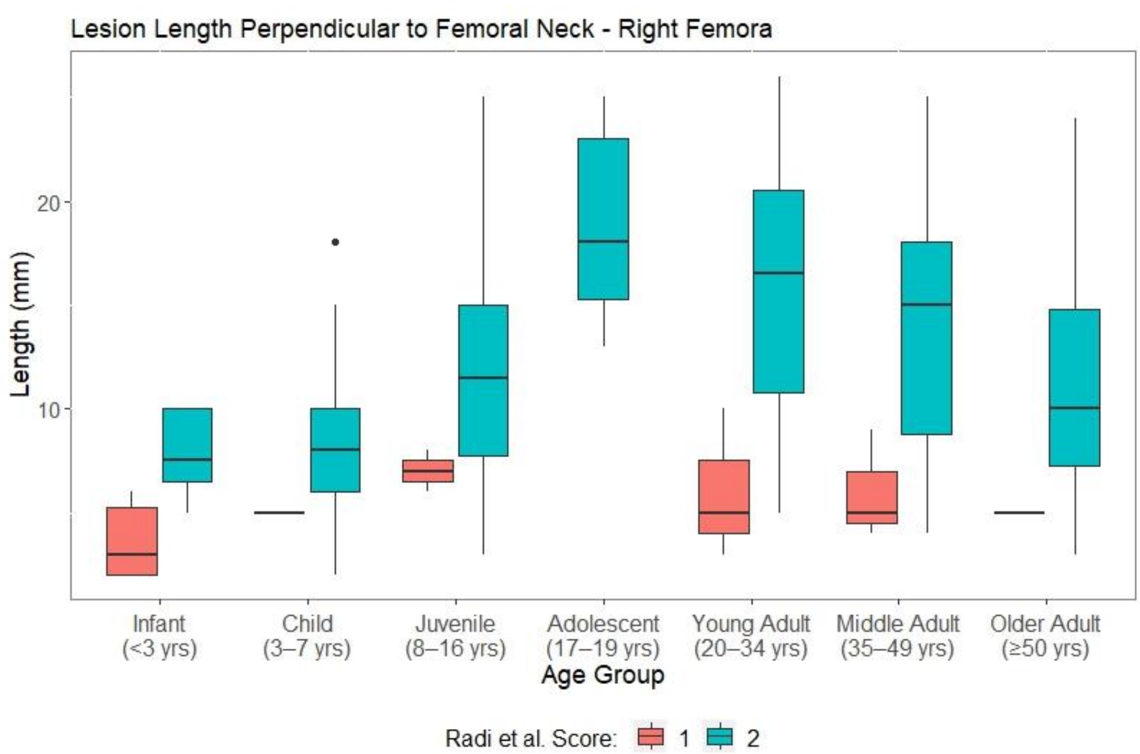

Figure 6.9: Boxplot of lesion length perpendicular to the femoral neck between lesions categorized as Radi et al. Score 1 or 2 for right femora, separated by age group.

Lesions with a Radi et al. Score 2 also tended to be larger in the dimension parallel to the femoral neck than lesions with a Radi et al. Score 1 in the same age group for both left and right femora (Table 6.41 and Figures 6.10 and 6.11). However, these differences were not as pronounced as those observed among the lesion measurements perpendicular to the femoral neck. Compared to the measurements perpendicular to the femoral neck between Radi et al. scores, the measurements parallel to the neck tended to be relatively closer between Radi et al. Scores 1 and 2. Additionally, the lesion measurements parallel to the femoral neck generally demonstrated smaller ranges for both Radi et al. scores.

Table 6.41: Summary statistics of lesion length parallel to the femoral neck between lesions categorized as Radi et al. Scores 1 and 2 for left and right femora, separated by age group.

	Parallel to Neck Measurements (mm)			
	Left femora		Right femora	
Age group	Score 1 Mean ± SD	Score 2 Mean ± SD	Score 1 Mean ± SD	Score 2 Mean ± SD
Infant (<3 yrs)	2.44 (±1.01) n = 9	5.00 (±1.36) n = 15	2.38 (±0.74) n = 8	4.92 (±0.79) n = 12
Child (3–7 yrs)	3.25 (±1.16) n = 8	6.11 (±1.98) n = 46	5 (±0.00) n = 1	6.53 (±1.93) n = 47
Juvenile (8–16 yrs)	4.00 (±0.00) n = 1	9.19 (±4.37) n = 26	5 (±0.00) n = 2	9.57 (±5.53) n = 28
Adolescent (17–19 yrs)	— n = 0	11 (±2.65) n = 5	— n = 0	10.6 (±5.37) n = 5
Young Adult (20–34 yrs)	4.92 (±3.14) n = 6	7.62 (±3.41) n = 21	7.00 (±5.20) n = 3	8.65 (±3.66) n = 17
Middle Adult (35–49 yrs)	5.67 (±1.53) n = 3	6.62 (±3.80) n = 26	3.33 (±0.58) n = 3	7.85 (±3.91) n = 20
Older Adult (≥50 yrs)	2.00 (±0.00) n = 1	6.00 (±4.60) n = 6	4.5 (±0.00) n = 1	6.67 (±3.67) n = 6

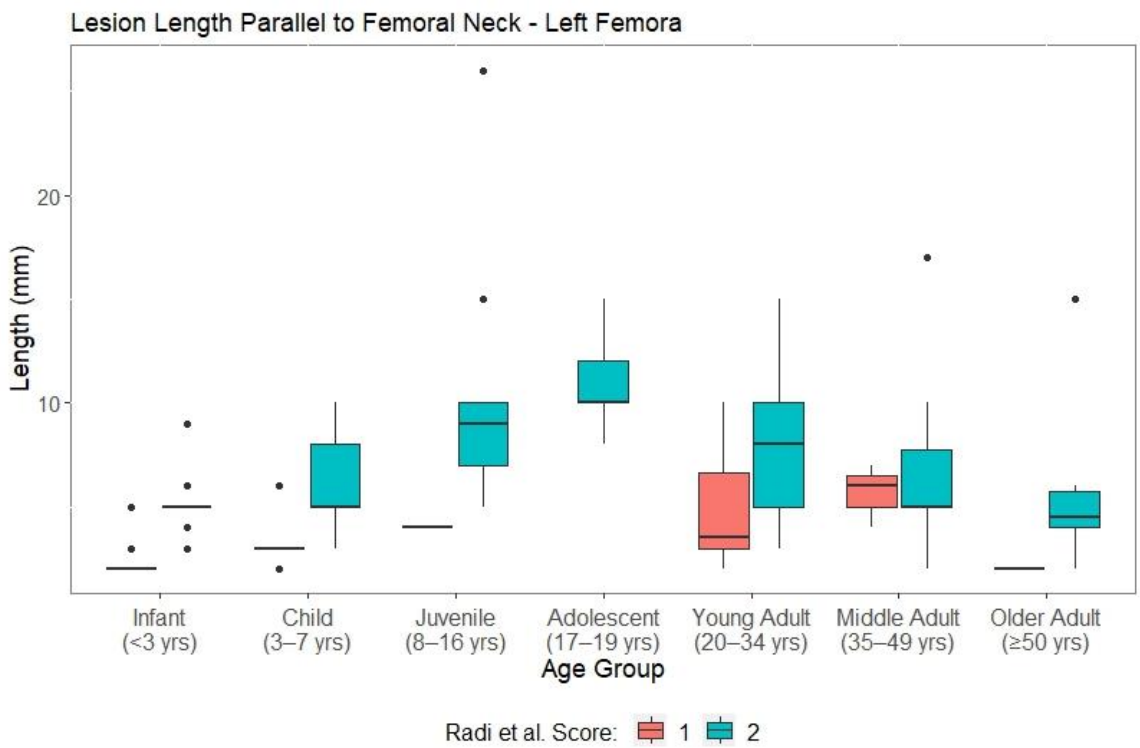

Figure 6.10: Boxplot of lesion length parallel to the femoral neck between lesions categorized as Radi et al. Score 1 or 2 for left femora, separated by age group.

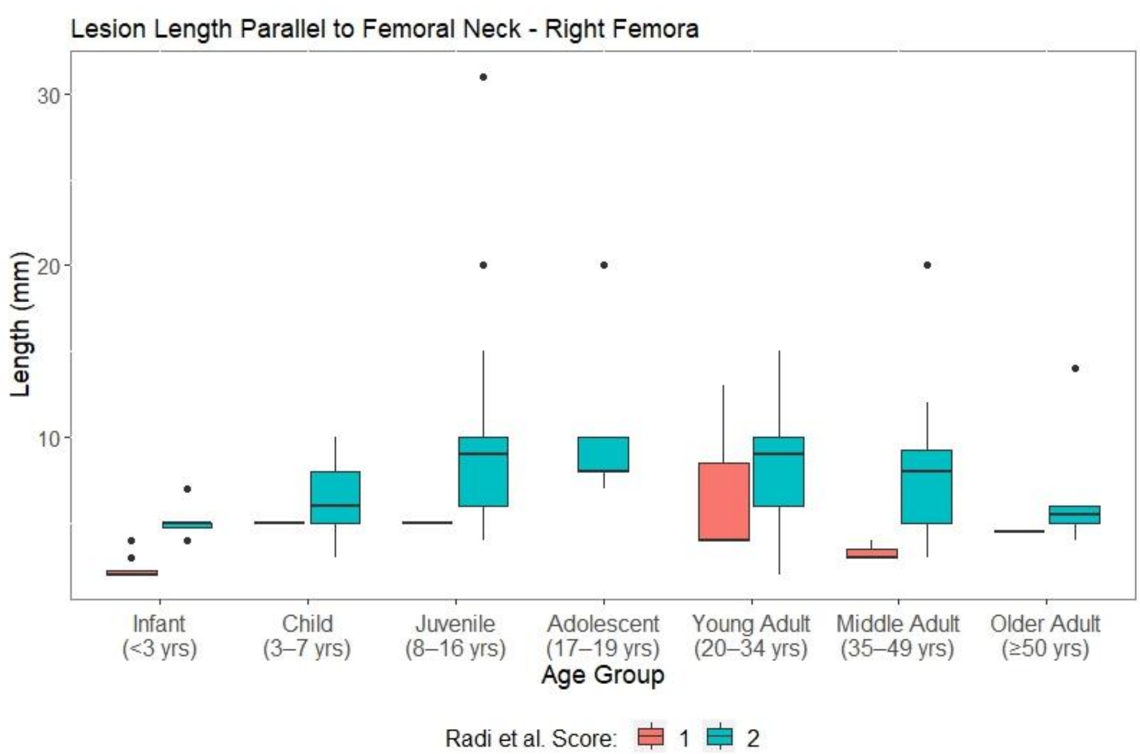

Figure 6.11: Boxplot of lesion length parallel to the femoral neck between lesions categorized as Radi et al. Score 1 or 2 for right femora, separated by age group.

Lesions with a Radi et al. Score 2 had larger measurements of femoral cribra perimeter compared to lesions with a Radi et al. Score 1 across age groups for both left and right femora (Table 6.42 and Figures 6.12 and 6.13). Additionally, the perimeter measurements for lesions displaying a Radi et al. Score 2 generally demonstrated larger ranges than the perimeter of lesions appearing as a Radi et al. Score 1.

Table 6.42: Summary statistics of lesion perimeter measurements between lesions categorized as Radi et al. Scores 1 and 2 for left and right femora, separated by age group.

	Perimeter Measurements (mm)			
	Left femora		Right femora	
Age group	Score 1 Mean ± SD	Score 2 Mean ± SD	Score 1 Mean ± SD	Score 2 Mean ± SD
Infant (<3 yrs)	8.00 (±3.84) n = 9	19.86 (±5.52) n = 14	8.88 (±3.98) n = 8	19.67 (±5.12) n = 12
Child (3–7 yrs)	12.50 (±3.63) n = 8	23.89 (±7.56) n = 46	14.00 (±0.00) n = 1	23.19 (±7.50) n = 47
Juvenile (8–16 yrs)	14.00 (±0.00) n = 1	40.19 (±15.91) n = 26	27.50 (±10.61) n = 2	35.22 (±14.58) n = 27
Adolescent (17–19 yrs)	— n = 0	53.80 (±16.81) n = 5	— n = 0	46.00 (±14.16) n = 5
Young Adult (20–34 yrs)	16.83 (±7.17) n = 6	34.14 (±15.61) n = 21	20.67 (±15.89) n = 3	43.56 (±15.52) n = 16
Middle Adult (35–49 yrs)	21.67 (±2.08) n = 3	36.00 (±16.43) n = 25	12.00 (±4.00) n = 3	38.70 (±15.46) n = 20
Older Adult (≥50 yrs)	10.00 (±0.00) n = 1	26.50 (±19.49) n = 6	13.00 (±0.00) n = 1	34.17 (±17.41) n = 6

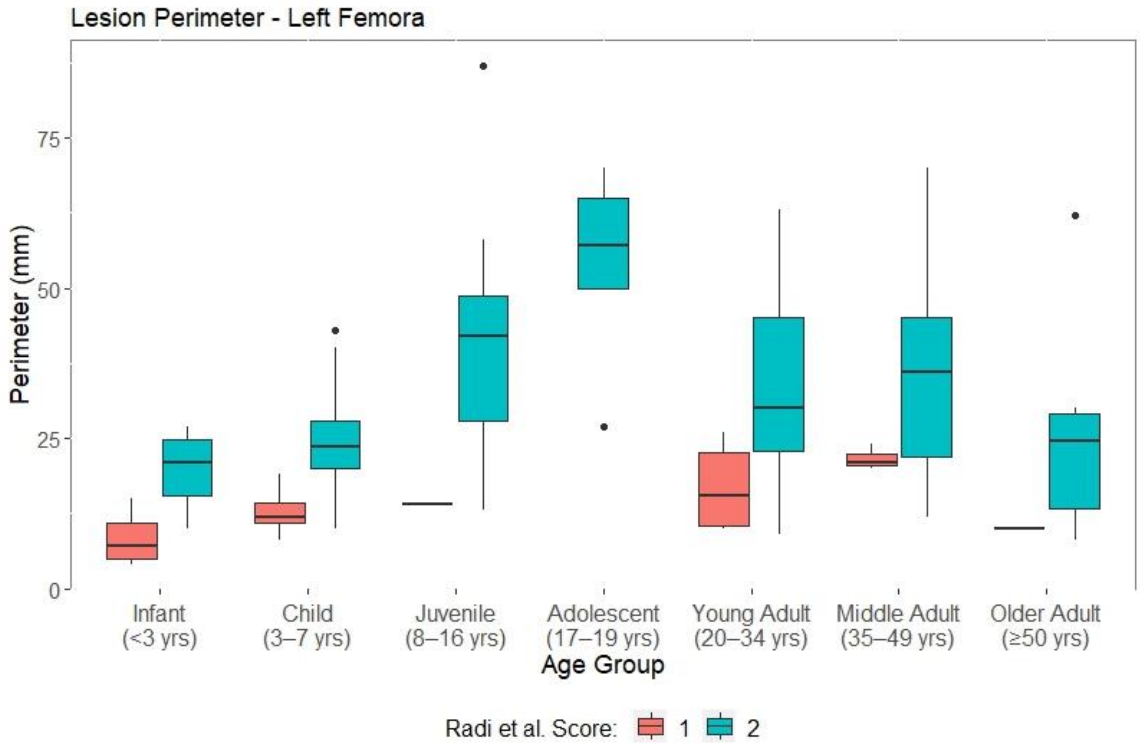

Figure 6.12: Boxplot of lesion perimeter measurements between lesions categorized as Radi et al. Score 1 or 2 for left femora, separated by age group.

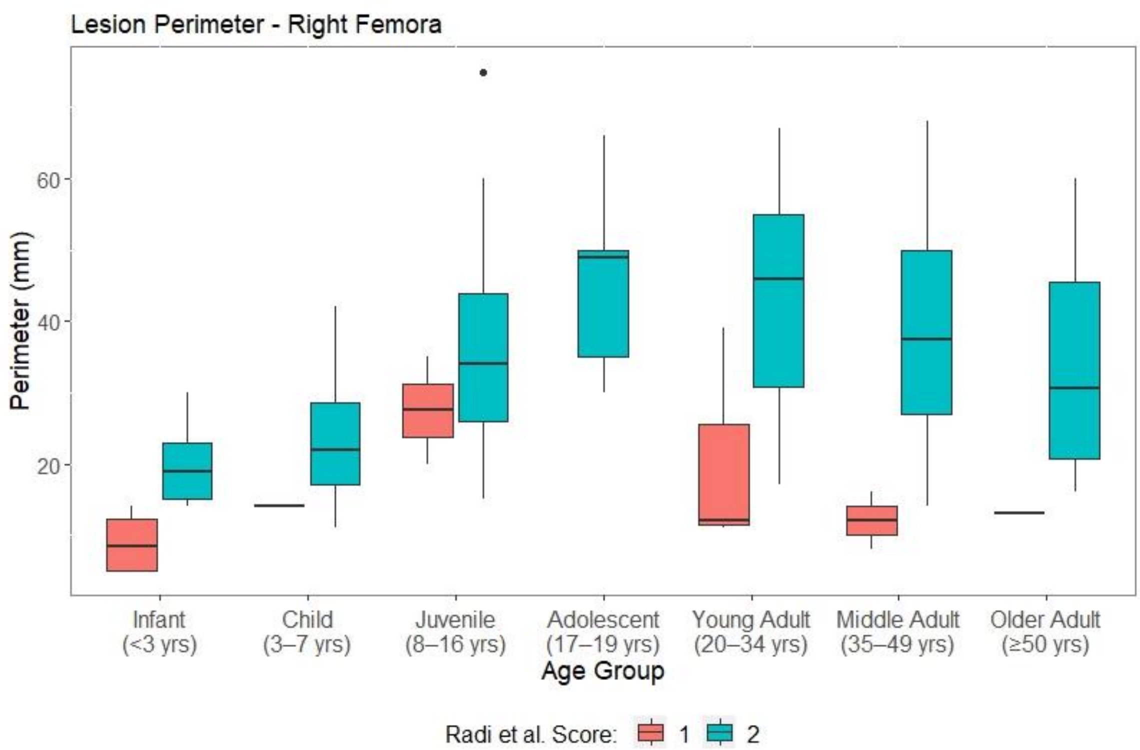

Figure 6.13: Boxplot of lesion perimeter between lesions scored as Radi et al. Score 1 or 2 for right femora, separated age group.

Research Question 6a & 6b

Research Question 6a: *Are there differences in trabecular microarchitecture at the anterior-inferior femoral neck between unaffected individuals and affected individuals displaying femoral cribra with varying degrees of skeletal remodeling (i.e., "activity")?*

Unaffected femora vs. affected femora with active or healing lesions

Figures 6.14, 6.15, 6.16, 6.17, and 6.18 represent grouped bar graphs for the five trabecular variables organized by comparative pairs between unaffected individuals and affected individuals displaying lesions hypothesized to be either active or healing. Of the 17 total comparison pairs, nine were between unaffected individuals and affected individuals with a lesion appearing active on the external surface, and eight were between unaffected individuals and affected individuals with a lesion demonstrating signs of healing. Tables 6.43, 6.44, 6.45, 6.46, and 6.47 summarize the number comparisons in which the trabecular measures for the affected femora, with either active or healing lesions, were greater or less than those obtained from unaffected femora.

Figure 6.14 displays the values of bone volume density (BV/TV) for each of the 17 pairs. In all nine comparisons between unaffected individuals and affected individuals with an estimated active lesion, BV/TV in active lesions were less than the unaffected counterparts. Of the eight comparisons between unaffected individuals and affected individuals with a lesion thought to be healing, five cases demonstrated lower BV/TV values in the healing lesions. The other three comparisons between unaffected individuals and individuals with a healing lesion showed higher BV/TV values in healing lesions compared to the unaffected counterparts; however, the values were very similar in one of those pairs (Pair 1).

Table 6.43: Number of comparison pairs in which BV/TV values of affected femora, hypothesized to have active or healing lesions, were greater or less than unaffected femora.

	BV/TV	
	Affected is greater than unaffected	Affected is less than unaffected
Unaffected vs. Affected Active	0/9	9/9
Unaffected vs. Affected Healing	3/8*	5/8

*BV/TV values for Pair 1 femora are similar

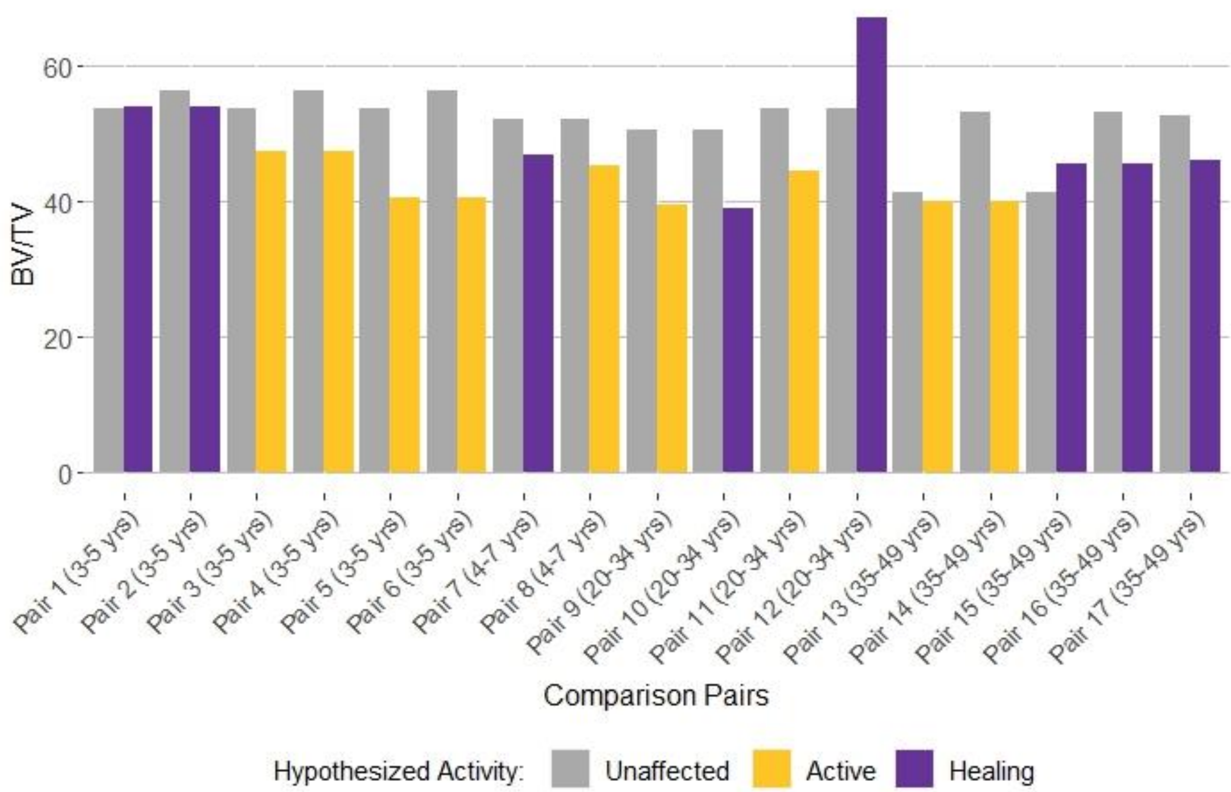

Figure 6.14: Group bar plot for BV/TV by comparison pairs of unaffected femora and affected femora with lesions hypothesized to be active or healing.

The values for specific bone surface (BS/BV) were compared between unaffected individuals and affected individuals with hypothesized active and healing lesions in Figure 6.15. Of the nine pairs in which individuals with estimated active lesions were compared to unaffected individuals, BS/BV values were greater in the active lesions compared to unaffected femora in seven cases. The remaining two pairs demonstrated lower values of BS/BV in active lesions compared to femora without lesions. In comparing BS/BV values between unaffected individuals and affected individuals with estimated healing lesions, four of the eight pairs demonstrated lower values in healing lesions compared to femora without a lesion. Of the remaining pairs, BS/BV values were greater in individuals with healing lesions compared to unaffected individuals in three cases, and BS/BV values were identical in one comparison pair (Pair 16).

Table 6.44: Number of comparison pairs in which BS/BV values of affected femora, hypothesized to have active or healing lesions, were greater or less than unaffected femora.

	BS/BV	
	Affected is greater than unaffected	Affected is less than unaffected
Unaffected vs. Affected Active	7/9	2/9
Unaffected vs. Affected Healing*	3/8	4/8

*BS/BV values for Pair 16 femora are the same

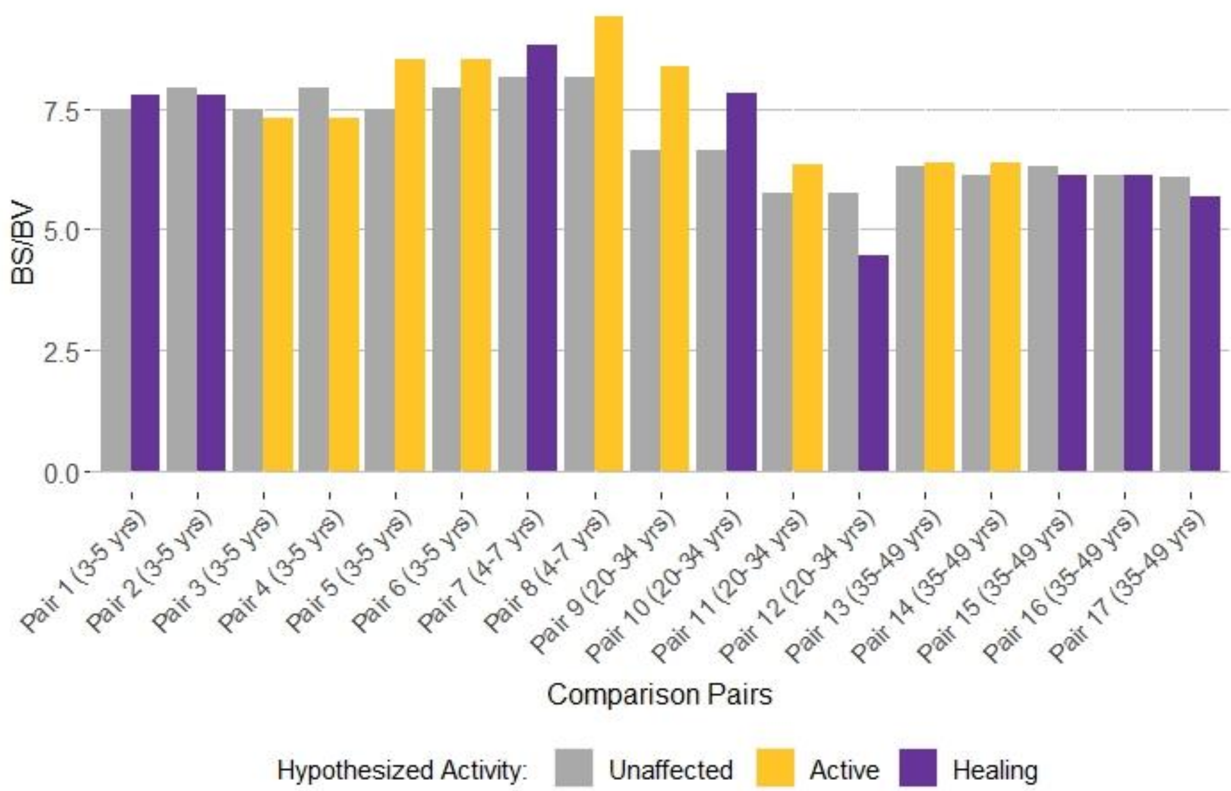

Figure 6.15: Group bar plot for BS/BV by comparison pairs of unaffected femora and affected femora with lesions hypothesized to be active or healing.

Figure 6.16 presents measures of trabecular thickness (Tb.Th.) for the pairs comparing unaffected individuals and affected individuals with active or healing lesions. Six of the nine pairs comparing femora with hypothesized active lesions to unaffected femora revealed higher values of Tb.Th. in the individuals with active lesions. The remaining three pairs showed lower values of Tb.Th. in active lesions compared to unaffected femora. Of the eight pairs comparing individuals with estimated healing lesions and their unaffected counterparts, Tb.Th. was greater in the affected femora with healing lesions in seven comparisons. Consequently, trabecular thickness in individuals with healing lesions was less than unaffected individuals in only one of the eight comparison pairs.

Table 6.45: Number of comparison pairs in which Tb.Th. values of affected femora, hypothesized to have active or healing lesions, were greater or less than unaffected femora.

	Tb.Th.	
	Affected is greater than unaffected	Affected is less than unaffected
Unaffected vs. Affected Active	6/9	3/9
Unaffected vs. Affected Healing	7/8	1/8

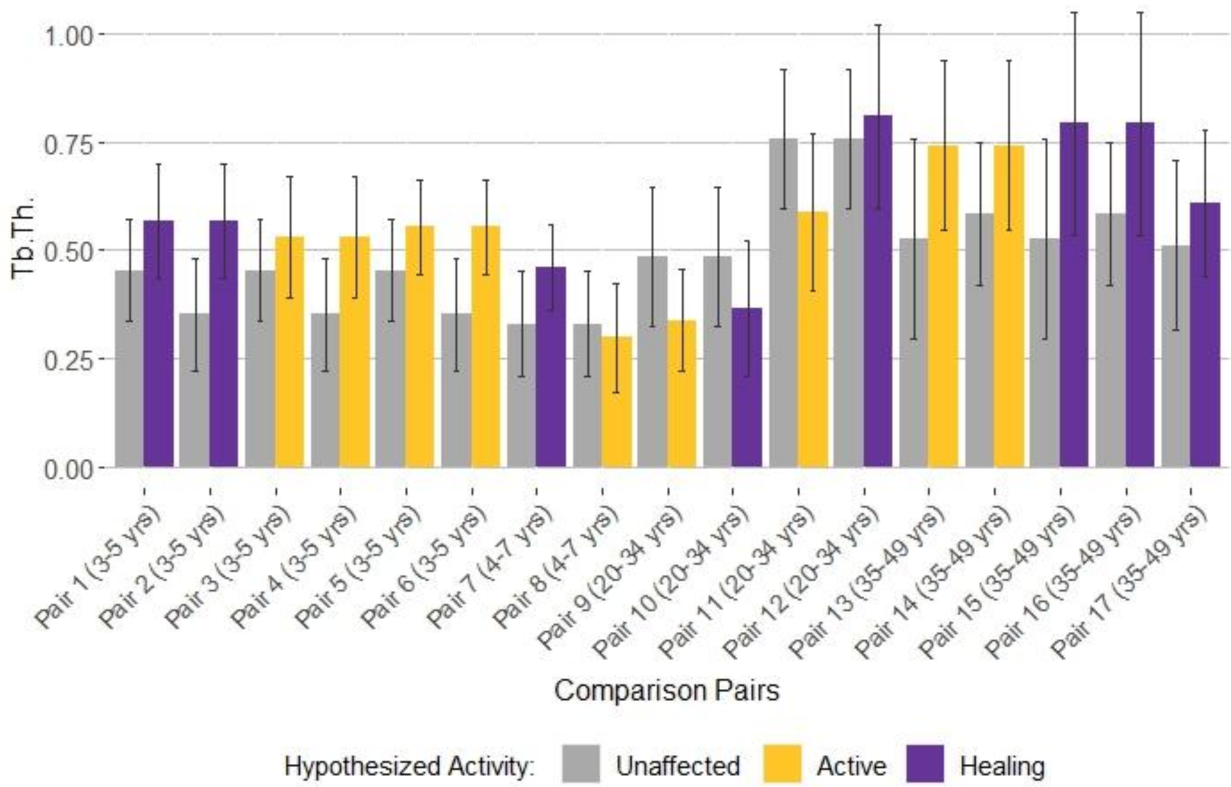

Figure 6.16: Group bar plot for Tb.Th. by comparison pairs of unaffected femora and affected femora with lesions hypothesized to be active or healing.

The mean values of trabecular number (Tb.N.) were compared between unaffected individuals and individuals with either active or healing femoral cribra in Figure 6.17. In seven of nine comparisons, Tb.N. in affected femora with hypothesized active lesions was less than that in femora without the lesion. The remaining two comparisons between unaffected individuals and individuals with active lesions revealed higher Tb.N. values in the active lesions. Of the eight comparisons between unaffected individuals and individuals with estimated healing lesions, half of the pairs showed higher values of Tb.N. in the healing lesions although three pairs had relatively similar values. The other half of the eight pairs showed lower values of Tb.N. in healing lesions compared to the unaffected femora.

Table 6.46: Number of comparison pairs in which Tb.N. values of affected femora, hypothesized to have active or healing lesions, were greater or less than unaffected femora.

	Tb.N.	
	Affected is greater than unaffected	Affected is less than unaffected
Unaffected vs. Affected Active	2/9	7/9
Unaffected vs. Affected Healing	4/8	4/8

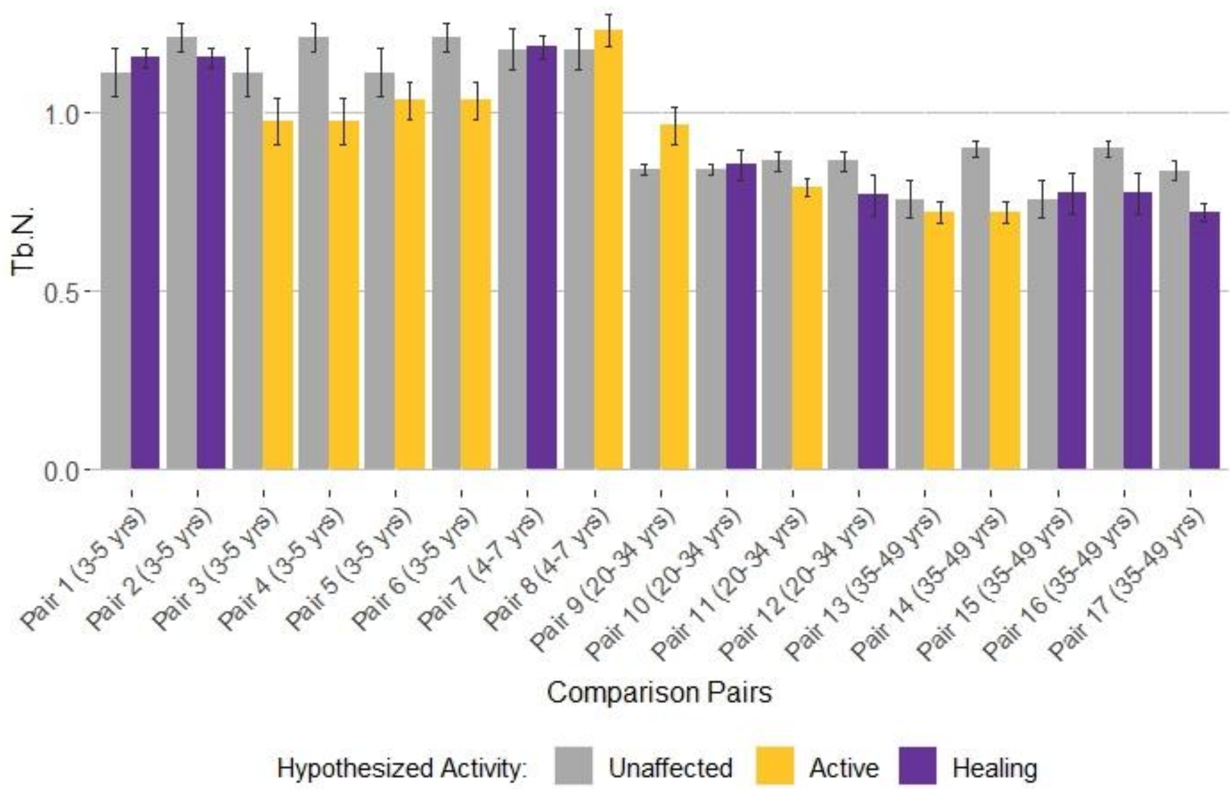

Figure 6.17: Group bar plot for Tb.N. by comparison pairs of unaffected femora and affected femora with lesions hypothesized to be active or healing.

In Figure 6.18, measures of trabecular spacing (Tb.Sp.) are compared between individuals without femoral cribra and individuals with hypothesized active or healing femoral cribra. Of the nine pairs comparing individuals with active lesions to the corresponding unaffected individuals, seven comparisons demonstrated higher Tb.Sp. values in the active lesions. In the remaining two comparisons, individuals with active lesions presented lower values of Tb.Sp. compared to their unaffected counterparts. Five of the eight pairs comparing individuals with healing femoral cribra to individuals without the lesion showed lower values of Tb.Sp. in the healing lesions. In the other three cases, Tb.Sp. in affected femora with healing lesions was greater than femora without the lesion.

Table 6.47: Number of comparison pairs in which Tb.Sp values of affected femora, hypothesized to have active or healing lesions, were greater or less than unaffected femora.

	Tb.Sp.	
	Affected is greater than unaffected	Affected is less than unaffected
Unaffected vs. Affected Active	7/9	2/9
Unaffected vs. Affected Healing	3/8	5/8

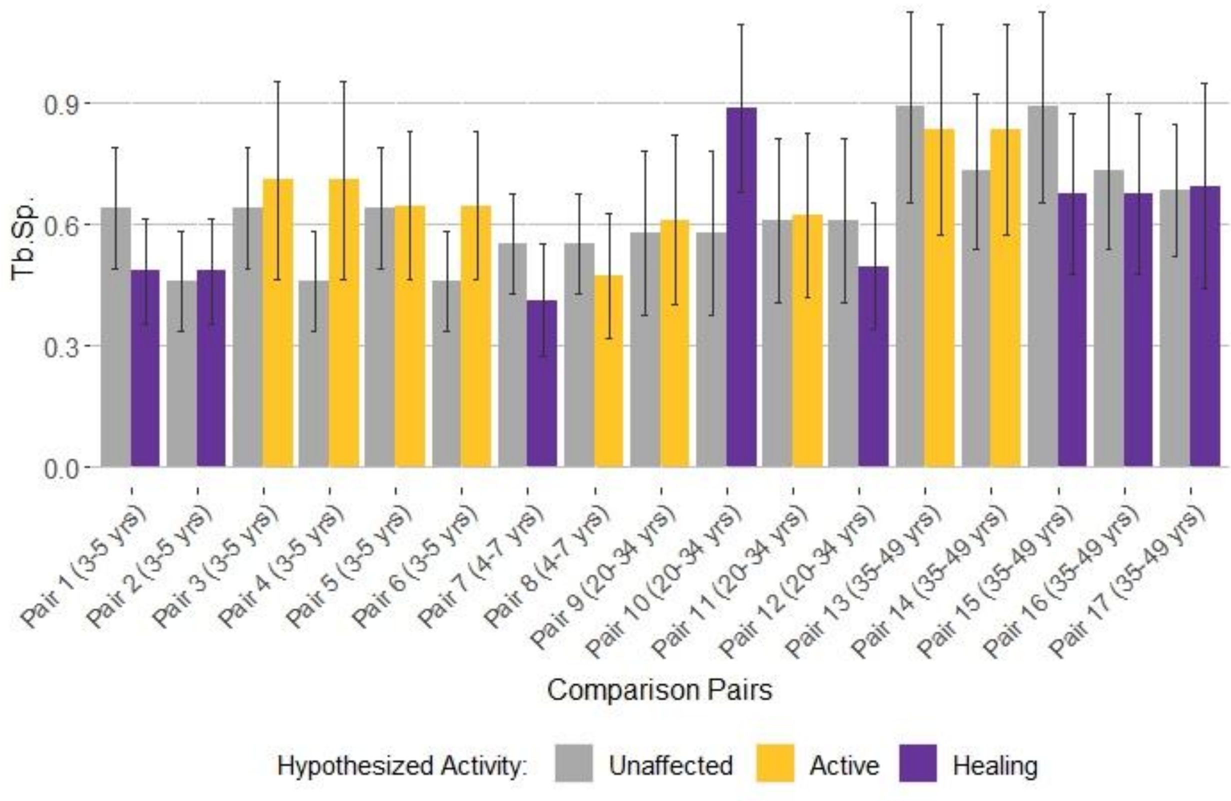

Figure 6.18: Group bar plot for Tp.Sp. by comparison pairs of unaffected femora and affected femora with lesions hypothesized to be active or healing.

Affected femora with active lesions vs. affected femora with healing lesions

Values for each of the five trabecular microarchitecture variables were compared between individuals with lesions hypothesized to be active and individuals with lesions thought to be healing, the results of which are summarized in Table 6.48. The comparisons across the five variables were conducted between seven pairs of individuals with each pair sharing the same estimated demographics (i.e., age-at-death and sex). In 6/7 of the comparison pairs, bone volume density (BV/TV) was greater in healing lesions compared to active lesions (Figure 6.19). The remaining comparison pair (Pair 5) revealed a lower BV/TV for the individual with a healing lesion compared to the individual with an active lesion; however, the values were very similar. In comparing specific bone surface (BS/BV), 6/7 comparisons showed lower values in healing lesions compared to active lesions (Figure 6.20). The other comparison pair demonstrated a higher BS/BV value in the healing lesion compared to the active lesion. All seven comparisons for trabecular thickness (Tb.Th.) showed higher values in healing lesions compared to active lesions (Figure 6.21). Healing lesions had greater mean values of trabecular number (Tb.N.) compared to active lesions in 4/7 comparisons, while lesions showing signs of healing had lower values of Tb.N. compared to lesions that appeared active in 3/7 comparisons (Figure 6.22). In the comparisons for trabecular spacing (Tb.Sp.), 6/7 pairs revealed lower values of Tb.Sp. in healing lesions compared to active lesions and only 1/7 pair demonstrated a higher value of Tb.Sp. in the healing lesion (Figure 6.23).

Table 6.48: Number of comparison pairs in which the trabecular measures of affected femora, hypothesized to have active or healing lesions, were greater or less than unaffected femora.

	Healing is greater than active	Healing is less than active
BV/TV	6/7	1/7*
BS/BV	1/7	6/7
Tb.Th.	7/7	0/7
Tb.N.	4/7	3/7
Tb.Sp.	1/7	6/7

*BS/BV values for Pair 5 femora are similar

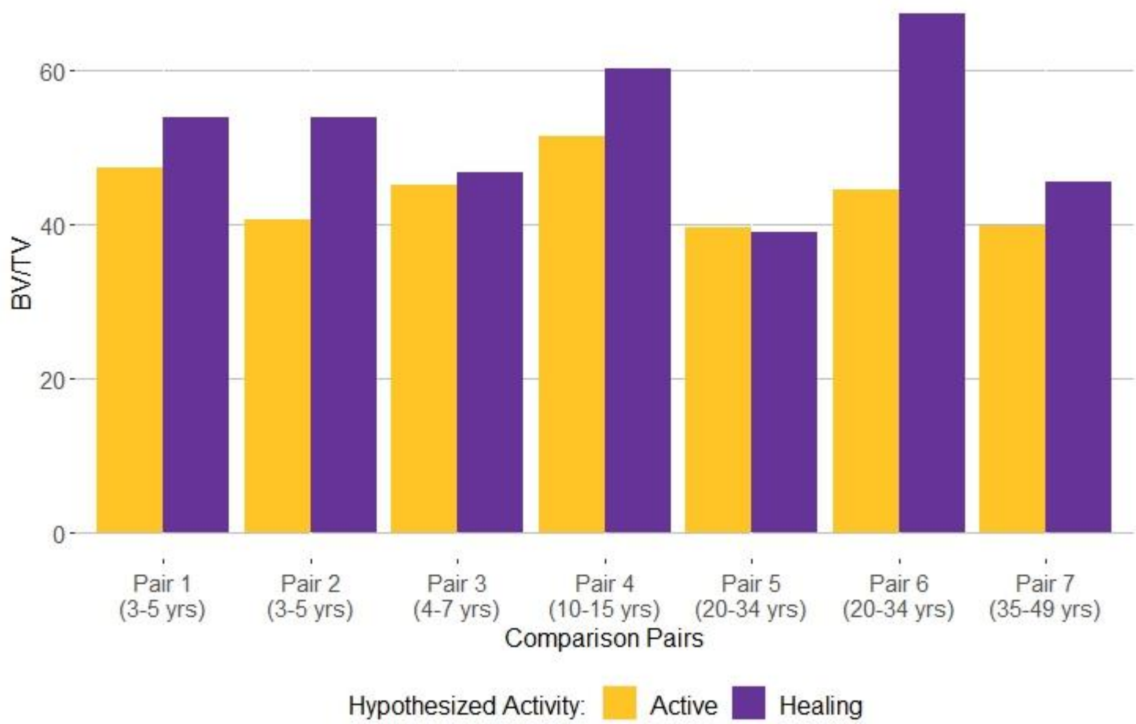

Figure 6.19: Group bar plot for BV/TV by comparison pairs of affected femora with lesions hypothesized to be active and healing.

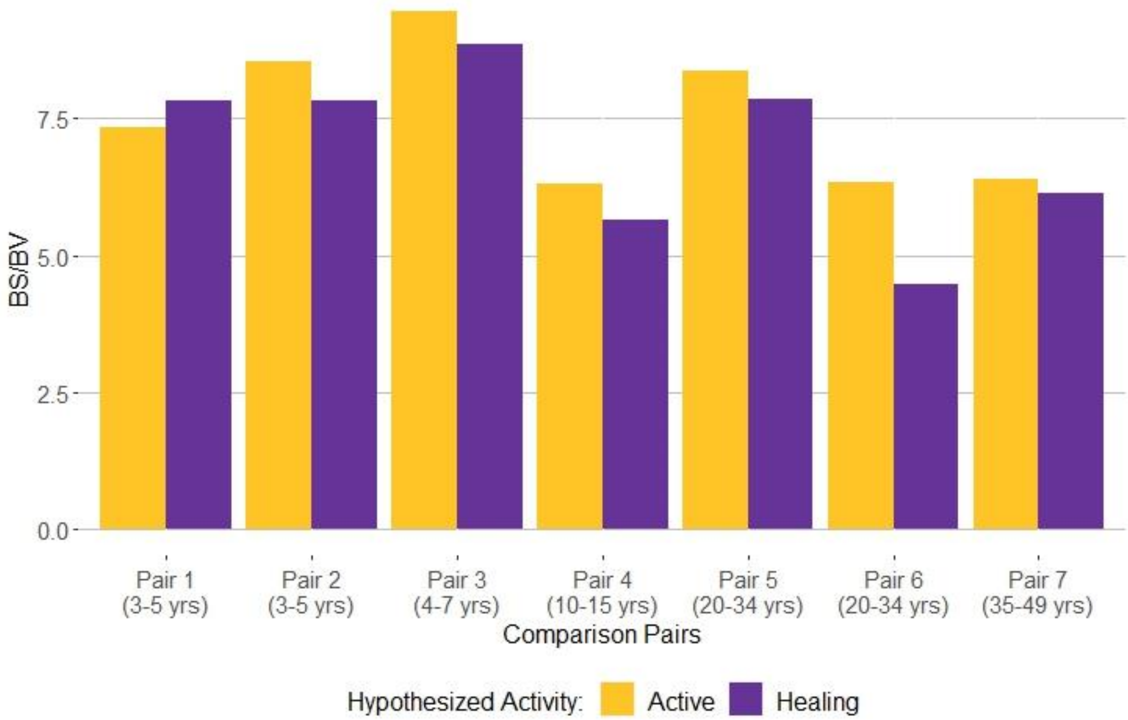

Figure 6.20: Group bar plot for BS/BV by comparison pairs of affected femora with lesions hypothesized to be active and healing.

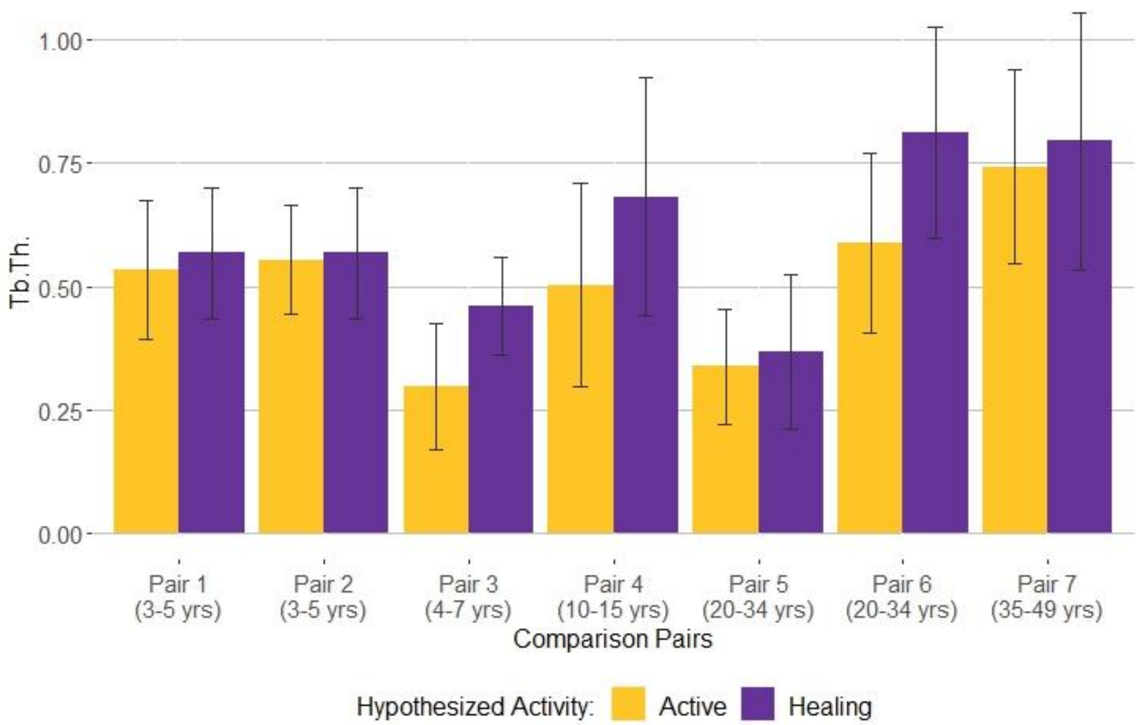

Figure 6.21: Group bar plot for Tb.Th. by comparison pairs of affected femora with lesions hypothesized to be active and healing.

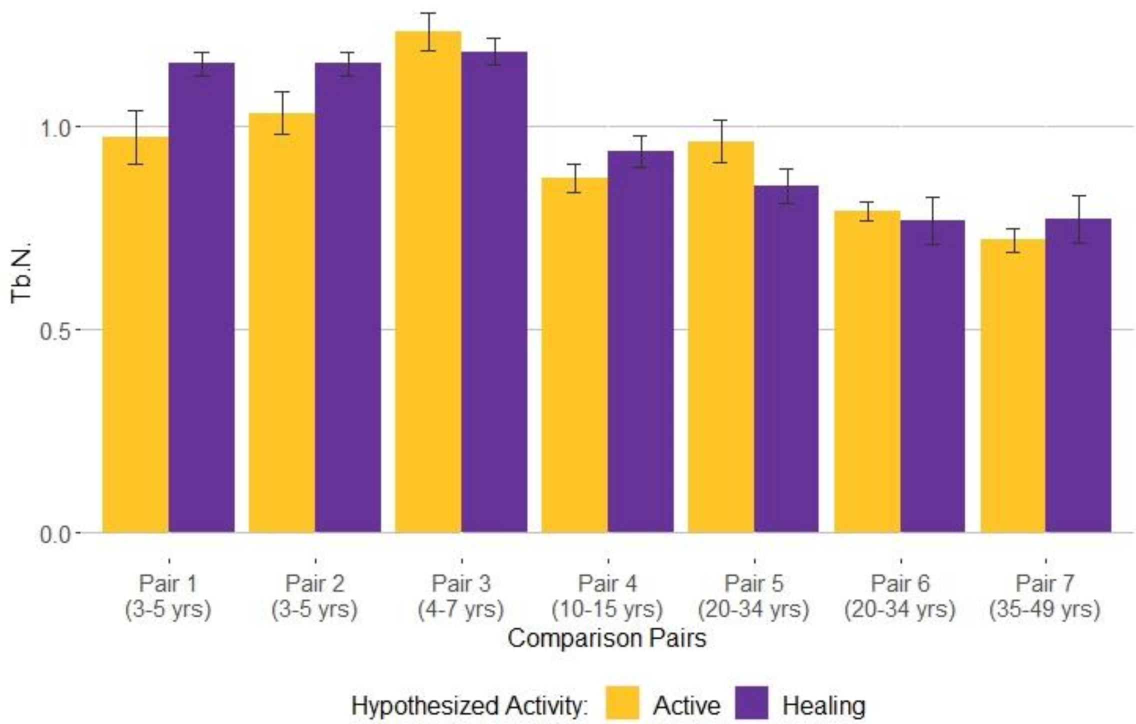

Figure 6.22: Group bar plot for Tb.N. by comparison pairs of affected femora with lesions hypothesized to be active and healing.

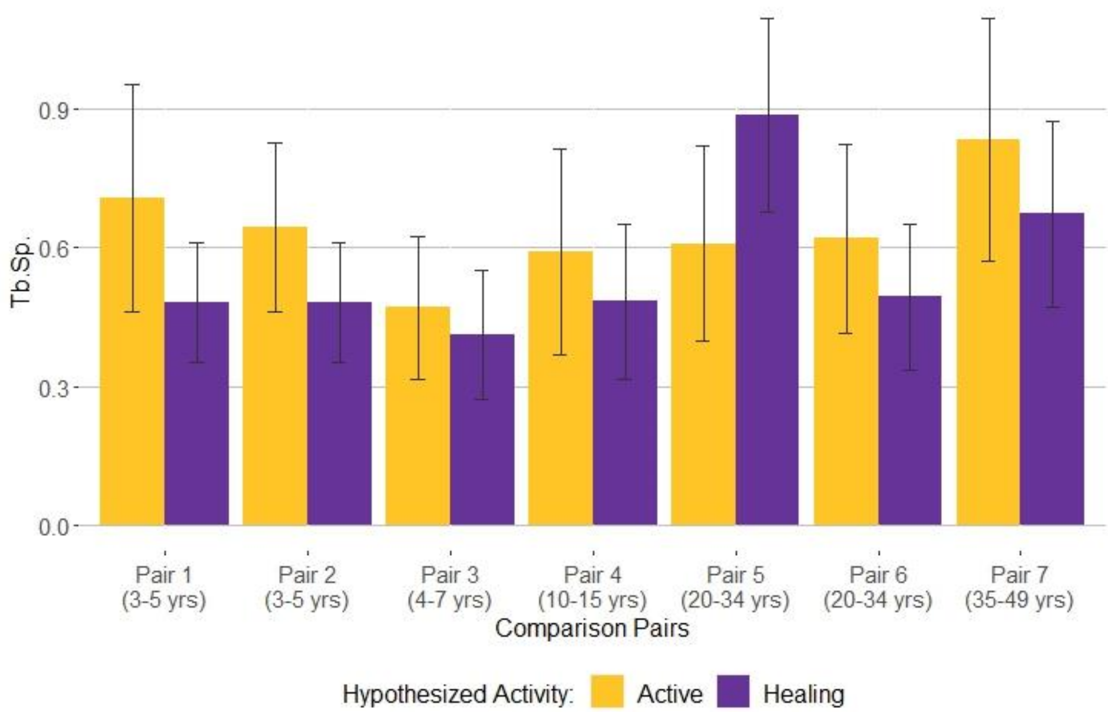

Figure 6.23: Group bar plot for Tb.Sp. by comparison pairs of affected femora with lesions hypothesized to be active and healing.

Research Question 6b: *Are there differences in trabecular microarchitecture at the anterior-inferior femoral neck between unaffected individuals and affected individuals displaying varying extents of femoral cribra (i.e., "severity")?*

Unaffected femora vs. affected femora with "less severe" or "more severe" lesions

The five trabecular variables were compared between pairs of unaffected individuals and affected individuals displaying femoral cribra hypothesized to be either less severe or more severe. Each comparison pair was between individuals from the same age cohort. Of the ten comparison pairs, five pairs were between unaffected individuals and affected individuals with a lesion appearing less severe from the surface, and five pairs were between unaffected individuals and affected individuals with a lesion displaying a more severe external surface.

Figure 6.24 shows the values of bone volume density (BV/TV) compared between unaffected individuals and affected individuals with lesions hypothesized to be less or more severe, the results of which are summarized in Table 6.49. In 3/5 comparisons between unaffected individuals and affected individuals with a less severe lesion, BV/TV values were lower in the affected femora with less severe lesions. The other two comparisons, which were between pairs of individuals in the youngest age group (2–3 years), demonstrated higher values of BV/TV in the affected femora with less severe lesions compared to their unaffected counterparts. In comparing BV/TV between unaffected femora and affected femora with more severe lesions, 3/5 pairs showed lower values in the femora with the lesion. The other two comparisons between unaffected femora and femora with more severe lesions were between individuals of the youngest age cohort (2–3 years). One of these pairs demonstrated a higher BV/TV in the affected individual compared to the unaffected individual, and the other pair had similar values.

Table 6.49: Number of comparison pairs in which BV/TV values of affected femora, with lesions hypothesized to be less severe or more severe, were greater or less than unaffected femora.

	BV/TV	
	Affected is greater than unaffected	Affected is less than unaffected
Unaffected vs. Affected "less severe" lesion	2/5	3/5
Unaffected vs. Affected "more severe" lesion*	1/5	3/5

*BS/BV values for Pair 4 femora are similar

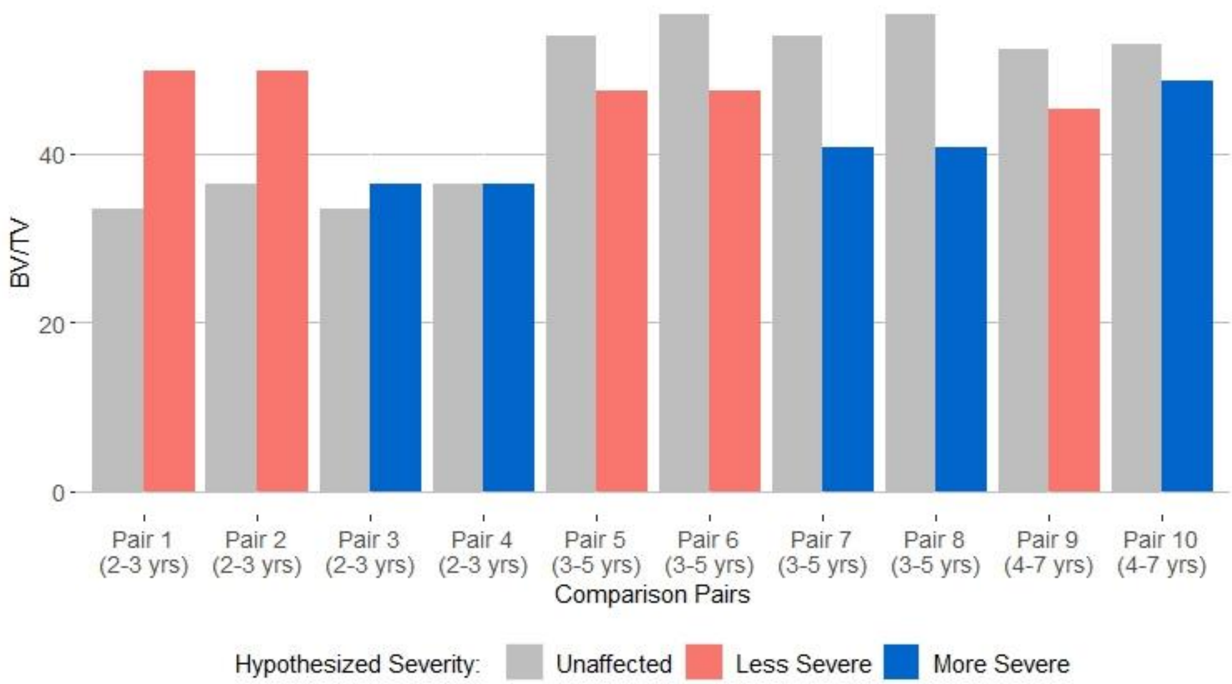

Figure 6.24: Group bar plot for BV/TV by comparison pairs of unaffected femora and affected femora with lesions hypothesized to be less severe or more severe.

The values for specific bone surface (BS/BV) were compared between unaffected individuals and affected individuals with lesions thought to be less severe or more severe in Figure 6.25, the outcomes of which are summarized in Table 6.50. Of the five comparisons between unaffected femora and femora with a lesion estimated to be less severe, four pairs demonstrated slightly lower values of BS/BV in the affected femora. The other pair, which was between individuals from the 4–7 years cohort, displayed a higher value of BS/BV in the femur with femoral cribra. Of the five comparisons between unaffected femora and femora with a lesion thought to be more severe, the affected femora had lower values of BS/BV in 3/5 pairs. In the remaining two comparisons, specific bone surface was greater in the affected femora with more severe lesions than in the unaffected femora.

Table 6.50: Number of comparison pairs in which BS/BV values of affected femora, with lesions hypothesized to be less severe or more severe, were greater or less than unaffected femora.

	BS/BV	
	Affected is greater than unaffected	Affected is less than unaffected
Unaffected vs. Affected "less severe" lesion	1/5	4/5
Unaffected vs. Affected "more severe" lesion	2/5	3/5

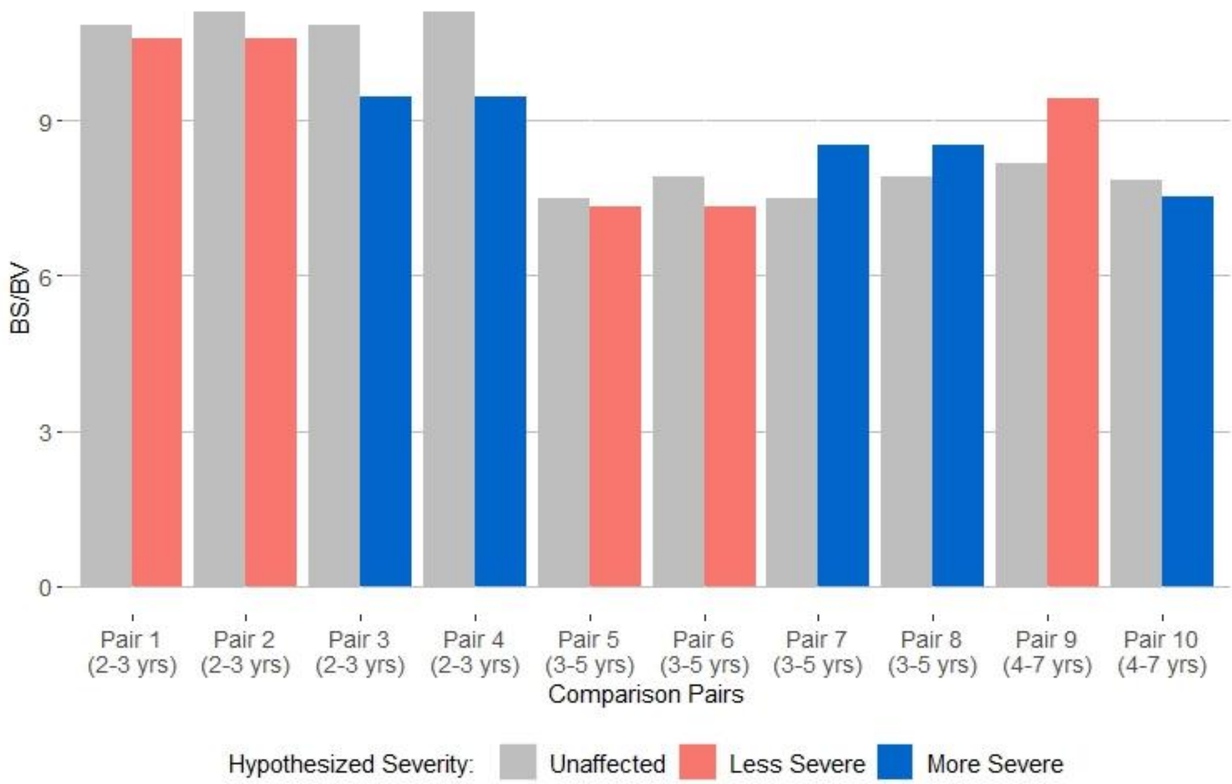

Figure 6.25: Group bar plot for BS/BV by comparison pairs of unaffected femora and affected femora with lesions hypothesized to be less severe or more severe.

The values for trabecular thickness (Tb.Th.) were compared between unaffected individuals and individuals with femoral cribra hypothesized to be either less severe or more severe in Figure 6.26. As summarized in Table 6.51, 3/5 comparisons between unaffected femora and femora with lesions that appeared less severe demonstrated higher values of trabecular thickness in the affected femora. Of the remaining two comparisons, one pair had similar values (Pair 2, 2–3 years) and the other pair (Pair 9, 4–7 years) showed a lower value for Tb.Th. in the affected femur with a less severe lesion. A similar pattern was observed in comparing unaffected femora and affected femora with lesions that appeared more severe (Table 6.51). Three of the five comparisons between femora without lesions and femora with more severe lesions demonstrated greater Tb.Th. values in the affected femora. Of the other two comparisons, one pair had similar values (Pair 4, 2–3 years) and the other pair showed a lower measure of Tb.Th. in the femur with a more severe lesion compared to the unaffected femur.

Table 6.51: Number of comparison pairs in which Tb.Th. values of affected femora, with lesions hypothesized to be less severe or more severe, were greater or less than unaffected femora.

	Tb.Th.	
	Affected is greater than unaffected	Affected is less than unaffected
Unaffected vs. Affected "less severe" lesion	4/5*	1/5
Unaffected vs. Affected "more severe" lesion*	3/5	1/5

*Tb.Th. values for Pair 2 femora and for Pair 4 femora are similar

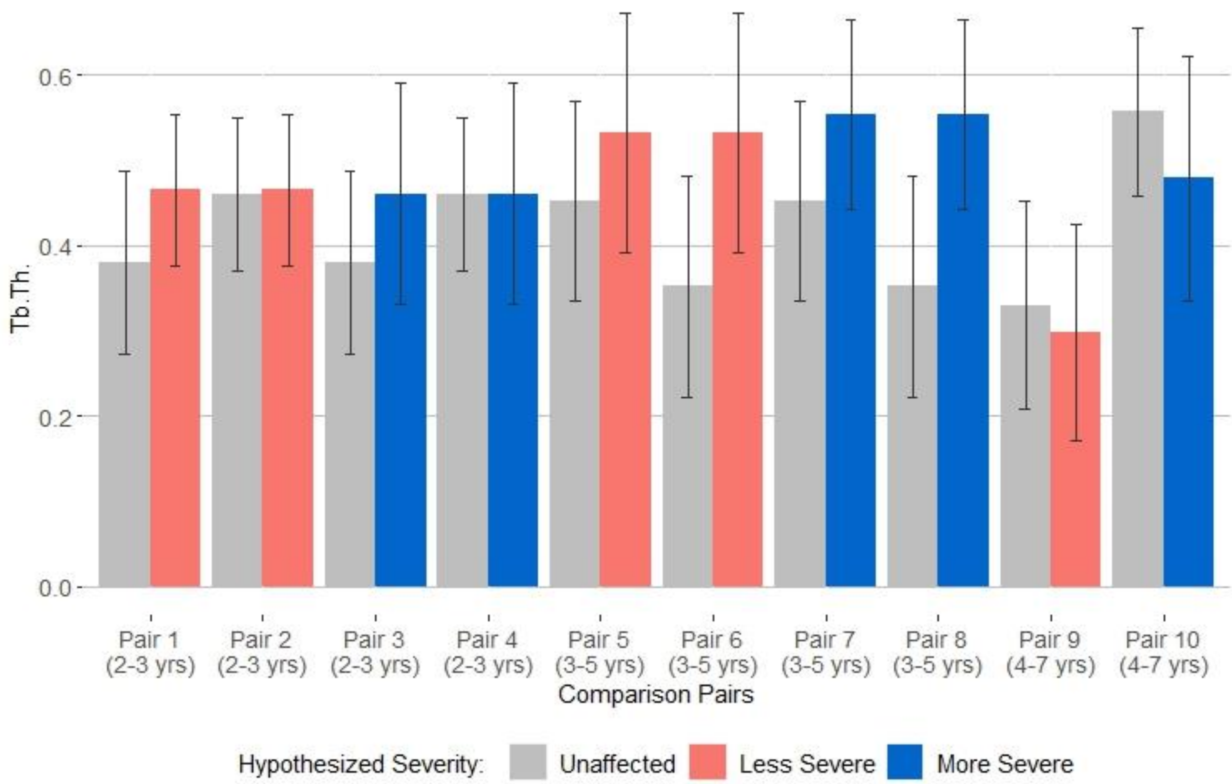

Figure 6.26: Group bar plot for Tb.Th. by comparison pairs of unaffected femora and affected femora with lesions hypothesized to be less severe or more severe.

Figure 6.27 presents mean values of trabecular number (Tb.N.) for the pairs comparing unaffected individuals and affected individuals with lesions thought to be more severe or less severe. Of the five comparisons between femora without lesions and femora with less severe lesions, three resulted in higher values of trabecular number for the affected femora whereas two demonstrated lower values for the affected femora (Table 6.52). In all five comparisons between unaffected femora and affected femora with more severe lesions, the affected femora demonstrated lower values for trabecular number than unaffected femora, although one of these displayed only slight difference (Pair 3, 2–3 years).

Table 6.52: Number of comparison pairs in which Tb.N. values of affected femora, with lesions hypothesized to be less severe or more severe, were greater or less than unaffected femora.

	Tb.N.	
	Affected is greater than unaffected	Affected is less than unaffected
Unaffected vs. Affected "less severe" lesion	3/5	2/5
Unaffected vs. Affected "more severe" lesion	0/5	5/5

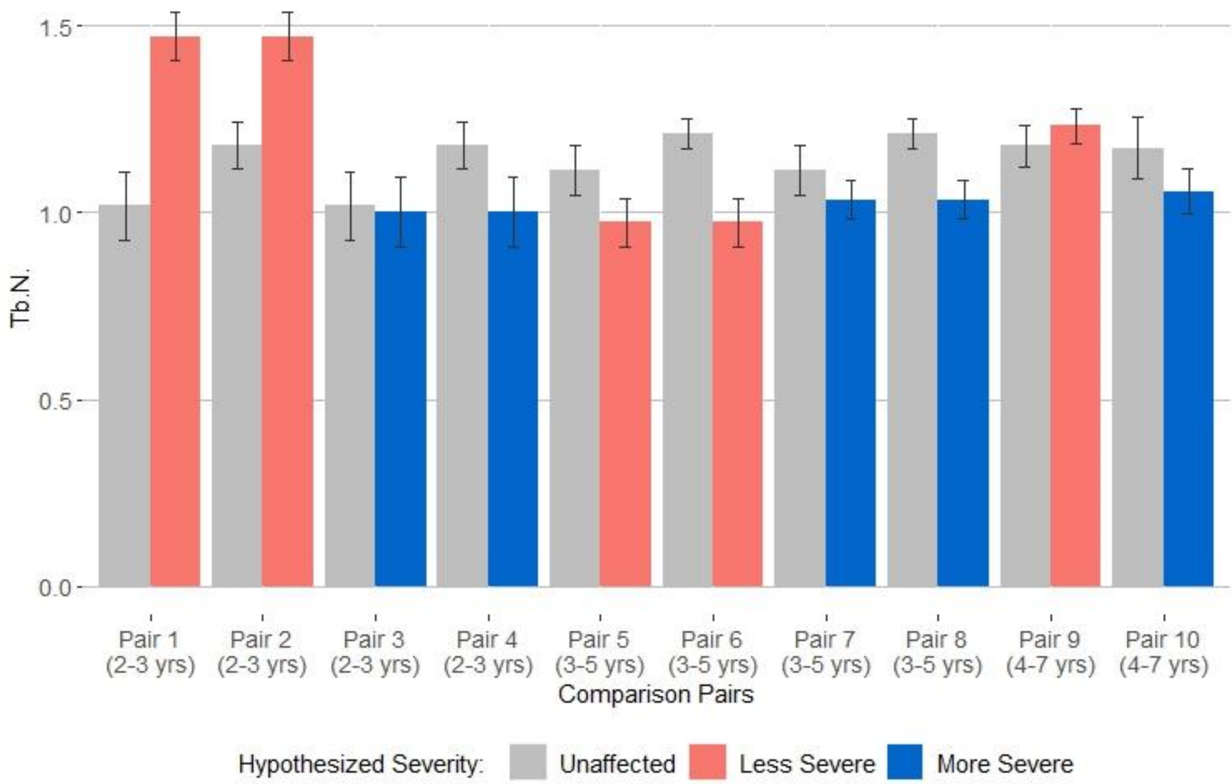

Figure 6.27: Group bar plot for Tb.N. by comparison pairs of unaffected femora and affected femora with lesions hypothesized to be less severe or more severe.

The values for trabecular spacing (Tb.Sp.) are compared between individuals without femoral cribra and individuals with the lesion that appeared less severe or more severe in Figure 6.28. In 3/5 comparisons between unaffected femora and affected femora hypothesized to be less severe, the values for trabecular spacing were lower among the femora with less severe lesions (Table 6.53). The remaining two pairs demonstrated higher values of trabecular spacing for the affected femora compared to the unaffected femora. When femora without the lesion were compared to femora displaying more severe lesions, 3/5 pairs demonstrated higher measures of Tb.Sp. in the femora with more severe lesions, although the values for Pair 7 (3–5 years) were close (Table 6.53). The other pair in this group (Pair 3, 2–3 years) had similar values of trabecular spacing between the unaffected femur and the affected femur with a lesion thought to be more severe.

Table 6.53: Number of comparison pairs in which Tb.Sp. values of affected femora, with lesions hypothesized to be less severe or more severe, were greater or less than unaffected femora.

	Tb.Sp.	
	Affected is greater than unaffected	Affected is less than unaffected
Unaffected vs. Affected "less severe" lesion	2/5	3/5
Unaffected vs. Affected "more severe" lesion*	3/5*	1/5

*Tb.Sp. values for Pair 3 femora and Pair 7 femora are similar

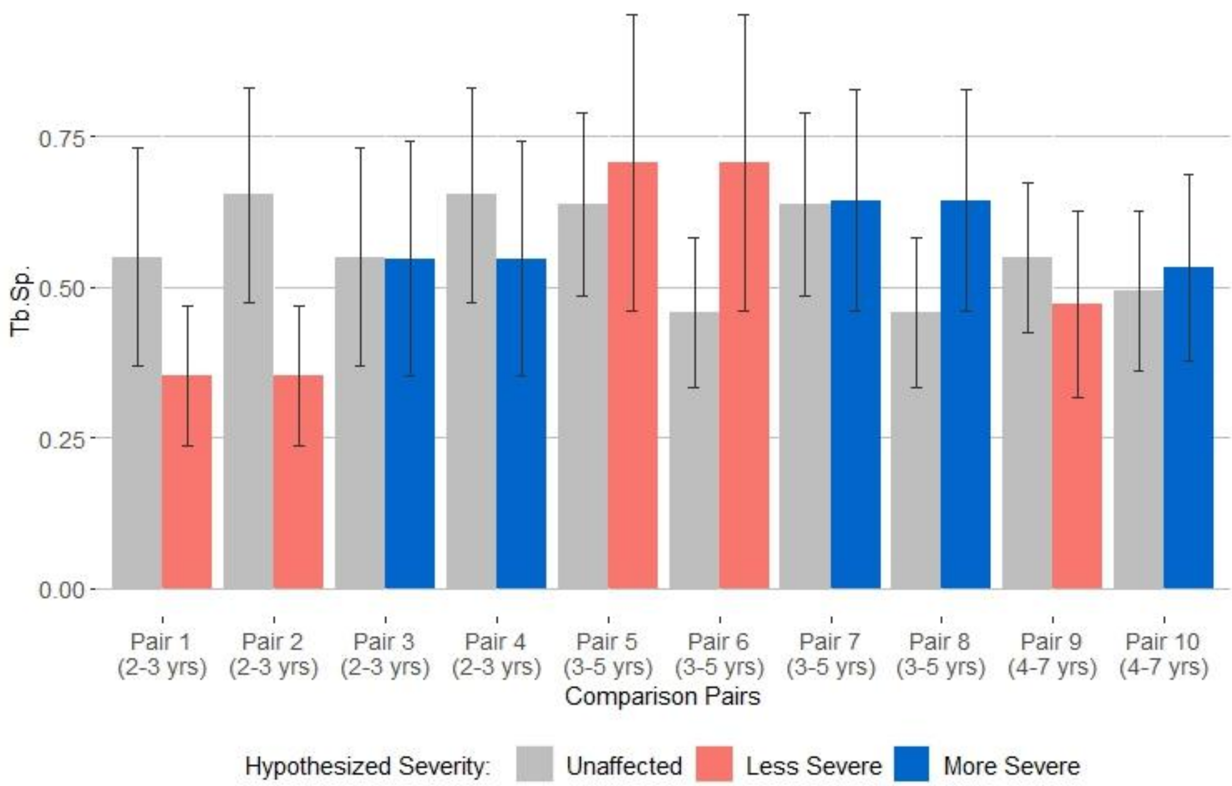

Figure 6.28: Group bar plot for Tb.Sp. by comparison pairs of unaffected femora and affected femora with lesions hypothesized to be less severe or more severe.

Affected femora with "less severe" lesions vs. affected femora with "more severe" lesions

The five trabecular variables were compared between femoral cribra lesions hypothesized to be less severe and more severe in three pairs of individuals from the same estimated age groups. The outcomes of these comparisons are summarized in Table 6.54. In all three comparison pairs (3/3), bone volume density (BV/TV) was lower in the lesions thought to be more severe than those thought to be less severe (Figure 6.29). Comparisons of specific bone surface (BS/BV) demonstrated higher values for more severe lesions in 2/3 comparisons, whereas the youngest pair (Pair 1, 2–3 years) demonstrated a lower BS/BV value for the more severe lesion (Figure 6.30). Measures of trabecular thickness (Tb.Th.) were lower in the more severe lesion for Pair 3, slightly higher in the more severe lesion of Pair 2, and similar between the less severe and more severe lesions in Pair 1 (Figure 6.31). In 2/3 comparisons trabecular number (Tb.N.) was greater in the more severe lesions than the less severe lesions (Pairs 2 & 3), whereas in the other comparison (Pair 1) trabecular number was lower in the more severe lesion (Figure 6.32). Values for trabecular spacing (Tb.Sp.) were lower in the more severe lesions in 2/3 comparisons (Pairs 2 & 3) and higher in the more severe lesion of the other pair (Pair 1) (Figure 6.33).

Table 6.54: Number of comparison pairs in which the trabecular measures of affected femora, with lesions hypothesized to be less severe or more severe, were greater or less than unaffected femora.

	"More severe" is less than "less severe"	"More severe" is greater than "less severe"
BV/TV	3/3 (Pair 1, Pair 2, Pair 3)	0/3
BS/BV	1/3 (Pair 1)	2/3 (Pair 2 & Pair 3)
Tb.Th.*	1/3 (Pair 3)	1/3 (Pair 2)
Tb.N.	1/3 (Pair 1)	2/3 (Pair 2 & Pair 3)
Tb.Sp.	2/3 (Pair 2 & Pair 3)	1/3 (Pair 1)

*Tb.Th. values for Pair 1 femora are similar

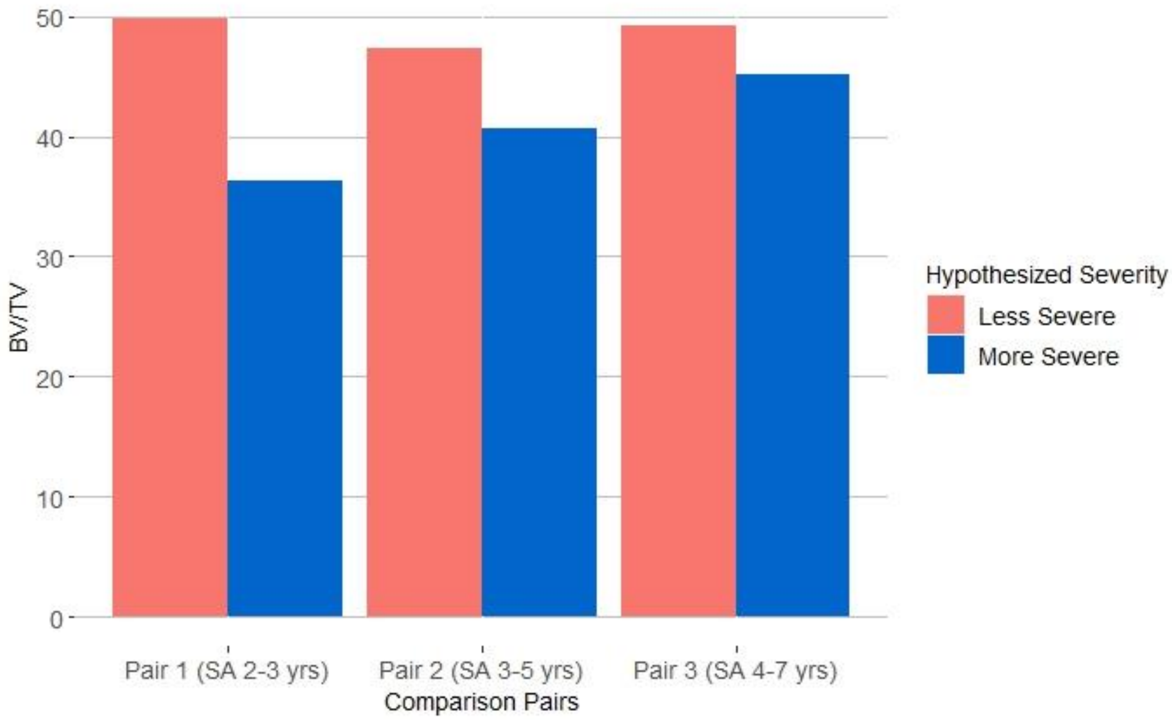

Figure 6.29: Group bar plot for BV/TV by comparison pair of affected femora with lesions hypothesized to be less severe and more severe.

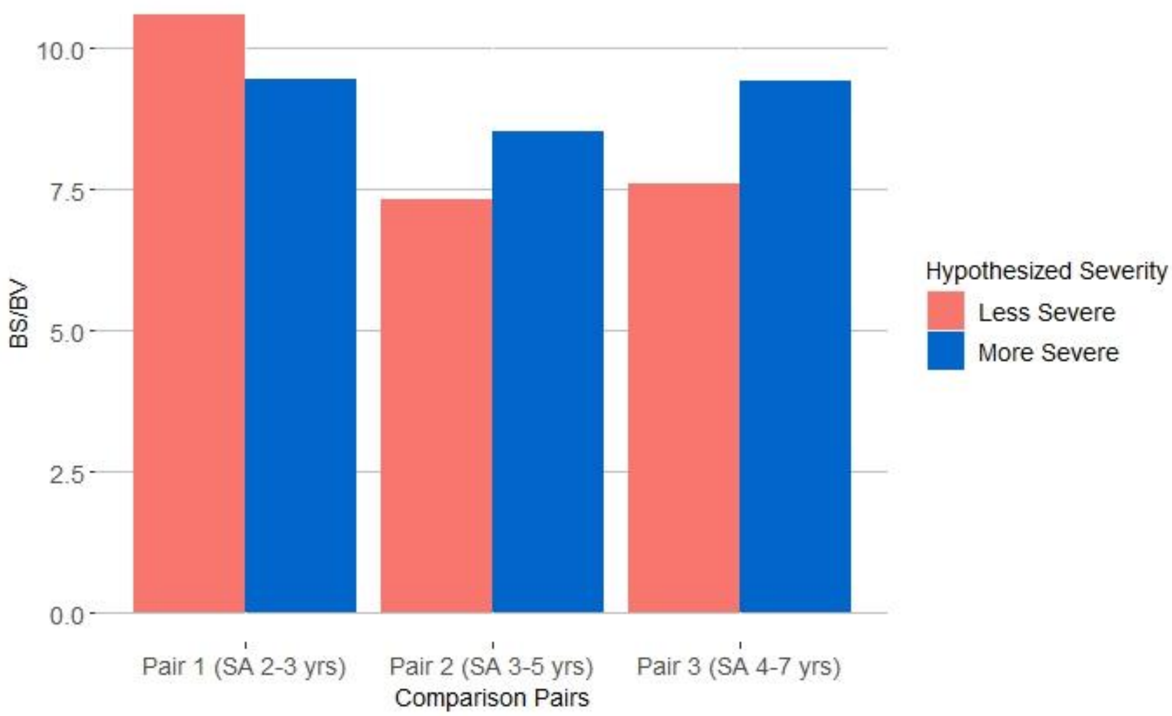

Figure 6.30: Group bar plot for BS/BV by comparison pairs of affected femora with lesions hypothesized to be less severe and more severe.

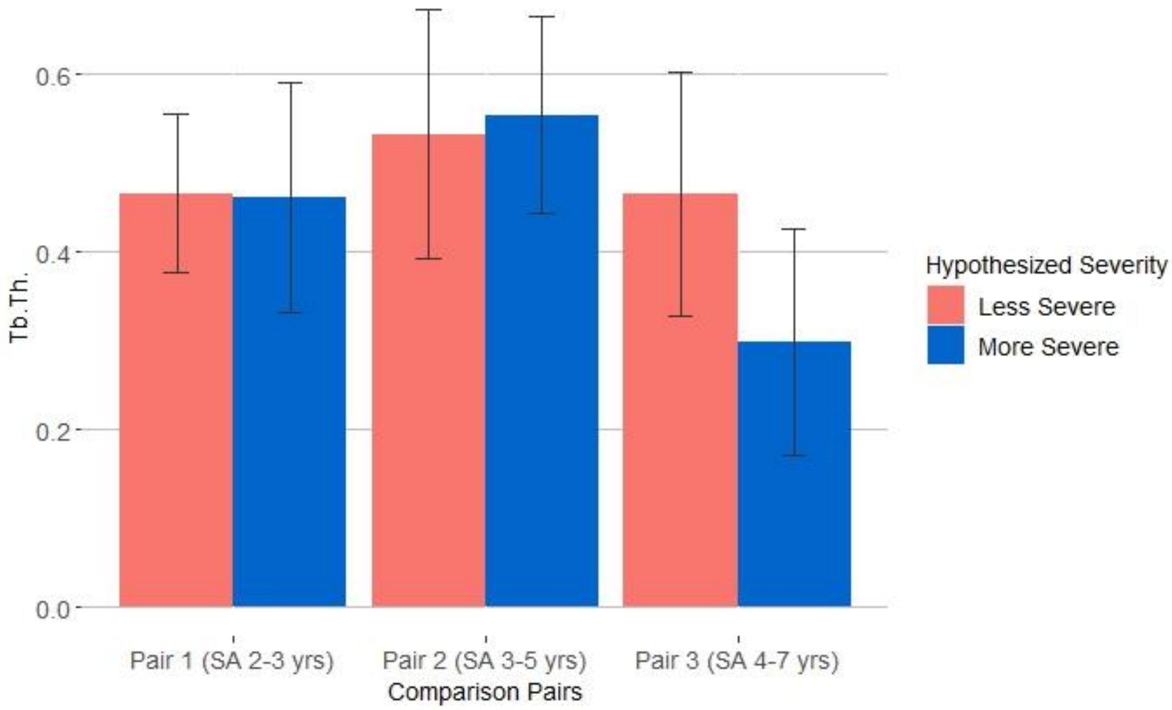

Figure 6.31: Group bar plot for Tb.Th. by comparison pairs of affected femora with lesions hypothesized to be less severe and more severe (error bars represent SD).

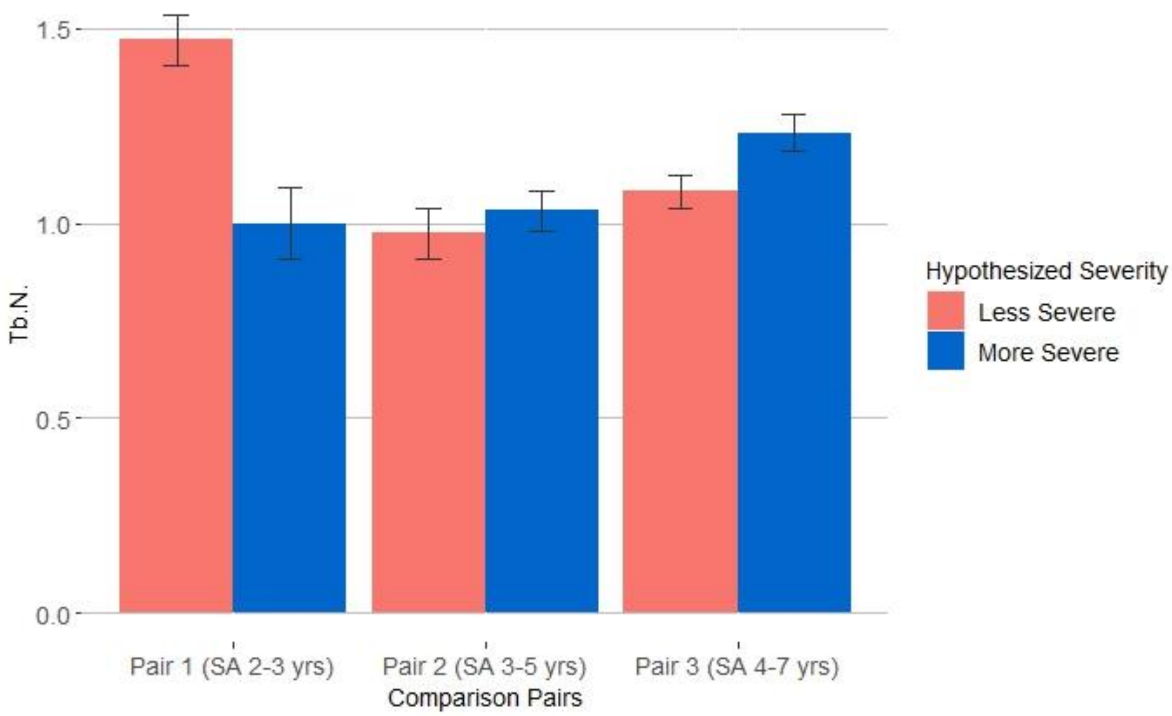

Figure 6.32: Group bar plot for Tb.N. by comparison pairs of affected femora with lesions hypothesized to be less severe and more severe (error bars represent SD).

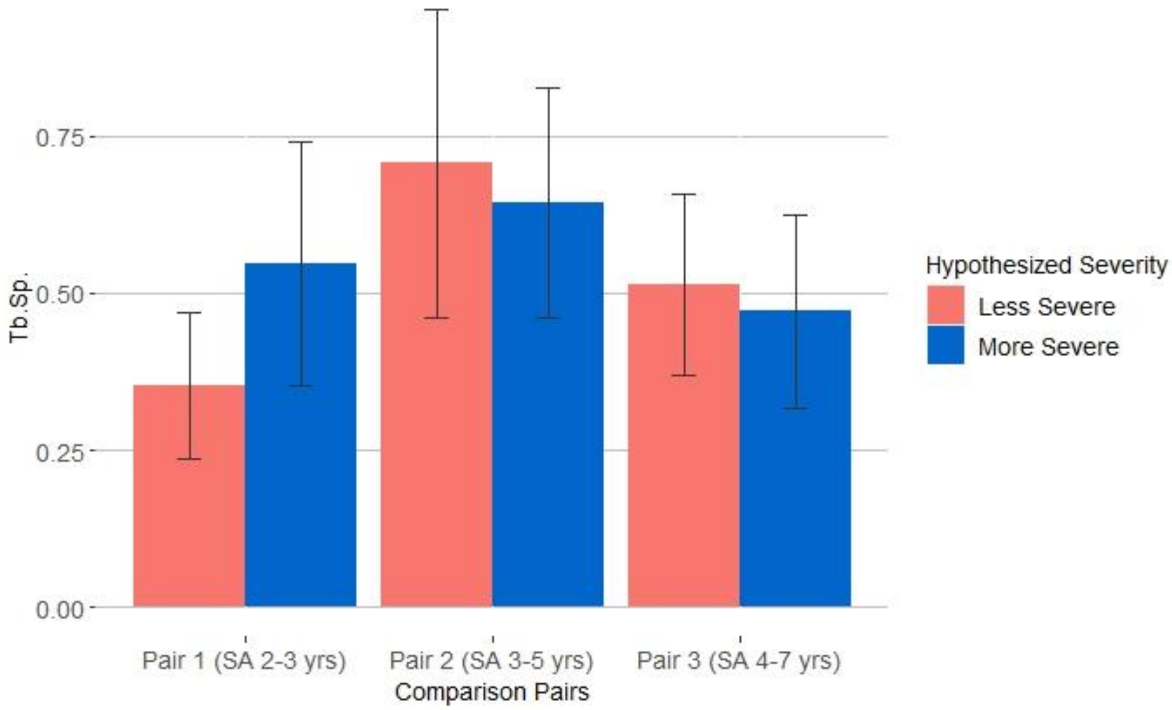

Figure 6.33: Group bar plot for Tb.Sp. by comparison pairs of affected femora with lesions hypothesized to be less severe and more severe (error bars represent SD).

CHAPTER SEVEN: DISCUSSION AND CONCLUSIONS

In this chapter, the results of the data analyses presented in the previous chapter are interpreted and concluding thoughts are provided at the end. The first section discusses the results regarding the hypothesized prevalence of malaria at Mis Island within the larger context of the medieval period. The estimated dynamics of malaria at Mis Island during the medieval period are then discussed from comparing cemeteries 3-J-10 and 3-J-11, and comparing sex and age cohorts. The second section interprets the results on the skeletal lesions of interest in this dissertation. The suite of five skeletal lesions used to study the presence of malaria are first discussed, followed by the macroscopic and microscopic findings on femoral cribra.

Hypothesized malaria at Mis Island

The results of the five skeletal lesions' frequencies and the application of Smith-Guzmán's (2015a) algorithm support the presence of malaria at Mis Island during the medieval period and suggest a relatively high prevalence of the disease. In comparing the frequencies of skeletal lesions between Mis Island and those reported by Smith-Guzmán (2015a) from the other two samples—one endemic for malaria and the other malaria-free—the Mis Island sample was closer to the sample endemic for malaria. The frequencies of these lesions in the Mis Island sample were not only more similar to those of the sample endemic for malaria (Smith-Guzmán, 2015a), but rather exceeded the endemic sample for all lesions except spinal porosity, which was intermediate between the other two samples. Of particular note was the comparison between the samples for femoral cribra, in which the frequency observed at Mis Island was almost twice as much as that reported for the sample endemic for malaria. This finding supports the potential presence of malaria at Mis Island, especially as there were no cases of femoral cribra reported by Smith-Guzmán (2015a) in the malaria-free sample.

In applying Smith-Guzmán's (2015a) algorithm to investigate the potential presence of malaria for each individual, 75%, or conservatively 78%, of the scorable individuals met the algorithmic criteria for malaria and therefore had possibly been infected with the disease. This high estimate for potential malarial infection in the sample supports its presence at Mis Island during the medieval period and suggests that these individuals interred in the site's cemeteries may have been substantially impacted by the disease. The frequency of individuals demonstrating signs of potential infection are especially prominent when compared to the frequencies reported for the sites of Tombos (~1400–650 BCE) located at the Third Cataract in Upper Nubia (Buzon and Sanders, 2016) and the South Tombs Cemetery (1349–1332 BCE) at Amarna, Egypt (Smith-Guzmán et al., 2016). When compared with Mis Island, the closest reported frequency from the other sites was associated with the skeletal remains dating to the Third Intermediate and Napatan periods at Tombos (48% or 56%), followed by the South Tombs Cemetery at Amarna (50%), and lastly the skeletal remains dating to the New Kingdom from Tombos (30% or 35%). The comparatively lower frequencies of individuals demonstrating signs of possible malarial infection from Tombos and the South Tombs Cemetery could indicate that these communities experienced a lower prevalence of malaria. Alternatively, these results could reflect a higher prevalence of malaria, but more individuals who did not survive long enough for skeletal lesions to develop as compared to Mis Island. The higher frequency of individuals displaying skeletal lesions hypothesized to be associated with malarial infection at Mis Island, however, could be interpreted as a high prevalence of malaria with more continuous transmission that could result in elevated cases of estimated chronic malaria. This difference therefore may reflect the conditions believed to have been particularly conducive to mosquito vector populations in the region during the medieval period associated with the introduction and expansion of *saqia* irrigation.

The timing of *saqia* irrigation's introduction in ancient Nubia has been a topic of some disagreement, with propositions estimating its presence in Nubia around the 3^{rd} century CE during the Meroitic period (Fuller and Lucas, 2020) and others suggesting its arrival later during the early post-Meroitic period (Edwards, 2004). Despite this discrepancy, the spread and subsequent intensification of this agricultural technology in Nubia is considered a primary factor in the restructuring of subsistence systems and population patterns in the post-Meroitic period (Fuller and Lucas, 2020). Indication of *saqia* waterwheel irrigation at Mis Island during the medieval period is supported by remnants of the *qadus* jar uncovered at the medieval settlement 3-J-19 on Mis Island (Thomas, 2008). Additional evidence of *saqia* irrigation in the area is associated with a potentially earlier date from the large Meroitic site adjacent to Mis Island at Umm Muri, where numerous fragments of *qadus* were excavated (Ahmed, 2014). With a relative lack of *seluka* land present along the Nile, the adoption of *saqia* irrigation fostered agricultural shifts with year-round cultivation, new crops, and more reliable food resources (Edwards, 2004). These changes allowed for a growth in population and territorial settlement, as well as an expansion of arable land (Edwards, 2004; Fuller and Lucas, 2020; Welsby, 2002); however, this anthropogenic influence may have affected dynamics with mosquitoes as malarial vectors.

The intensification of *saqia* irrigation leading into and during the medieval period is cited as a primary factor in settlement growth around the Fourth Cataract region which in turn, is suggested to have increased mosquito vector populations and concomitantly malarial risk. In the Fourth Cataract region, the totality of the uncovered Kushite material culture indicates a relatively isolated rural society during the Napatan and Meroitic periods (Ahmed, 2014).

However, the Middle Nile Valley witnessed a substantial expansion of settlements and population between 375–1500 CE. Settlement patterns intensified in the Fourth Cataract region and adjacent western Abu Hamed Reach in the post-Meroitic and medieval periods (Malcolm et al., 2007) and rural settlements increased along the Dongola Reach during the 6th century CE (Obłuski, 2020). This growth in population and settlement density is largely attributed to the more extensive implementation of *saqia* irrigation, which allowed for expansion of agricultural activity in areas previously less inhabited and during extended periods of time (Malcolm et al., 2007; Obłuski, 2020). However, these settlement patterns may have contributed to a context in which mosquito populations and malarial transmission could be more supported (Malcolm et al., 2007), as compared to areas of particularly low population density in which the lack of people may not support or sustain transmission (Tatem et al., 2008).

In addition to changes in settlement patterns and human population density, the implementation of *saqia* irrigation may have further supported mosquito vector populations by providing more artificial breeding sites. The use of *saqia* irrigation is thought to have resulted in an agricultural revolution in Nubia during the post-Meroitic and early medieval periods, in which the amount of arable land increased and year-round cultivation could be maintained (Edwards, 2004; Welsby, 2002). The *saqia* waterwheels enabled irrigation of water from the Nile into more elevated areas inland, whereas previously most of the cultivatable land would have likely included the flooded *seluka* areas potentially accompanied by hand-watering methods and/or the *shaduf* tool that lifts water from the source (Dalton et al., 2023). However, the increase in the amount and duration of irrigated land may have provided additional breeding sites for mosquito vectors beyond the river's edge and the naturally available *seluka* land. Irrigation canals and associated artificial sources of water involved in agriculture provide additional breeding sites for mosquito vectors (Coates and Redding-Coates, 1981), which can support their population and promote their proliferation (Fuller et al., 2012). Observations of such artificial water sources in regions around the Fourth and Third cataracts have revealed that *An. arabiensis* vectors use these breeding sites especially during the months when the river levels are high, and therefore provide suitable breeding opportunities located further from the river's disruption (Ageep et al., 2009; Dukeen and Omer, 1986).

The communities associated with the more urban sites of Tombos and the South Tombs Cemetery at Amarna predate the estimated implementation of *saqia* irrigation in ancient Nubia and Egypt, and thus may not have experienced the extent of influences for malarial risk hypothesized to have accompanied this agricultural technology. Occupation of Tombos at the Third Cataract occurred before the estimated introduction of *saqia* irrigation in Nubia and Napatan agriculture was likely similar to Middle Kingdom and New Kingdom Egyptian occupations in Nubia (Fuller and Lucas, 2020). Additionally, while settlement during the Napatan period was focused along the Dongola Reach with centers around Tabo and Kawa south of the Third Cataract (Edwards, 2004), the Napatan settlement patterns below the Third Cataract in the Dongola Reach were relatively isolated and likely were not as conducive to mosquito populations (Malcolm et al., 2007). In ancient Egypt, the *saqia* waterwheel is believed to have been introduced during the second century BCE and the hydraulic noria is thought to have appeared by the fourth century BCE (Elmesery, 2020), both of which occurred after the period associated with the South Tombs Cemetery.

The closer frequency of estimated malarial infection from Tombos during the Third Intermediate/Napatan periods and the South Tombs Cemetery with the Mis Island sample compared that of the skeletal remains from Tombos during the New Kingdom may be associated with differences in habitual activities and inferred social status. Recent interpretations of Tombos during the New Kingdom suggest its establishment as an Egyptian fortress during the New Kingdom occupation with both Egyptian and local Nubian inhabitants (Gibbon and Buzon, 2018). Analyses of inferred activity levels at Tombos have been interpreted as indication that the New Kingdom inhabitants may have included more administrative workers, whereas comparatively higher activity levels hypothesized for the local inhabitants during the Third Intermediate/Napatan period are attributed in part to heightened agricultural activity (Gibbon and Buzon, 2018). Interpretations of the skeletal remains from the South Tombs Cemetery have suggested the individuals interred in this non-elite cemetery experienced relatively high levels of physical activity (Kemp et al., 2013). These heightened amounts of activity in the two samples may have been associated with more exposure to mosquito breeding sites and thus, potentially influenced the higher frequencies of estimated malaria that were closer to that observed from the Mis Island sample.

Comparing cemeteries 3-J-10 and 3-J-11

The comparable frequencies of individuals demonstrating signs of potential malarial infection from cemeteries 3-J-10 and 3-J-11 suggest similar exposure to the disease between these cemetery groups at Mis Island. Overall, the estimates of hypothesized malaria were similarly elevated between cemeteries 3-J-10 and 3-J-11 at 71% and 77%, respectively. As cemetery 3-J-10 reflects burials from the late medieval period (~1100–1500 CE) and cemetery 3-J-11 represents burials spanning pre-medieval to late medieval years (~300–1400 CE), these results suggest that there may not have been substantial differences in risk of infection between the duration of the medieval period and the late medieval period. Upon closer examination, equivalent frequencies were observed when each age cohort from one cemetery was compared to the corresponding age group in the other cemetery. When individuals associated with estimated biological sex were compared between cemeteries, no significant difference was found in comparing males from cemetery 3-J-10 and males from cemetery 3-J-11 and the frequencies of hypothesized malaria were nearly identical. The comparison between females from cemetery 3-J-10 and females from cemetery 3-J-11 revealed a higher frequency observed among females from cemetery 3-J-11; however, this difference was not statistically significant despite approaching significance. One factor that could have influenced this outcome was the difference in subsample sizes, as there were fewer individuals from cemetery 3-J-10 available for analysis and therefore could be underrepresented in the comparisons between cemeteries.

In comparing the five skeletal lesions between cemeteries 3-J-10 and 3-J-11, significantly higher frequencies of cribra orbitalia and spinal porosity were observed in cemetery 3-J-11 which suggests potentially higher stress and/or more chronic pathological insult experienced by these individuals. For cribra orbitalia, higher frequencies were observed across age groups of individuals from cemetery 3-J-11 compared to 3-J-10, which parallels Hurst's (2013) finding of significantly higher prevalence of cribra orbitalia among subadult individuals from cemetery 3-J-11. While the skeletal lesions studied by Hurst (2013) other than cribra orbitalia were not statistically significant between subadults from both cemeteries, Hurst also observed an overall greater prevalences of other skeletal stress indicators in cemetery 3-J-11. In the current research, differences in the prevalence of spinal porosity between the cemeteries were most pronounced in the adult age groups. When individuals with a biological sex estimate were compared, both males and females from cemetery 3-J-11 demonstrated significantly higher frequencies of spinal porosity than males and females from cemetery 3-J-10, respectively. As was found in a subsequent analysis for Research Question 4, spinal porosity was observed at peak frequencies in the adolescent and young adult age groups which may suggest a relatively longer formation compared to the other porous lesions, or a later onset of formation in response to the health insult. The higher frequency of spinal porosity among the adults in particular from cemetery 3-J-11 may indicate greater pathological insult experienced either during younger ages that manifested in the skeleton over time in those individuals who survived, or during more recent adolescent or adult ages.

While changes in the Nile River's levels during the medieval period may not have affected estimated prevalence of malarial infection visible in the skeletal remains as hypothesized, these environmental changes may have contributed to the higher prevalence of these lesions in cemetery 3-J-11. During the late medieval period, levels of the Nile River are thought to have been relatively high, with particularly prominent floods between approximately 1300 and 1522 CE (Edwards, 2004; Malcolm et al., 2007). However, prior to this time, particularly low levels of the Nile are thought to have been present between 828–837 CE and again between 939–948 CE (Edwards, 2004). In noting how low levels of the Nile River and drought could have deleterious effects on cultivation and subsistence, Hurst suggests that some portion of cemetery 3-J-11 may represent elevated amounts of morbidity and mortality from such times of hardship. Given malaria's synergistic relationship with other pathologies (White, 2018), the combined results of the inter-cemetery comparisons may reflect the effects of comorbidities and their interactions on an individual's health. Such co-occurrence of harmful health factors may have contributed to the higher frequency of estimated malaria among females from cemetery 3-J-11, although not statistically significant, as malaria poses a particular risk to pregnant women who are in an immunosuppressed state (Carter and Mendis, 2002).

Comparing sex and age cohorts

The results of comparing the prevalence of hypothesized malaria between males and females, overall and by age group, indicate that there may not have been a substantial difference in exposure to mosquito vectors based on sex at Mis Island during the medieval period. While the frequency of estimated malarial infection was slightly higher in females compared to males, the prevalences were similarly elevated and no statistically significant difference was found. Therefore, these findings suggest a lack of differential proximity to mosquito vectors and their habitat between males and females at Mis Island that could have markedly influenced malarial risk.

A similar exposure to malaria between males and females is further supported by the absence of statistically significant differences for the majority of the skeletal lesions examined; however, a significantly higher frequency of femoral cribra was observed in the female group, albeit a weak relationship. The prevalence of femoral cribra was greater across age groups for females compared to males, but the larger subsample size of observable femora among female individuals may have influenced this result. While some previous studies investigating this lesion have not found this relationship (Schats, 2021; Smith-Guzmán, 2015a), Radi and colleagues (2013) also observed a significantly higher prevalence of femoral cribra among females compared to males in their 20th century skeletal sample from a cemetery in Bologna, Italy. The higher amount of femoral cribra in females may indicate differential stress experienced earlier in life, although Soler (2012) observed comparably elevated levels of non-specific skeletal indicators between males and females. Interpretation of this difference between males and females for the single lesion therefore is difficult beyond acknowledged sample size differences. However, this pattern for femoral cribra could be related to the immunosuppression experienced by women during pregnancy (Carter and Mendis, 2002) or possibly differences were present that could have affected the remodeling process of the lesion leading to a more sustained expression.

The statistically significant age-related pattern of prevalence of hypothesized malaria indicates an elevated level of chronic condition rather than acute status. An overall trend was found in the frequency of estimated malaria that increased with age to the adolescent age group, followed by a high prevalence in the young adult cohort, and decreased with age in the middle and older adult age groups. Additionally, the frequencies across age groups were high with the child, adolescent, and young adult cohorts over 80% and the infant, middle adult, and older adult groups over 50%. These results may reflect a greater prevalence of malarial infection in younger age groups with comparatively less prevalence in older age groups and/or some degree of lesion remodeling in those individuals who survived into adulthood.

This pattern across the age cohorts is potentially suggestive of a high prevalence of more chronic malaria in which some degree of immunity was likely acquired with age or duration of contact. Visible skeletal lesions implicated in malarial infection are likely more indicative of chronic rather than acute conditions, as some time would presumably be involved for skeletal signs to manifest (Wood et al., 1992) and chronic malaria is associated with increased marrow cellularity and erythroid hyperplasia (Wickramasinghe and Abdalla, 2000). Therefore, individuals with these lesions may represent those who survived for a variable amount of time and thus likely developed some degree of immunity. Repeated exposure to malaria can induce partial immunity that can decrease symptomatic expressions, although still involve carrying of the parasite (Ratti and Wallace, 2020; Tumwiine et al., 2007). This acquired immunity, however, can fluctuate and disappear without recurrent exposure (Ratti and Wallace, 2020; Tumwiine et al., 2007) and thus, is associated with age of the individual. Newborn infants whose mothers obtained some acquired immunity inherit a degree of protection for approximately six months, after which time they become susceptible to infection and build their own immune defense to infections (Ratti and Wallace, 2020). While acquired antimalarial immunity is less likely during the youngest ages, older children and adults may be more able to develop such immunity (Carter and Mendis, 2002). With repeated exposure, adult individuals can also develop a protection that suppresses the parasite, which can take about one or two decades to build and could be slowly lost with breaks in exposure (Ratti and Wallace, 2020). Achieving and maintaining some degree of acquired antimalarial protection, however, depends on the endemicity of malaria and the regularity of exposure.

The pattern and frequencies of estimated malaria across age groups suggests a primarily endemic type of malaria at Mis Island during the medieval period rather than strictly epidemic malaria. Epidemic malaria takes place in non-endemic areas that typically have no or minimal transmission and involve an increase in transmission with "low or absent" protective immunity in all age groups (Carter and Mendis, 2002:567). Individuals experiencing epidemic malaria may therefore be less likely to survive before skeletal indication of malaria could manifest, whereas individuals in areas of endemic malaria would be more likely to experience chronic anemia that might be visible in the skeleton (Smith-Guzmán et al., 2016). Given the high frequency of individuals displaying signs of possible infection and skeletal lesions across the cohorts at Mis Island, the primary type of endemicity is unlikely to be epidemic.

Endemic malaria can further be classified as stable or unstable. In stable malaria, immunity is high in older individuals as the continuous effects of malaria may lead to sustained immunity, whereas in unstable malaria immunity is inconstant in older individuals as fluctuations in transmission can interrupt acquired antimalarial protection (Carter and Mendis, 2002). A lack of insight into the severity and activity of all five skeletal lesions at this time limits conclusive considerations on the possible onset and chronic status that might be associated with relative immunity. However, the high frequency of middle and older adult individuals displaying signs of possible malarial infection may reflect periods of unreliable immunity status associated with unstable endemic malaria.

Skeletal lesions implicated in hypothesized malaria

Association between skeletal lesions and age

In the Mis Island skeletal sample, cribra orbitalia, humeral cribra, femoral cribra, and spinal porosity were significantly associated with age of the individual with generally greater prevalences in the younger age groups. The highest frequencies of cribra orbitalia were observed in the infant, child, and adolescent cohorts, with similar prevalences across the three groups, and the lowest frequencies were seen in the adult age groups. Rather than demonstrating a heightened prevalence in the infant age group, frequencies of humeral and femoral cribra increased to peak prevalences in the child and adolescent groups and were then lower in the adult age groups. This distribution of lesion prevalence across age groups is similar to that observed by Schats (2021) in skeletal remains from the medieval/early modern Netherlands (800–1600 CE). For cribra orbitalia, humeral cribra, and femoral cribra, Schats (2021) reports frequencies reaching a peak in the child age group (4–12 years) with slightly lower prevalence in the adolescent (13–19 years) age group. The similarities in age distribution for these lesions between the samples may reflect a common tendency for them to form during childhood and subsequently persist into adulthood. In the Mis Island sample, the age distribution of spinal porosity demonstrated a different pattern with increasing frequencies reaching peak prevalence in the adolescent age cohort, followed by the young adult group, and decreasing frequencies in the middle and older adult groups. Compared to the other porous lesions, this finding may tentatively indicate a longer period of formation for spinal porosity or a later onset.

The association between the porous lesions and age of the individual, and the distribution of the lesions across age groups, are consistent with the hypothesis that their formation may be related to anemia. In anemia, skeletal lesions are thought to primarily result from red bone marrow expansion in order to promote red blood cell production (Brickley, 2018). Given the changes in red marrow distribution with age, the presence of skeletal lesions resulting from anemia are considered to represent formation during younger ages when red marrow is present, and only in regions where red or mixed marrow remains. Marrow throughout the skeleton is red in infancy but progressively converts to yellow marrow, such that the adult pattern of distribution is obtained by 25 years old and red marrow generally remains in the skull, vertebrae, sternum and ribs, pelvis, and proximal humeri and femora (Kricun, 1985). Based on the pattern observed in the Mis Island skeletal sample, the porous lesions may have formed during younger ages when red marrow was still present and thus could have resulted from anemia. The age distribution of spinal porosity peaking in adolescent and young adult ages, rather than the younger age groups as demonstrated by the cribrous lesions, may be associated with the relative extents of red marrow with increasing age. Larger amounts of red marrow persist in the vertebrae into adulthood and are therefore sites in which hyperplasia may be more likely to occur in adult individuals with anemia (Brickley et al., 2020).

If these porous lesions tend to form during younger ages, the presence of the lesions observed in adult individuals could represent their persistence over time from continued chronic insult or incomplete resorption. The relatively lower prevalence of these lesions in adult individuals may be due to remodeling of previous lesions such that they are obscured in older ages. Additionally, the lower prevalence of the lesions in adult age groups could be associated with nonsurvival of individuals during childhood.

While the four porous lesions were significantly associated with age, periosteal reaction did not demonstrate a significant relationship with age of the individual. Instead, this lesion was observed at a relatively consistent prevalence across age groups with the highest frequency in the infant cohort. Hurst (2013) observed varying patterns of lesion activity for periosteal reaction between age groups at Mis Island and suggests that in this population, periosteal reaction may be more related to individual circumstances rather than an overarching experience. Therefore, rather than a close association with biological variables tied to age (e.g., red marrow distribution), the results reflect that periosteal reaction can be the result of multiple factors that result in disturbance of the periosteum (e.g., infection and trauma).

Association among skeletal lesions

In examining the association between pairs of the five lesions of interest in all individuals regardless of age, significant associations were observed primarily among the porous lesions; however, these patterns were influenced by age. When the relationships between lesions were examined separately in subadult and adult groups, significant associations were found between pairs of lesions among subadults, but no significant associations were observed among adults. This finding supports the previous discussion on the connection between age of the individual and lesion expression.

For the three cribrous lesions implicated in the "cribrous syndrome", significant associations were observed between each pair of cribrous lesion (CO-HC, CO-FC, HC-FC) when all individuals regardless of age were examined. The investigation into patterns among these lesions in subadult individuals also revealed significant associations between the pairs of cribrous lesion, except between cribra orbitalia and humeral cribra. The frequency of the three cribrous lesions co-occurring in the Mis Island sample is higher compared to other studies. While 27% of the individuals scorable for all three lesions at Mis Island displayed the combination of lesions, a frequency of 4.9% was observed by Schats (2021) in a sample of subadults and adults from the medieval/early modern Netherlands (800–1600 CE). When the simultaneous presence of the three lesions is examined in subadults only, Mis Island also demonstrates elevated prevalence with 44% compared to 33.3% observed by Djuric and colleagues (2008) and 13.2% reported by Schats (2021). Additionally, while significant associations were found between cribra orbitalia and the postcranial cribrous lesions in the Mis Island sample, no significant association between cribra orbitalia and humeral and femoral cribra was found by Smith-Guzmán (2015a) in the endemic malaria sample, or by Schats (2021) in the sample from the medieval/early modern Netherlands.

The significant associations found between cribra orbitalia and the postcranial cribrous lesions in the Mis Island sample, not observed in previous studies, could be due to various factors. Given the high frequencies of cribra orbitalia and femoral cribra in the Mis Island sample, the significant associations could be an artifact of the greater likelihood for co-occurrence when the prevalence of one lesion is high. Regarding possible etiology, the associations may reflect shared pathological processes and origins including anemia. Alternatively, some proportion of cribra orbitalia may be due to different processes that were simultaneous with the those producing the postcranial cribrous lesions. This possibility is based on previous studies that did not find significant associations between the lesions and the non-specific characterization of cribra orbitalia which has been attributed to multiple conditions. In the Mis Island sample, Hurst (2013:230) observed a “relatively common occurrence” of scurvy in subadults and a significant association between skeletal indication of scurvy and cribra orbitalia. In an effort to avoid inclusion of cribra orbitalia more likely associated with scurvy in the current study, cribra orbitalia was scored as present when there was perforation through the cortical bone and a lack of subperiosteal new bone formation (Smith-Guzmán et al., 2018). However, cribra orbitalia matching that description and possibly resulting from processes other than marrow hyperplasia may account for some cases. With malaria and its concomitant anemia as a posited etiology for the porous lesions observed at Mis Island, comorbidities may be possible as malarial infection has a synergistic relationship with other conditions and pathologies (White, 2018).

In addition to the current research, previous studies have found significant associations between humeral cribra and femoral cribra, including in Smith-Guzmán's (2015a) malaria endemic sample and Schats's (2021) sample of subadult remains from the medieval/early modern Netherlands. Furthermore, Schats (2021:87) observes that "cribra humeri does not occur without cribra femora being present", which was a pattern also found by Garcia and colleagues (2002) who observed 100% association between humeral cribra and femoral cribra in skeletal remains from a Late Roman (3rd–5th centuries CE) necropolis in Tarragona, Spain. A similar relationship between humeral cribra and femoral cribra was observed in the Mis Island sample, in that of the individuals with humeral cribra who could also be scored for femoral cribra (n=91), 95% displayed both lesions. These findings suggest that humeral cribra may be unlikely to form in isolation without the simultaneous presence of femoral cribra. Therefore, humeral cribra may form during a shared etiology and process in the formation of femoral cribra. The appearance of femoral cribra without humeral cribra could be related to the potential for thinner cortical bone thickness in the femoral neck as observed in adults (Schats, 2021).

The significant associations found between the two postcranial cribrous lesions and spinal porosity (HC-SP and FC-SP) suggest that they are involved in a similar etiological response. This result was observed when all individuals were analyzed and when subadults were assessed separately but was not observed in the adult cohort. Therefore, a possible common etiology is likely age-related. These findings support a shared process of formation during younger ages which is consistent with the hypothesis that anemia might be a cause.

Periosteal reaction demonstrated a significant association with humeral cribra (PR-HC) when examined in all individuals combined, and with femoral cribra and spinal porosity (PR-FC and PR-SP) when these pairings were investigated in subadults only. However, the association between periosteal reaction and these porous lesions was an inverse relationship. This result is contrary to Smith-Guzmán's findings from the malaria endemic sample, in which the presence of periosteal reaction was found to be associated with femoral cribra and spinal porosity (2015a). Smith-Guzmán interpreted these results as suggestion that the three lesions could be part of "the same inflammatory response" (2015a:629). Therefore, instances of periosteal reaction in the Mis Island sample may represent various etiological responses in addition to the hypothesized malarial infection.

Femoral cribra

Indicators suggestive of lesion activity

Observations of estimated lesion activity from the external surface of femoral cribra resulted in an age-related pattern consistent with the expected outcomes for "active" and "healed" lesion status. To investigate signs of lesion activity, this research used an approach based on Mensforth and colleagues' (1978) method for porotic hyperostosis in which femoral cribra displaying sharp edges was estimated as "active" and femoral cribra presenting smooth-edged bone was hypothesized to be "healing". The significant association found between age of the individual and estimated activity of femoral cribra, in which signs of "healing" increased with age, supports the proposition that these features of femoral cribra are indicative of the lesion's activity. The results from the current research are similar to those reported by Mangas-Carrasco and López-Costas (2021) who also observed a healing pattern of femoral cribra with age. Using a scoring system of active, mixed, or inactive based on the lesion's degree of expression, Mangas-Carrasco and López-Costas found that signs attributed to healing increased with age in remains excavated from late medieval archaeological sites in NW Spain. Additionally, the results of lesion size for "active" and "healing" femoral cribra observed in each age group revealed clustering of relatively larger lesions in the juvenile and adolescent cohorts with primarily active-looking lesions compared to the more varied sizes of primarily healing lesions in the adult cohorts. These findings support the anticipated age-related pattern of the lesion's formation and progression.

With origins considered to be primarily pathological in nature, the higher prevalence of more active-looking femoral cribra in younger individuals could reflect the expectation that subadults represent more "frail" individuals who did not survive health insults. Conversely, the greater frequency of femoral cribra that appears healing in the adult age groups could represent those individuals who survived prior stress and experienced some degree of recovery. This pattern is also consistent with the proposed etiology of anemia, in that femoral cribra may tend to form during younger ages and therefore appear active in subadult individuals and demonstrate signs of healing over time with increasing age and survivorship. However, the cases of femoral cribra in adult individuals that appear active could reflect the retainment of red bone marrow in the proximal femur into adulthood (Kricun, 1985). Additionally, active-looking femoral cribra in older adult cohorts could represent the potential for reconversion of yellow marrow into red marrow during conditions such as chronic anemia—especially hemolytic anemia—in response to a need for heightened hematopoiesis (Kricun, 1985). While the results of lesion activity indicators from femoral cribra's external surface are consistent with expectations of "active" and "healing" states, an examination of the quantitative measures reflecting the underlying bony structure contributes to these findings.

The results of the trabecular microarchitecture variables derived from micro-CT scans of unaffected individuals and affected individuals with varying degrees of activity support indications of the lesion being active or healing observed on the surface. In comparing unaffected femora with femora thought to have "active" lesions, the "active" lesions within the comparison pairs demonstrated the following pattern: all had lower values for bone volume density (BV/TV), most had higher values for specific bone surface (BS/BV), most had higher values for trabecular thickness (Tb.Th.), most had lower values for trabecular number (Tb.N.), and most had higher values for trabecular spacing (Tb.Sp.). Based on the expected changes to these trabecular variables involved in resorptive, formative, and mixed processes (Morgan, 2014), these active femoral cribra lesions are most consistent with mixed cellular activity. However, when unaffected femora and affected femora with lesions hypothesized to be "healing" based on the external appearance were compared, this pattern was not as consistent. Compared to the unaffected femora, the affected femora with "healing" lesions demonstrated generally similar occurrences of lower and higher values of all trabecular variables except for trabecular thickness (Tb.Th.), which was greater in the "healing" femora compared to the unaffected femora in all but one comparison pair. This lack of an overall pattern could reflect various stages of healing in these affected femora, as the differences in the variables for some pairs were suggestive of more mixed or resorptive processes in the affected femora, while other comparison pairs were indicative of more formative processes in the affected femora. The latter pairs were observed particularly in the adult cohorts and may suggest more advanced healing with age.

The comparisons between the trabecular variables of affected femora with lesions hypothesized to be "active" or "healing" further support the correlation between indications of activity from the external surface with underlying bone processes. A relatively consistent pattern was observed across the comparison pairs in which the "healing" lesions demonstrated the following relative to the "active" lesions: almost all had higher values for bone volume density (BV/TV), all but one had lower values for specific bone surface (BS/BV), all had higher values for trabecular thickness (Tb.Th.), and almost all had lower values for trabecular spacing (Tb.Sp.). Trabecular number (Tb.N.) was the only variable in which the results were divided relatively evenly with the "healing" lesions displaying higher or lower values. Based on the anticipated changes in trabecular variables for the types of bone processes (Morgan, 2014), this trend in the relative differences of trabecular microarchitectural variables suggests that the lesions that appear "healing" on the surface may have undergone more formative processes compared to the lesions that appear "active" on the surface. Qualitative observations of the micro-CT scans between these comparison pairs support the quantitative findings. As reflected in Figure 7.1, the lesion that appears "healing" displays a relatively greater amount of trabecular bone volume, the trabeculae are thicker and appear more numerous in this case, and there is less spacing between the trabeculae.

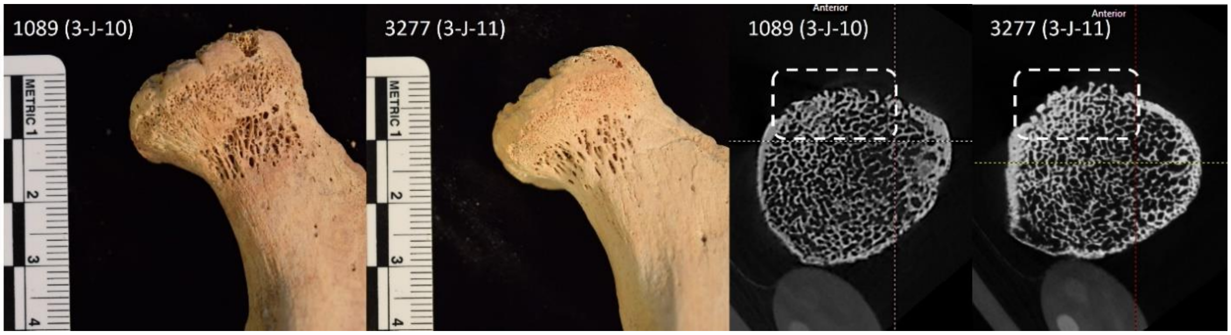

Figure 7.1: External and internal features of a lesion hypothesized to be active (1089) and a lesion hypothesized to be healing (3277) from Comparison Pair 4 (10–15 yrs).

In further investigation of femoral cribra's activity status, the presence of a raised margin adjacent to the area of porosity or exposed trabeculae, referred to as a "cortical window" in the current research, may be consistent with lesion "healing" in the Mis Island skeletal sample. This cortical window was significantly associated with signs of healing in the affected porous area and when present, was observed primarily with lesions estimated to be healing. Additionally, the cortical window was virtually absent in subadult individuals and was observed with increasing frequency with age in the adult individuals. These results support the hypothesis that the cortical window is indicative of a healing process that can occur over time.

While this feature was significantly associated with lesions estimated to be healing, the occurrence of its expression was relatively low. The absence of a cortical window in lesions thought to be healing could be attributed to a potentially faster rate of remodeling and healing processes in trabecular bone compared to cortical bone (Oftadeh et al., 2015; Sandberg and Aspenberg, 2016), such that signs of "healing" in trabecular bone may precede a cortical window in femoral cribra. Although mainly observed in combination with signs of healing from the porous bone or trabeculae, there were several instances in which it was observed with lesions estimated to be active. These cases could be a result of a process impeding porous or trabecular remodeling, reactivity of a previously healing lesion, or a different origin of the cortical window from the proposed cause.

The comparisons of trabecular microarchitecture variables obtained from micro-CT scans involving femoral cribra with cortical windows and estimated to be healing generally support this feature's association with indication of healing activity observed from the surface. When compared to affected femora with active-looking lesions, and to some extent with unaffected femora, most of the femora with cortical windows demonstrated differences in the trabecular measures that were consistent with formative processes. However, one femur with a cortical window did not follow this trend and when compared to its unaffected counterpart (Pair 10), seemed to reflect more resorptive processes. Additionally, when compared to an affected femur with a lesion estimated to be active (Pair 5), the femur with the cortical window estimated to be healing had relatively similar trabecular measures except lower trabecular number (Tb.N.) and greater trabecular spacing (Tb.Sp.). While possible factors behind the results for this particular lesion with the cortical window are currently unclear, this individual may have experienced an especially severe condition, or some contributing factor may have been influencing trabecular bone processes.

In discussing variation in skeletal features of the anterior femoral neck, Göhring (2021) contends that convex porous lesions lacking cortical borders should be considered separate from concave lesions of exposed trabeculae with evident cortical margins. Göhring suggests that the former is "cribra femoris" and is pathological in nature, whereas the latter should be identified as Allen's fossa which Göhring describes as likely caused by "friction of the zona orbicularis" of the hip joint capsule during activity (2021:4). In the current research, instances in which cortical windows were scored as present likely overlap with Göhring's definition of Allen's fossa as a depressed nonmetric trait. Additionally, all cortical windows observed in the Mis Island sample were associated with Radi et al. 2 scores, and therefore displayed trabecular exposure. While the effects of the zona orbicularis on features of the femoral neck are not dismissed in this discussion, this structure's involvement in the expression of cortical windows observed in the studied skeletal remains is currently questioned. The zona orbicularis is a set of curved fibers associated with the hip joint capsule perpendicular to the joint axis at the narrowest part of femoral neck which aid in joint stability and do not attach directly to bone (Tsutsumi et al., 2021; Wagner et al., 2012). The morphology of this structure, however, has been a subject of investigation and uncertainty with some studies finding that it is absent or less prominent anteriorly (Malagelada et al., 2015; Wagner et al., 2012) and may not be part of the "local collar" (Tsutsumi et al., 2021:1163). Therefore, a connection between the zona orbicularis and formation of cortical windows around femoral cribra as defined in the current research is currently unclear. This reservation especially pertains to observed cases of femoral cribra with small, focal windows on the anterior neck, as well as areas of exposed trabeculae with windows that are not isolated to the narrowest section of the femoral neck.

Indicators suggestive of lesion severity

In examining the patterns of femoral cribra's cortical disruption using Radi and colleagues' (2013) scoring system, the results suggest that the lesion's expression as a grouping of pores on the surface (Radi et al. Score 1) may represent a less severe and earlier stage of formation whereas the lesion's appearance with trabecular exposure (Radi et al. Score 2) may reflect a more severe stage. The Radi et al. Score 1 expression of femoral cribra was most frequently observed in the infant cohort and represented almost half of the cases in that age group, whereas this score was seen at lower frequencies in the other age groups. This score also clustered closer to the active lesion status than the healing lesion status in the MCA for left femora. Conversely, the Radi et al. Score 2 expression accounted for most of the lesions observed in the child, adolescent, and adult age groups. Radi and colleagues (2013) did not examine subadult remains in their study and therefore the subadult frequencies observed in the current research cannot be compared. However, a greater prevalence of the Radi et al. Score 1 expression was reported among the adult individuals in Radi and colleagues' research compared to the adult individuals of Mis Island. Therefore, the Radi et al. Score 1 does not seem to be a strictly age-related expression of femoral cribra, but rather may reflect a less severe lesion state.

These indications of femoral cribra's potential severity are further supported by the results of lesion size. Comparing measurements of the lesion—perpendicular and parallel to the femoral neck and perimeter—between the two scores generally revealed smaller dimensions for the Radi et al. Score 1 lesions and larger dimensions for the Radi et al. Score 2 lesions. These differences were most pronounced for the size of lesion perpendicular to the femoral neck and consequently perimeter of the lesion. The trend of Radi et al. Score 2 lesions displaying particularly larger dimensions perpendicular to the neck compared to Radi et al Score 1 lesions, but relatively more similar dimensions parallel to the neck, may tentatively indicate a propensity of femoral cribra to expand perpendicular to the neck in its progression. However, the small subsample size of Radi et al. Score 1 lesions in the current research may not represent potential variation in this measurement.

The comparisons of trabecular microarchitecture variables obtained from micro-CT scans between unaffected femora and affected femora thought to be "less severe" or "more severe" support this finding for the Radi et al. scores. The comparison pairs involving subadult individuals with age-at-death estimates between 2–3 years included the only available example of a lesion assessed as a Radi et al. Score 1 that could fit in the sample sled and be scanned. As a result, the "less severe" lesion in the comparison pairs from this age cohort (subadult 2–3 yrs) represents a lesion assessed as a Radi et al. Score 1 (1352) and the "more severe" lesion was evaluated as a Radi et al. Score 2 (5013) (Figure 7.2). In comparing these affected femora with the unaffected femora from this age group, both the "less severe" (Radi et al. Score 1) and "more severe" (Radi et al. Score 2) lesions demonstrated differences in the trabecular variables that are suggestive of more formative processes. While the "less severe" and "more severe" lesions displayed similar trends compared to the femora without the lesion in this cohort, the differences in the trabecular variables demonstrated by the "less severe" lesion are potentially suggestive of more formative activity compared to the "more severe" lesion (Morgan, 2014). Of these, larger differences in the unaffected vs. "less severe" femoral cribra comparison pairs were noted in the higher bone volume density (BV/TV) and trabecular number (Tb.N.) measures, and the lower trabecular spacing (Tb.Sp.) values.

Furthermore, in comparing these "less severe" (Radi et al. Score 1) and "more severe" (Radi et al. Score 2) lesions, the "more severe" lesion with a Radi et al. Score 2 showed lower bone volume density (BV/TV), specific bone surface (BS/BV), and trabecular number (Tb.N.), similar trabecular thickness (Tb.Th.), and higher trabecular spacing (Tb.Sp.). If femoral cribra lesions displaying a Radi et al. Score 1 reflect a less severe and earlier stage of formation, and lesions with a Radi et al. Score 2 represent greater severity in femoral cribra's progression, the findings from this series of micro-CT scans suggest that at this age formative processes may be involved in the lesion's appearance; however, more resorptive processes may potentially be part of femoral cribra's subsequent expression with exposed trabeculae. This proposed model of processes is visualized in the micro-CT scans (Figure 7.2), in that compared to the lesion with the Radi et al. Score 1 (1352), the lesion with the Radi et al. Score 2 (5013) displays less bone volume density, specific bone surface, trabecular number, and higher trabecular spacing in the area of the lesion. As these comparisons between Radi et al. scores were only attainable for subadult individuals with age-at-death estimates of 2-3 years, further research is required to better understand potential differences.

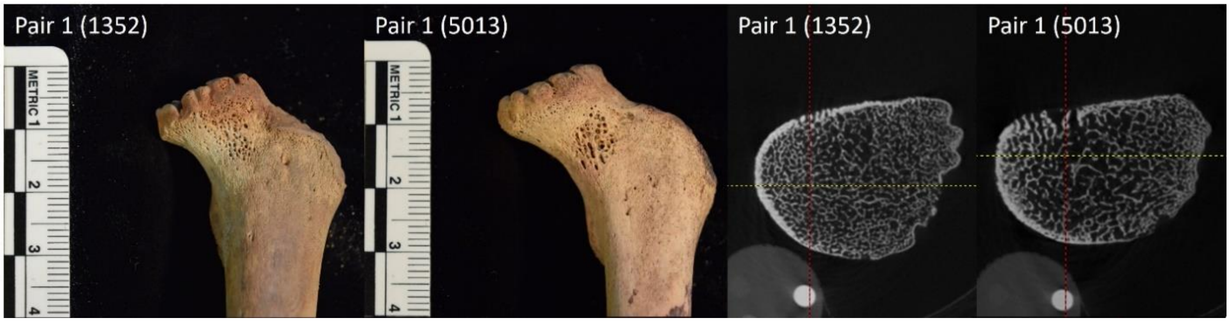

Figure 7.2: External and internal features of a lesion hypothesized to be "less severe" (1352) and a lesion hypothesized to be "more severe" (5013) from Comparison Pair 1 (2–3 yrs).

The comparisons between unaffected femora and femora with lesions that appeared "less severe" or "more severe" for individuals with age-at-death estimates of 3–5 years or 4–7 years included lesions that were all assessed as a Radi et al. Score 2, but displayed different extents of trabecular exposure on the surface. Regardless of estimated severity, the affected femora in these cohorts demonstrated the following compared to the unaffected counterparts: all displayed lower bone volume density (BV/TV), and all but one femur had lower values for trabecular number (Tb.N.) and higher measures of trabecular spacing (Tb.Sp.). The values for specific bone surface (BS/BV) and trabecular thickness (Tb.Th.) varied with no apparent association with the hypothesized severity. The results of these comparisons suggest that the presence of the lesions reflect resorptive or mixed processes; however, no clear pattern between the different estimated lesion severities for these femora compared to the unaffected femora was observed in this subsample.

In comparing these Radi et al. Score 2 lesions hypothesized to be "less severe" or "more severe" based on the degree of trabecular exposure on the surface (Comparison Pairs 2 and 3), the "more severe" lesions displayed lower values of bone volume density (BV/TV) and trabecular spacing (Tb.Sp.), and higher values of specific bone surface (BS/BV) and trabecular number (Tb.N.). The "more severe" lesion in Comparison Pair 3 had a lower trabecular thickness (Tb.Th.) value than the "less severe" lesion in that pair and while the average for the "more severe" lesion in Comparison Pair 2 was slightly higher than the "less severe" lesion, the values were similar. These trabecular differences in the "more severe" looking lesions that demonstrate greater exposure of the trabeculae may represent the simultaneous processes of bone resorption and formation during marrow hyperplasia. As discussed for lesions of the cranium, this process may involve thinning of trabeculae while osteoblastic activity is delegated to restoring the resorbed outer cortical bone with increased number of trabeculae, which can create the "hair-on-end" appearance (Morgan, 2014; Stuart-Macadam, 1987). This interpretation may be supported by visual observations of the "more severe" lesions' micro-CT images (Figure 7.3) which display some radial trabeculation towards the surface lacking cortical bone. These results tentatively suggest that more pronounced differences in the degree of trabecular exposure observed on the surface might reflect various stages of marrow hyperplasia in the lesion's progression of severity. However, further research is required as these interpretations are based on a small number of femora and potential responses during these particular subadult ages.

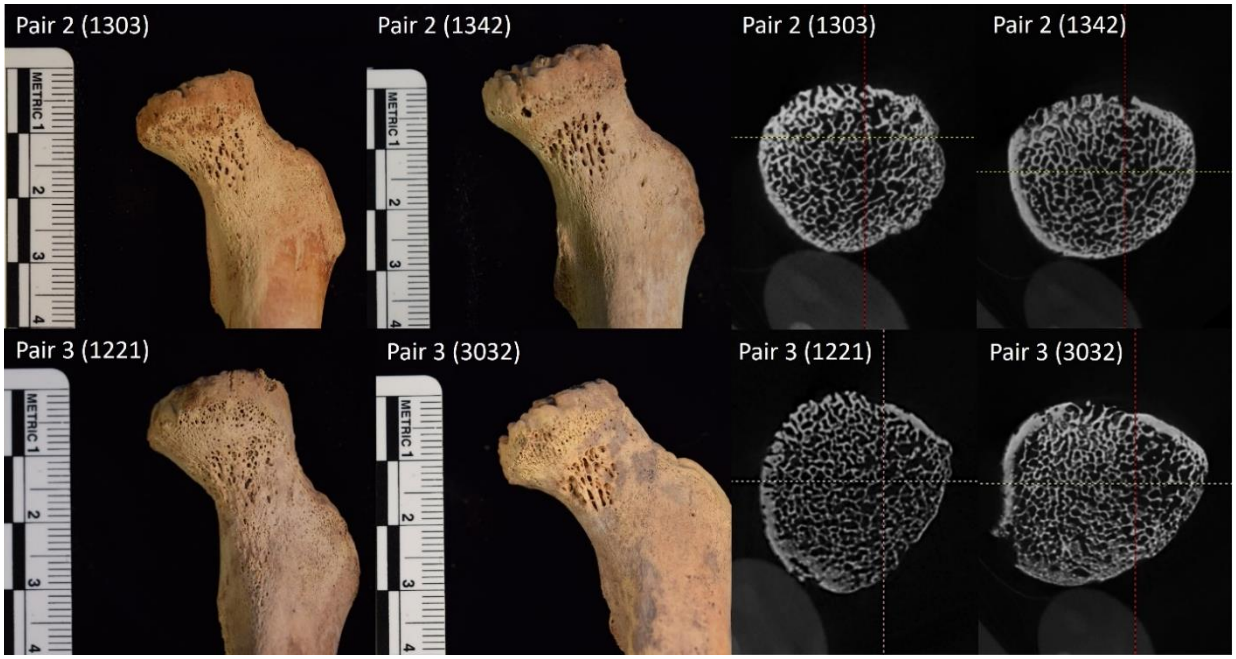

Figure 7.3: External and internal features of lesions hypothesized to be "less severe" (1303 and 1221), and lesions hypothesized to be "more severe" (1342 and 3032) from Comparison Pair 2 (3–5 yrs) and Comparison Pair 3 (4–7 yrs).

Anemia as a possible etiology of femoral cribra

The investigation on the trabecular microarchitecture of femoral cribra yielded insights that support a possible etiology of chronic anemia associated with the lesion. The majority of active-looking femoral cribra lesions examined in this research demonstrated trabecular features that may indicate mixed cellular processes possibly associated with marrow hyperplasia, and resorptive processes. In the cohorts older than the subadult 2–3 years age group, "active" femoral cribra lesions tended to demonstrate lower bone volume density, fewer number of trabeculae, and increased trabecular spacing. The observations from the current study are consistent with Djuric and colleagues' (2008) qualitative findings from histological analyses of subadult femoral cribra lesions. Djuric et al. observed thinned and porous cortical bone, expansion of the intertrabecular space, and extension of trabeculae perpendicular to the surface, which led the researchers to propose chronic anemia as a potential cause of femoral cribra due to marrow expansion. While qualitative observations on the orientation of the trabeculae were not made for every lesion in the current study, such indications are visible in the micro-CT images including those in this chapter.

Conclusions and future research directions

The relatively high estimated prevalence of malaria at Mis Island, particularly in comparison to the sites of Tombos and the South Tombs Cemetery at Amarna, is consistent with the hypothesis of heightened malaria associated with the effects of settlement growth and expansion of irrigated land that accompanied *saqia* irrigation intensification in the medieval period. While a significant difference in estimated malarial infection between cemeteries 3-J-10 and 3-J-11 was not observed, higher prevalences of cribra orbitalia and spinal porosity in cemetery 3-J-11 in the current research parallel Hurst's (2013) findings and contribute to the suggestion of heightened stress prior to the late medieval period possibly associated with lower levels of the Nile River. The investigation into potential dynamics of malaria at Mis Island during the medieval period suggest a seemingly pervasive exposure to malaria shared among the site's inhabitants in the context of endemic malaria.

While the method used in this dissertation research suggests the presence of malarial infection in the skeletal remains, one limitation of the study is that the disease does not produce "pathognomonic lesions in the skeleton" (Schats, 2023:34) and its presence at the Fourth Cataract during the medieval period has not been confirmed. Therefore, future inquiry into malaria in ancient Nubia during the medieval period would benefit from confirmatory testing for the disease in skeletal remains using methods such as aDNA or immunological testing. Additionally, insight into the potential effects of anthropogenic influences on malaria in ancient Nubia would be supplemented by studying the possible prevalence of malaria at other sites. In particular, additional sites from the Meroitic, Post-Meroitic, and medieval periods could provide a more detailed view on malarial dynamics during the time in which *saqia* irrigation is thought to have been introduced and subsequently intensified. Future research on malaria at Mis Island could include testing the association between the skeletal lesions associated with malaria and the skeletal lesions and indicators studied by Soler (2012) and Hurst (2013) for a closer examination of potential co-morbidities.

The association between the porous lesions studied in this dissertation and age of the individual is consistent with a hypothesized etiology of anemia. Furthermore, significant associations among these lesions suggest shared processes involved in their formation. The three cribrous lesions demonstrated associations in the Mis Island sample, although the relationship between cribra orbitalia and the postcranial cribrous lesions may depend on the population. However, as observed in other studies, humeral cribra seems to form from shared processes with femoral cribra. Understandings of this relationship and the process of their formation would benefit from assessing the role of cortical thickness at these lesions' locations. While spinal porosity has not received as much attention as the cribrous lesions, the findings from this dissertation suggest its association with the other porous lesions but may potentially be related to older subadult age groups. Finally, the association between periosteal reaction and the porous lesions may vary between populations and reflect a different response to malarial infection, as well as more varied etiological responses. One limitation in examining the skeletal lesions of interest is the potential for co-existing conditions influencing the expression of these lesions. Future research could focus on closely examining the relationship between lesions suggestive of malaria and those associated with other conditions to better understand the interaction of processes leading to their formation. Finally, while the cribrous lesions have been a focus of recent research, understandings of the five skeletal lesions implicated in malarial infection as a whole would benefit from investigating their patterns in additional skeletal samples from varied contexts, including those involving other types of endemicity for malaria.

The investigation on femoral cribra regarding its potential activity and severity provided preliminary support for interpreting the lesion's status using features from the external surface. Applying Mensforth and colleagues' (1978) approach to lesion activity, the sharp-edged femoral cribra lesions estimated to be active and the smooth-edged femoral cribra lesions estimated to be healing followed the expected age-related pattern that would support these designations. Furthermore, micro-CT analyses of a selected subsample of femora demonstrated trabecular differences that are consistent with the lesions that appear "healing" from the surface to have undergone more formative processes as compared to lesions that look "active". The cortical window observed in the femora from the Mis Island sample may be associated with and accompany "healing" of the porous lesion; however, may not be a sign on which to base an interpretation.

Regarding possible severity of femoral cribra, examination of Radi and colleagues' (2013) scoring system revealed that these scores may represent "less severe" and "more severe" stages in the development of the lesion. In addition to the larger lesion size observed with the higher score, results of the micro-CT analysis tentatively suggests a progression of severity between the two scores that may involve resorptive processes. Furthermore, when lesions scored as a Radi et al. Score 2 with different extents of trabecular exposure were examined, the trabecular differences tentatively suggest varying stages of possible marrow hyperplasia in the score's expression. However, a limitation of the micro-CT research component of this dissertation was the small subsample sizes, as well as a focus solely on subadults with age-at-death estimates between 2–7 years for the investigation into severity.

Therefore, current understandings of femoral cribra would benefit from continued research into its trabecular microarchitecture in a greater number of femora across age groups, as well as from different populations. This line of work would also be aided by the inclusion of additional femora without the lesion, as processes that did not result in alterations on the bone's surface may have still influenced the trabecular bone used in the comparisons. Finally, the micro-CT investigation of femoral cribra was consistent with a possible etiology of anemia and thus potentially associated with the hypothesized malaria in this skeletal sample. Future micro-CT research from other populations could contribute further etiological considerations on femoral cribra, as well as humeral cribra and the association between the two lesions.

LITERATURE CITED

Adams WY. 1964. Post-Pharaonic Nubia in the light of archaeology I. J Egypt Archaeol 50:102–120.

Adams WY. 1965. Post-Pharaonic Nubia in the light of archaeology II. J Egypt Archaeol 50:160–178.

Adams WY. 1966. Post-Pharaonic Nubia in the light of archaeology III. J Egypt Archaeol 50:147–162.

Adams WY. 1974. Sacred and Secular Polities in Ancient Nubia. World Archaeol 6:39–51.

Adams WY. 1991. The United Kingdom of Makuria and Nobadia: A Medieval Nubian Anomaly. In: Davies WV, editor. Egypt and Africa: Nubia from Prehistory to Islam. London: British Museum Press in association with the Egypt Exploration Society. p 257–263.

Adams WY. 1998. Toward a comparative study of Christian Nubian burial practice. Archeologie du Nil Moyen 8:13–41.

Adams WY. 2001. Meinarti II: The Early and Classic Christian Phases. Oxford, England: Archaeopress.

Ageep TB, Cox J, Hassan MM, Knols BGJ, Benedict MQ, Malcolm CA, Babiker A, El Sayed BB. 2009. Spatial and temporal distribution of the malaria mosquito Anopheles arabiensis in northern Sudan: influence of environmental factors and implications for vector control. Malaria Journal 8:123.

Ahmed SM. 2014a. An introduction to the Merowe Dam Archaeological Salvage Project (MDASP). In: Anderson JR, Welsby DA, editors. The Fourth Cataract and Beyond: Proceedings of the 12th International Conference for Nubian Studies. Leuven: Peeters. p 5–8.

Ahmed SM. 2014b. Kushites at the Fourth Cataract. In: Anderson JR, Welsby DA, editors. The Fourth Cataract and Beyond: Proceedings of the 12th International Conference for Nubian Studies. Leuven: Peeters. p 111–118.

Al-Khafif GD, El-Banna R, Khattab N, Rashed TG, Dahesh S. 2018. The immunodetection of non-falciparum malaria in ancient Egyptian bones (Giza Necropolis). BioMed Research International 1–6.

Allen H. 1882. A System of Human Anatomy, Sec. II, Bones and Joints. Philadelphia.

Analyze 14.0 (AnalyzeDirect, Overland Park, KS)

Angel JL. 1964. The reaction area of the femoral neck. Clin Orthop Relat Res 32:130–142.

Angel JL. 1966. Porotic hyperostosis, anemias, malarias and marshes in the prehistoric Eastern Mediterranean. Science (153):760–763.

Aufderheide AC, Rodríguez-Martin C. 1998. The Cambridge Encyclopedia of Human Paleopathology. Cambridge: Cambridge University Press.

Bain BJ, Clark DM, Wilkins BS. Infection and Reactive Changes. 2019. In: Bone Marrow Pathology, Fifth Edition. Hoboken, New Jersey: John Wiley & Sons, Ltd. p 109–184.

Barbour KM. 1961. The Republic of the Sudan: A Regional Geography. London: University of London Press.

Bianucci R, Mattutino G, Lallo R, Charlier P, Jouin-Spriet H, Peluso A, Hingham T, Torre C, Ramino Massa E. 2008. Immunological evidence of Plasmodium falciparum infection in an Egyptian child mummy from the Early Dynastic Period. Journal of Archaeological Science 35:1880–1885.

Blondiaux J, de Broucker A, Colard T, Haque A, Naji S. 2015. Tuberculosis and survival in past populations: A paleo-epidemiological appraisal. Tuberculosis 95:S93–S100.

Brass M. 2015. Interactions and pastoralism along the southern and southeastern frontiers of the Meroitic State, Sudan. J World Prehist 28:255–288.

Brickley M, Ives R. 2006. Skeletal manifestations of infantile scurvy. American Journal of Physical Anthropology 129:163–172.

Brickley MB. 2018. Cribra orbitalia and porotic hyperostosis: A biological approach to diagnosis. American Journal of Physical Anthropology 167:896–902.

Brickley MB, Ives R, Mays S. 2020. The Bioarchaeology of Metabolic Bone Disease. Elsevier.

Buikstra JE, Ubelaker DH. 1994. Standards for Data Collection from Human Skeletal Remains. Fayetteville: Arkansas Archaeological Survey.

Butzer KW. 1976. Early Hydraulic Civilization in Egypt: A Study in Cultural Ecology. Chicago: University of Chicago Press.

Buzon MR, Sanders KS. 2016. Skeletal evidence of malaria at Tombos: disease patterns from the New Kingdom through Napatan Periods in Upper Nubia. Poster session presented at the American Association of Physical Anthropologists, Atlanta, GA.

Carter R, Mendis KN. 2002. Evolutionary and historical aspects of the burden of malaria. Clinical Microbiology Reviews 15(4):564–594.

Coates D, Redding-Coates TA. 1981. Ecological problems associated with irrigation canals in the Sudan with particular reference to the spread of bilharziasis, malaria and aquatic weeds and the ameliorative role of fishes. International Journal of Environmental Studies 16:207–212.

Dalton M, Spencer N, Macklin MG, Woodward, JC, Ryan P. 2023. Three thousand years of river channel engineering in the Nile Valley. Geoarchaeology 38:565–587.

DeWitte SN, and Stojanowski CM. 2015. The Osteological Paradox 20 Years Later: Past Perspectives, Future Directions. Journal of Archaeological Research 23:397–450.

Djuric M, Milovanovic P, Janovic A, Draskovic M, Djukic K, Milenkovic P. 2008. Porotic lesions in immature skeletons from Stara Torina Late Medieval Serbia. International Journal of Osteoarcheology 18:458–75.

Djuric M, Janovic A, Milovanovic P, Djukic K, Milenkovic P, Draskovic M, Roksandic M. 2010. Adolescent health in medieval Serbia: signs of infectious diseases and risk of trauma. Journal of Comparative Human Biology 61:130–149.

Djuric M, Zagorac S, Milovanovic P, Djonic D, Nikolic S, Hahn M, Zivkovic V, Bumbasirevic M, Amling M, Marshall RP. 2013. Enhanced trabecular micro-architecture of the femoral neck in hip osteoarthritis vs. health controls: a micro-computed tomography study in postmenopausal women. International Orthopaedics 37:21–26.

Dukeen MYH, Omer SM. 1986. Ecology of the malaria vector Anopheles arabiensis Patton (Diptera: Culiciadae) by the Nile in northern Sudan. Bulletin of Entomological Research 76:451–467.

Edwards DN. 1994. Post Meroitic (‘X-Group’) and Christian burials at Sesebi, Sudanese Nubia. J Egypt Archaeol 80:159–178.

Edwards DN. 1996. The Archaeology of the Meroitic State: New Perspectives on its Social and Political Organization. Oxford: Tempus Reparatum: Distributed by Hadrian Books.

Edwards DN. 1999. Meroitic Settlement. In: Welsby DA, editor. Recent Research in Kushite History and Archaeology: Proceedings of the 8th International Conference for Meroitic Studies. British Museum Occasional Paper. London: British Museum Press. p 19–67.

Edwards DN. 2001. The Christianisation of Nubia: some archaeological pointers. Sudan & Nubia 5:89–96.

Edwards DN. 2004. The Nubian Past: an archaeology of the Sudan. London, United Kingdom: Routledge.

Edwards DN. 2014. Medieval Nobadia. In: Anderson JR, Welsby DA, editors. The Fourth Cataract and Beyond: Proceedings of the 12th International Conference for Nubian Studies. Leuven; Paris; Wapole, MA: Peeters. p 171–182.

El-Najjar MY, Ryan DJ, Turner CG, and Lozoff B. 1976. The etiology of porotic hyperostosis among the prehistoric and historic Anasazi Indians of Southwestern United States. American Journal of Physical Anthropology 44:477–487.

el-Tayeb M. 2010. The Post-Meroitic from Kirwan to the present. Sudan & Nubia 14:2–14.

Elmesery. 2020. Evolution of irrigation system, tools, and technologies. In: Omran EE, Negm AM, editors. Technological and Modern Irrigation Environment in Egypt: Best Management Practices and Evaluation. p 59–73.

Fajardo RJ, Müller R. 2001. Three-dimensional analysis of nonhuman primate trabecular architecture using micro-computed tomography. American Journal of Physical Anthropology 115:327–336.

Farfour E, Charlotte F, Settegrana C, Miyara M, Buffet P. 2012. The extravascular compartment of the bone marrow: a niche for Plasmodium falciparum gametocyte maturation? Malaria Journal 11(285):1–4.

Finnegan M. 1978. Non-metric variation of the infracranial skeleton. Journal of Anatomy 125:23–37.

Finnegan M, Faust MA. 1974. Variants of the femur. Research Report 14: Bibliography of Human and Non-human, Non-Metric Variation. 3.

Fuller DO, Parenti MS, Hassan AN, Beier JC. 2012. Linking land cover and species distribution models to project potential ranges of malaria vectors: an example using Anopheles arabiensis in Sudan and Upper Egypt. Malaria Journal 11:264.

Fuller DQ, Lucas L. 2020. Savanna on the Nile: Long-term agricultural diversification and intensification in Nubia. In: Emberling G, Williams BB, editors. The Oxford Handbook of Ancient Nubia. New York: Oxford University Press. p 927–953.

Garcia E, Berrocal MI, Baxarias J, Campillo D, Subirá ME. 2002. Cribra and trace elements in the Prat de la Riba Necropolis (Tarragona, Spain, 3rd–5th centuries AD). Antropologia Portuguesa 19: 71–83.

Gibbon VE, Buzon MR. 2018. A diachronic examination of biomechanical changes in skeletal remains from Tombos in ancient Nubia. Journal of Comparative Human Biology 69:158–166.

Ginns A. 2006. Preliminary report on the excavations conducted on Mis Island (AKSC), 2005–2006. Sudan & Nubia, 10:13–19.

Ginns A. 2007. Preliminary report on the second season of excavations conducted on Mis Island (AKSC). Sudan & Nubia 11:20–26.

Ginns A. 2010a. Medieval cemetery 3-J-10. Sudan Archaeol. Res. Soc. Draft publications.

Ginns A. 2010b. Medieval cemetery 3-J-11. Sudan Archaeol. Res. Soc. Draft publications.

Godlewski W. 2014. The Kingdom of Makuria. In: Anderson JR, Welsby DA, editors. The Fourth Cataract and Beyond: Proceedings of the 12th International Conference for Nubian Studies. Leuven; Paris; Wapole, MA: Peeters. p 155–170.

Göhring A. 2021. Allen's fossa—An attempt to dissolve the confusion of different nonmetric variants on the anterior femoral neck. International Journal of Osteoarchaeology. https://doi.org/10.1002/oa.2968

Gomes RAMP, Petit J, Dutour O, Santos AL. 2022. Frequency and co-occurrence of porous skeletal lesions in identified non-adults from Portugal (19th to 20th centuries) and its association with respiratory infections as cause of death. International Journal of Osteoarchaeology 32:1061–1072.

Gowland RL, Western AG. 2012. Morbidity in the marshes: using spatial epidemiology to investigate skeletal evidence for malaria in Anglo-Saxon England (AD 410–1050). American Journal of Physical Anthropology 147:301–311.

Hawass Z, Gad YZ, Ismail S, Khairat R, Fathalla D, Hasan N, Ahmed A, Elleithy H, Ball M, Gaballah F, et al. 2010. Ancestry and pathology in King Tutankhamun's family. JAMA: The Journal of the American Medical Association 303:638–647.

Hengen OP. 1971. Cribra orbitalia: pathogenesis and probable etiology. Journal of Human Evolution 22:57–75.

Hildebrand T, Laib A, Müller R, Dequeker J, Rüegsegger P. 1999. Direct three-dimensional morphometric analysis of human cancellous bone: microstructural data from spine, femur, iliac crest, and calcaneus. Journal of Bone and Mineral Research 14(7):1167–1174.

Holland TD, and O'Brien MJ. 1997. Parasites, porotic hyperostosis, and the implications of changing perspectives. American Antiquity 62(2):183–193.

Hurst CV. 2013. Growing up in Medieval Nubia: health, disease, and death of a medieval juvenile sample from Mis Island, PhD dissertation. East Lansing: Michigan State University.

Joice R, Nilsson SK, Montgomery J, Dankwa S, Egan E, Morahan B, Seydel KB, Bertuccini L, Alana P, Williamson KC, et al. 2014. Plasmodium falciparum transmission stages accumulate in the human bone marrow. Science Translational Medicine 6(244):244re5.

Judd M. 2004. Gabati: Health in Transition. Sudan & Nubia 8:84–89.

Kate BR. 1963. The incidence and cause of cervical fossa in Indian femora. Journal of the Anatomical Society of India 12(2):69–76.

Kemp B, Stevens A, Dabbs GR, Zabecki M, Rose JC. 2013. Life, death and beyond in Akhenaten's Egypt: excavating the South Tombs Cemetery at Amarna. Antiquity 87(335):64.

Kirwan L. 1984. The birth of Christian Nubia: some archaeological problems. Revista degli Studi Orientali 63:119–134.

Kirwan L. 2002. Post-Meroitic Nubia—A Reappraisal. In: Kirwan L, Hägg T, Törö, L, Welsby DA, editors. Studies on the History of Late Antique and Christian Nubia. Aldershot: Ashgate Publishing Limited. p 1–9.

Kivell TL, Skinner MM, Lazenby R, Hublin J. 2011. Methodological considerations for analyzing trabecular architecture: an example from the primate hand. Journal of Anatomy 218:209–225.

Kotsick E.L. 1963. Facets and imprints on the upper and lower extremities of femora from a Western Nigerian population. J. Anat. 97(3): 393–402.

Kricun ME. 1985. Red-yellow marrow conversion: Its effect on the location of some solitary bone lesions. Skeletal Radiology 14:10–19.

Lalremruata A, Ball M, Bianucci R, Welte B, Nerlich AG, Kun J.F.J, Pusch CM. 2013. Molecular identification of falciparum malaria and human tuberculosis co-infections in mummies from the Fayum Depression (Lower Egypt). PLoS ONE 8(4):e60307.

Lamikanra AA, Brown D, Potocnik A, Casals-Pascual C, Langhorne J, Roberts DJ. 2007. Malaria anemia: of mice and men. Blood 110(1):18–28.

Lazenby RA, Skinner MM, Kivell TL, Hublin J. 2011. Scaling VOI size in 3D μCt studies of trabecular bone: a test of the over-sampling hypothesis. American Journal of Physical Anthropology 144:196–203.

Lee MSJ, Maruyama K, Fujita Y, Konishi A, Lelliott PM, Itagaki S, Horii T, Lin J, Khan SM, Kuroda E, et al. 2017. Plasmodium products persist in the bone marrow and promote chronic bone loss. Science Immunology 2:eaam8093.

Lewis M. 2018. Hemopoietic and metabolic disorders. In: Paleopathology of Children: Identification of Pathological Conditions in the Human Skeletal Remains of Non-Adults. London, United Kingdom: Academic Press. p 193–223.

Lohwasser A. 2014. Kush and Her Neighbors Beyond the Nile Valley. In: Anderson JR, Welsby DA, editors. The Fourth Cataract and Beyond: Proceedings of the 12th International Conference for Nubian Studies. Leuven; Paris; Wapole, MA: Peeters. p 125–134.

Loufouma-Mbouaka A, Binder M, Noedl H, Gamble M. 2020. Evaluation of rapid diagnostic tests and Enzyme Linked Immunoassay in the detection of malaria in ancient human remains. Journal of Archaeological Science 116:105118

Malagelada F, Tayar R, Barke S, Stafford G, Field RE. 2015. Anatomy of the zona orbicularis of the hip: a magnetic resonance study. Surgical and Radiologic Anatomy 37:11–18.

Malcolm CA, Welsby DA, El Sayed BB. 2007. SIT for the malaria vector Anopheles arabiensis in northern state, Sudan: an historical review of the field site. In: Vreysen MJB, Robinson AS, Hendrichs J, editors. Area-Wide Control of Insect Pests. From Research to Rield Implementation. Dordrecht: Springer. p 361–372.

Mangas-Carrasco E, López-Costas O. 2021. Porotic hyperostosis, cribra orbitalia, femoralis and humeralis in Medieval NW Spain. Archaeological and Anthropological Sciences 13:169.

Mann RW, Hunt DR, Lozanoff S. 2016. Photographic regional atlas of nonmetric traits and anatomical variants in the human skeleton. Springfield, Illinois: Charles C. Thomas Publisher, Ltd.

Marchand C, Chen H, Buschmann MD, Hoemann CD. 2011. Standardized three-dimensional volumes of interest with adapted surfaces for more precise subchondral bone analyses by micro-computed tomography. Tissue Engineering 17(4):475–484.

Marciniak S, Herring DA, Sperduti A, Poinar HN, Prowse TL. 2018. A multi-faceted anthropological and genomic approach to framing Plasmodium falciparum malaria in Imperial period central-southern Italy (1st-4th c. CE). Journal of Anthropological Archaeology 49:210–224.

Mays S. 2018. How should we diagnose disease in paleopathology? Some epistemological considerations. International Journal of Paleopathology 20:12–19.

McIlvaine BK. 2015. Implications of reappraising the iron-deficiency anemia hypothesis. International Journal of Osteoarchaeology 25:997–1000.

Mendiela S, Rissech C, Haber M, Pujol-Bayona A, Lomba J, Turbón D. 2014. Childhood growth and health in Camino del Molino (Caravaca de la Cruz, Murcia, Spain) a collective burial of the III Millennium cal. BC. A preliminary approach. In: Adés, Ao, editors. Estudis D’evolució Etolgia 101–106.

Mensforth RP, Lovejoy OC, Lallo JW, Armelagos GJ. 1978. The role of constitutional factors, diet, and infectious disease in the etiology of porotic hyperostosis and periosteal reactions in prehistoric infants and children. Medical Anthropology 2(1):1–59.

Meyer AW. 1924. The “cervical fossa” of Allen. American Journal of Physical Anthropology 7:257–269.

Meyer AW. 1934. The genesis of the fossa of Allen and associated structures. American Journal of Anatomy 55:469–510.

Miller RL, Ikram S, Armelagos GJ, Walker R, Harer WB, Shiff CJ, Bagget D, Carrigan M, Maret SM. 1994. Diagnosis of plasmodium falciparum infections in mummies using the rapid manual ParaSight™-F test. Transactions of the Royal Society of Tropical Medicine and Hygiene 88:31–32.

Miquel-Feucht MJ, Polo-Cerdá M, Villalaín-Blanco JD. 1999. El sindrome criboso: cribra femoral vs. cribra orbitaria. In: Sistematización metodológica en Paleopatología, Actas V Congreso Nacional AEP, Sánchez JA (ed.). Asociación Española de Paleopatología, Alcalá la Real: Jaén, Spain. p 221–37.

Molleson T, Andrews P, Boz B, Sofaer Derevenski J, Pearson J. 1998. Human remains up to 1998. Catalhoyuk 1998 Archive Report.

Moreau R, Malu DT, Dumais M, Dalko E, Gaudreault V, Roméro H, Martineau C, Kevorkova O, Dardon JS, Dodd EL, Bohle DS, Scorza T. 2012. Alterations in bone and erythropoiesis in hemolytic anemia: Comparative study in bled, phenylhydrazine-treated and *Plasmodum*-infected mice. PLoS ONE 7(9): e46101. doi:10.1371/journal.pone.0046101

Morgan JA. 2014. The methodological and diagnostic applications of micro-CT to paleopathology: A quantitative study of porotic hyperostosis, PhD thesis. London, Ontario: University of Western Ontario.

Naidoo S, London L, Burdorf A, Naidoo RN, Kromhout H. 2011. Occupational activities associated with a reported history of malaria among women working in small-scale agriculture in South Africa. American Journal of Tropical Medicine and Hygiene 85(5):805–810.

Näser C. 2007. The Humboldt University Nubian expedition 2005: Works on Sherari and Us. In: Näser C, Lange M, editors. Proceedings of the Second International Conference on the Archaeology of the Fourth Nile Cataract. Meroitica 23:118-133.

Nathan H, Haas N. 1966. "Cribra orbitalia" A bone condition of the orbit of unknown nature: Anatomical study with etiological considerations. Israel Journal of Medical Sciences 2(2):171–191.

Nerlich AG, Schraut B, Dittrich S, Jelinek T, Zink AR. 2008. Plasmodium falciparum in ancient Egypt. Emerging Infectious Diseases 14:1317–1319.

Obaldia N III, Meibalan E, Sa JM, Ma S, Clark MA, Mejia P, Moraes Barros RR, Otero W, Ferreira M, Mitchell JR, et al. 2018. Bone marrow is a major parasite reservoir in Plasmodium vivax infection. mBio 9(3):e00625-18.

Obłuski A. 2020. The Archaeology of Medieval Nubian Kingdoms. In: Emberling G, Williams BB, editors. The Oxford Handbook of Ancient Nubia. New York: Oxford University Press. p 829–846.

Odgers P.N.B. 1931. Two details about the neck of the femur: (1) The eminentia. (2) The empreinte. Journal of Anatomy 65:352–362.

Oftadeh R, Perez-Viloria M, Villa-Camacho JC, Vaziri A, Nazarian A. 2015. Biomechanics and mechanobiology of trabecular bone: a review. Journal of Biomechanical Engineering 137(1):010802-1–010802-15.

Ortner DJ. 2003. Identification of Pathological Conditions in Human Skeletal Remains. San Diego, CA: Academic Press.

Oxenham MF, Cavill I. 2010. Porotic hyperostosis and cribra orbitalia: the erythropoietic response to iron-deficiency anemia. Anthropological Science 118:199–200.

Paredes J, Ferreira MT, Wasterlain SN. 2015. Growth problems in a skeletal sample of children abandoned at Santa Casa da Misericórdia, Faro, Portugal (16^{th}–19^{th} centuries). Anthropological Science 123:49–59.

Posit team. 2022. RStudio: Integrated Development Environment for R. Posit Software, PBC, Boston, MA. URL http://www.posit.co/.

Rabino Massa E, Cerutti N, Marin A, Savoia D. 2000. Malaria in ancient Egypt: paleoimmunological investigation on predynastic mummified remains. Chungara 32(1):7–9.

Radi N, Mariotti V, Riga A, Zampetti S, Villa C, Belcastro MG. 2013. Variation of the anterior aspect of the femoral head-neck junction in a modern human identified skeletal collection. American Journal of Physical Anthropology 152:261–72.

Ratti V, Wallace DI. 2020. A malaria transmission model predicts holoendemic, hyperendemic, and hypoendemic transmission patterns under varied seasonal vector dynamics. Journal of Medical Entomology 57(2):568–584.

Redfern R. 2010. Human Bioarchaeological Database. London: The British Museum

Reisner GA. 1910. The Archaeological Survey of Nubia, Report for 1907–1908. Egypt Survey Department, Cairo.

Rivera F, Mirazón Lahr M. 2017. New evidence suggesting a dissociated etiology for *cribra orbitalia* and porotic hyperostosis. American Journal of Physical Anthropology 164:76–96.

Ruffini GR. 2012. Medieval Nubia: A Social and Economic History. New York; New York: Oxford University Press.

Sabbatani S, Manfredl R, Fiorino S. 2010. Malaria infection and human evolution. Le Infezioni in Medicina 1:56–74.

Sandberg OH, Aspenberg P. 2016. Inter-trabecular bone formation: a specific mechanism for healing in cancellous bone. Acta Orthopaedica 87(5):459–465.

Schats R. 2021. Cribriotic lesions in archaeological human skeletal remains. Prevalence, co-occurrence, and association in medieval and early modern Netherlands. International Journal of Paleopathology 35:81–89.

Schats R. 2023. Developing an archaeology of malaria. A critical review of current approaches and a discussion on ways forward. International Journal of Paleopathology. 41:32–42.

Scheidel W. 2001. Death on the Nile: Disease and the Demography of Roman Egypt. Leiden, Netherlands: Brill Academic Publishers.

Schofield G. 1959. Metric and morphological features of the femur of the New Zealand Maori. The Journal of the Royal Anthropological Institute of Great Britain and Ireland 89(1):89–105.

Setzer TJ. 2014. Malaria detection in the field of paleopathology: a meta-analysis of the state of the art. Acta Tropica 140:97–104.

Shinnie PL, Shinnie M. 1965. New light on medieval Nubia. J Afr Hist 6:263–273.

Smith NE. 2015. The paleoepidemiology of malaria in the Ancient Near East, PhD dissertation. Fayetteville: University of Arkansas.

Smith-Guzmán NE. 2015a. The skeletal manifestation of malaria: an epidemiological approach using documented skeletal collections. American Journal of Physical Anthropology 158:624–635.

Smith-Guzmán NE. 2015b. Cribra orbitalia in the ancient Nile Valley and its connection to malaria. International Journal of Paleopathology 10:1–12.

Smith-Guzmán NE, Rose JC, Kuckens K. 2016. Beyond the differential diagnosis: new approaches to the bioarchaeology of the Hittite plague. In: Zuckerman MK, Martin DL, editors. New Directions in Biocultural Anthropology. Hoboken, New Jersey: John Wiley & Sons, Inc. p 295–316.

Smith-Guzmán NE, Dabbs GR, Davis HS, Shidner AE. 2018. Distinguishing skeletal lesions of malaria from comorbidities and coexisting metabolic conditions at Amarna, Egypt. Poster presented at the 87th Annual Meeting of the American Association of Biological Anthropologists.

Snow RW, Guerra CA, Mutheu JJ, Hay SI. 2008. International funding for malaria control in relation to populations at risk of stable Plasmodium falciparum transmission. PLoS Med 5(7): e142.doi:10.1371/journal.pmed.0050142

Soler A. 2012. Life and death in a Medieval Nubian farming community: the experience at Mis Island, PhD dissertation. East Lansing: Michigan State University.

Spaulding J. 1995. Medieval Christian Nubia and the Islamic world: a reconsideration of the Baqt Treaty. Int J Afr Hist Stud 28:577–594.

Stuart-Macadam P. 1987. Porotic hyperostosis: new evidence to support the anemia theory. American Journal of Physical Anthropology 74:512–526.

Stuart-Macadam P. 1992. Anemia in past human populations. In: Stuart-Macadam P, and Kent S, editors. Diet Demography and Disease, Changing Perspectives on Anemia. New York: Aldine. p 151–170.

Tatem AJ, Guerra CA, Kabaria CW, Noor AM, Hay SI. 2008. Human population, urban settlement patterns and their impact on Plasmodium falciparum malaria endemicity. Malaria Journal 7:218.

Thomas R. 2008. The origin and use of ceramics on the islands of Mis and Umm Muri, in the Late Meroitic to Christian periods. Sudan & Nubia 12:64–73.

Trigger BG. 1969. The Royal tombs at Qustul and Ballana and their Meroitic antecedents. The Journal of Egyptian Archaeology 55:117–128.

Tsutsumi M, Nimura A, Utsunomia H, Akita K. 2021. Dynamic changes of the joint capsule in relation to the zona orbicularis: An anatomical study with possible implications for hip stability mechanism. Clinical Anatomy 34:1157–1164.

Tumwiine J, Mugisha JYT, Luboobi LS. 2007. On oscillatory pattern of malaria dynamics in a population with temporary immunity. Computational and Mathematical Methods in Medicine 8(3):191–203.

Wagner FV, Negráo JR, Campos J, Ward SR, Parviz H, Trudell DJ, Resnick D. 2012. Capsular ligaments of the hip: Anatomic, histologic, and positional study in cadaveric specimens with MR arthrography. Radiology 263(1):189–198.

Wagner WE, Gillespie BJ III. 2019. Using and interpreting statistics in the social, behavioral, and health sciences. Thousand Oaks, CA: SAGE Publications, Inc.

Walker PL, Bathurst RR, Richman R, Gjerdrum T, and Andrushko VA. 2009. The causes of porotic hyperostosis and cribra orbitalia: a reappraisal of the iron-deficiency anemia hypothesis. American Journal of Physical Anthropology 139:109–25.

Wapler U, Crubézy E, Schultz M. 2004. Is cribra orbitalia synonymous with anemia? Analysis and interpretation of cranial pathology in Sudan. American Journal of Physical Anthropology 123:333–339.

Welsby DA. 1996. The Kingdom of Kush: The Napatan and Meroitic Empires. London: Published for the Trustees of the British Museum by British Museum Press.

Welsby DA. 2002. The Medieval Kingdoms of Nubia: Pagans, Christians and Muslims Along the Middle Nile. London: British Museum Press.

Welsby DA. 2003. The Amri to Kirbekan Survey: the 2002–2003 season. Sudan Nubia 7:26–32.

Welsby DA. 2004. The Archaeology and History of Sudan. In: Welsby DA, Anderson JR, editors. Sudan: Ancient Treasures. British Museum Press. p 12–19.

Welsby DA. 2006. The Merowe Dam Archaeological Survey. Excavations in the vicinity of ed-Doma (AKSE), 2005–2006. Sudan Nubia 10:8–13.

Welsby DA. 2014. The Kingdom of Alwa. In: Anderson JR, Welsby DA, editors. The Fourth Cataract and Beyond: Proceedings of the 12th International Conference for Nubian Studies. Leuven; Paris; Wapole, MA: Peeters. p 183–200.

Welsh F. 2013. Architecture and life in villages of the Fourth Nile Cataract in the region of et-Tereif. Draft report.

White NJ. 2018. Anaemia and malaria. Malaria Journal 17:371 https://doi.org/10.1186/s12936-018-2509-9

Whitehouse WJ. 1975. Scanning electron micrographs of cancellous bone from the human sternum. Journal of Pathology 116:213–224.

Whitehouse WJ, Dyson ED. 1974. Scanning electron microscope studies of trabecular bone in the proximal end of the human femur. Journal of Anatomy 118:417–444.

Wickramasinghe SN, Abdalla SH. 2000. Blood and bone marrow changes in malaria. Bailliére's Clinical Haematology 13(2):277–299.

Wood JW, Milner GR, Harpending HC, and Weiss KM. 1992. The Osteological Paradox. Current Anthropology 33(4):343–370.

Żurawski B. 2006. Nubian mortuary complex of the Christian Period. In: Caneva I, Roccati A, editors. Acta Nubica: Proceedings of the X International Conference of Nubian Studies, Rome 9-14 September 2002. Rome: Universitá di Roma "La Sapienza."

Żurawski B. 2014. The Fourth Cataract in the Medieval Period. In: Anderson JR, Welsby DA, editors. The Fourth Cataract and Beyond: Proceedings of the 12th International Conference for Nubian Studies. Leuven; Paris; Wapole, MA: Peeters. p 135–154.