A Study in Paleo-Oncology:

On the Identification of Neoplastic Disease in Archaeological Bone

by

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A thesis

presented to the University of Waterloo

in fulfillment of the

thesis requirement for the degree of

Master of Arts

in

Public Issues Anthropology

Waterloo, Ontario, Canada, 2014

Declaration

I hereby declare that I am the sole author of this thesis. This is a true copy of the thesis, including any required final revisions, as accepted by my examiners. I understand that my thesis may be made electronically available to the public.

Abstract

Humans have experienced neoplastic disease since antiquity as evidenced by its frequent mentions in numerous ancient medical texts from diverse cultures. However, the skeletal record does not always corroborate this fact, as archaeological cases of neoplasms are not found as often as other more recognizable diseases. Numerous reasons have been given for this disparity ranging from cancer killing the individual before skeletal lesions could form to the idea that tumours simply do not survive in the archaeological record. As such neoplasms are not often considered when constructing a differential diagnosis and to a larger extent the disease is considered to be a product of the modern age.

This thesis examines the identification of neoplasms in archaeological bone using clinical data and comparison to medically diagnosed cancer cases from the University of Athens Human Skeletal Reference Collection. I also developed diagnostic criteria and data forms specifically designed to record and describe neoplastic lesions. This enabled me to develop differential diagnoses for suspected cancer cases in skeletons from the Athenian Agora, ancient Corinth, the Wiener Laboratory at the American School of Classical Studies in Athens and the Anthropology Department of the University of Waterloo. Using the comparative collection, I worked toward identifying characteristics that would make it possible to identify neoplastic lesions and distinguish between primary and secondary malignancies. An unexpected finding was demonstrating that lesions associated

with leukemia are similar to those of scurvy, a metabolic disease, and must be considered in differential diagnoses.

The methods I employed may be applied elsewhere to other suspected cases of cancer and thus enable more research in cancer's prevalence in antiquity. This will support the public issue that cancer is not a disease of modernity and that attempts to treat and understand this disease has always been a part of medical history.

Acknowledgements

First and foremost I would like to thank my supervisor, Dr. Maria Liston for her support and encouragement throughout this project. I would also like to thank my committee members, Dr. Nancy Barrickman and Dr. Sherry Fox.

Next I would like to thank the American School of Classical Studies in Athens, for allowing me to work in the Wiener Laboratory and have access to their comparative skeletal collection. I also thank Dr. John Camp and Dr. Guy Sanders for giving me access to the skeletal material at the Athenian Agora and at the Corinth excavations. From the University of Athens, I thank Dr. Sortiris Manolis for giving me permission to review the Athens Human Skeletal Reference Collection. I also thank Dr. Velissaria Vanna for her generosity and willingness to let me have extensive access to examine the cancer cases in the Athens Collection while she conducted her own project on the same material. I would also like to thank the Dr. Jonathan Tomlinson and the Canadian Institute in Greece for their courtesy and accommodations.

I thank the faculty and staff of the Anthropology Department at the University of Waterloo for their guidance and encouragement. Finally, thank you to the other students in my cohort, Kaleigh Eichel, Mithila Ruthralingam, David Gadzala and Beth Penney, for listening to my frustrations and suggesting beer as the ultimate remedy.

This thesis is dedicated to my parents, John and Alicja

Table of Contents

LIST OF FIGURES

CHAPTER 1: INTRODUCTION

The anthropological sub-discipline of paleopathology studies diseases experienced by humans in the past primarily by examining the skeletal remains of individuals and diagnosing pathological skeletal lesions that manifested during life. Other secondary lines of evidence include mummified remains, iconography and historical literature. Through this line of inquiry we are able to reconstruct the health of an individual or population and see how diseases were experienced historically, both biologically and culturally. This discipline establishes a framework to understand how a disease and its victims were understood in the past, and how a disease interacted with culture and society.

Broadly speaking, paleopathological studies focus on all types of disease, and often there is special interest in those that had great influence in history and antiquity, such as infectious diseases in the form of plagues. Focus has also been placed on joint and metabolic diseases that would have influenced the life of an individual, giving insight to their overall health and clues towards their diet and activity patterns. Other illnesses, most notably neoplastic diseases, have received less attention and are considered uncommon or rare in archaeological contexts.

This belief is echoed outside of the discipline. For instance, David (2010)[1] stated, "In industrialized societies, cancer is second only to cardiovascular disease as a cause of death. But in ancient times, it was extremely rare. There is nothing in the natural environment that can cause cancer. So it has to be a man-made disease, down to pollution and changes to our diet and lifestyle." This assertion has been broadcasted to the public via science

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[1] As found in University of Manchester 2010.

correspondents in the media and popular science websites and blogs, misinforming them about a prolific disease in present Western society (Alleyne 2010; Macrae 2010; Nordqvist 2010; Choi 2010). One of these websites conducted a poll of its readers asking, "Do you think cancer is primarily man-made?" The results of this poll indicated that 44.12% of respondents voted "No doubt," 40.57% voted "Maybe, but we need more research," and 15.31% voted "No way" (Choi 2010). From this poll it can be inferred that the general public, even those that subscribe to popular science media outlets, believe that cancer is a man-made disease that was absent in antiquity. Though organizations such as Cancer Research UK have replied to David's (2010) statement, claiming that cancer is not modern or man-made and that such claims are false and misleading to the public and cancer patients (Arney 2010), this belief persists.

Paleopathological research can examine the assumption that cancer is a disease of modernity, by providing evidence of its existence in archaeological skeletal remains and perhaps its prevalence. However, in paleopathology, the identification and diagnosis of neoplastic disease is hindered by the lack of precise diagnostic criteria and medically diagnosed comparative examples.

This thesis has four aims. First, I will review previously identified neoplastic lesions in modern and archaeological skeletal remains from Greece. Second I will develop diagnostic criteria to aid in identifying cancer in skeletal remains. Third I will create differential diagnoses that consider neoplasms as an option. And fourth, through this research I hope to determine if ancient cancers can be identified and diagnosed effectively. If I am successful then the methods I employ can be applied elsewhere to other suspected

cases of cancer and thus enable more research in cancer's prevalence in antiquity. This will

support the public issue that cancer is not a disease of modernity and that attempts to treat

and understand this disease always been a part of medical history.

CHAPTER 2: MODERN UNDERSTANDING OF NEOPLASTIC DISEASE

The designation of "neoplasm" refers to the category of disease that is distinguished by the uncontrolled, proliferative growth of cells. This category includes a broad spectrum, encompassing reactive focal and metabolic abnormalities, as well as miscellaneous growths, which range from large cysts to minor warts (Miller 2008: 663). Neoplasms are organized into two categories: benign and malignant. Benign neoplasms are characterized by restricted growth, little impact on the surrounding tissue and sharply demarcated margins (Auferheide and Rodríguez-Martín 1998: 371-372). These tumours often occur in characteristic locations in the skeleton and some have a predilection for sites of rapid bone growth (Miller 2008: 665). Malignant neoplasms are those that grow uncontrollably, interfere with the function of bodily systems and are distinguishable by their ability to infiltrate surrounding tissues. Malignancies are normally classified as either carcinoma or sarcoma. Carcinoma refers to a cancer that arises from the epithelial tissue that lines external and internal surfaces of the body, while sarcoma refers to a cancer that arises from any connective or supportive tissue, including bone. Tumours are further subdivided into three categories based on what type of tissue they develop from: osteoblastic tumours are those that develop in bone, chondroblastic are those from the cartilage and fibroblastic form in the collagen.

Causes of Cancer

Neoplasms develop from a single cell that has become cancerous due to the interaction between an individual's DNA and various carcinogenic factors in the environment. These factors cause damage to DNA, which in turn changes the normal

genetic coding for cellular mechanisms that oversee processes such as cell multiplication (Ames 1978: 1). The World Health Organization divides carcinogens into three broad categories: physical, chemical and biological.

Physical carcinogens include ultraviolet light and ionizing radiation caused by radon. Ultraviolet light is a naturally occurring form of radiation that is emitted from the sun. Upon reaching the Earth, UV rays are absorbed by proteins resulting in modification or destruction of DNA. Humans and other animals have developed adaptive features in the skin that protect the body from ultraviolet radiation (de Gruijl 2000: 2004) but they are still at risk of developing skin cancer. This risk is higher for individuals who sunburn easily and never tan (de Gruijl 2000: 2005). Radon is a product of the radioactive decay of naturally occurring uranium in the Earth's crust and it affects indoor air quality (Mossman 2007: 152). Radon can accumulate within homes and is consequently breathed in by humans; in cases where there are high levels of radon, lung cancer may result (Mossman 2007: 152).

The chemical category of carcinogens is much larger. Lung cancers can develop from frequent inhalation of asbestos fibres (Reeves 1976) and chronic exposure to arsenic can lead to cancer of the skin, lung and bladder (Liu and Waalkes 2008: 24). Components of tobacco smoke, such as formaldehyde and cadmium, also fall under this category (Hecht 2006: 606). The risk of developing cancer increases with the time an individual has smoked and the number of cigarettes smoked per day (Hecht 2006: 604). For instance, smokers have been noted to have a 10% increased risk of cancer, while heavy smokers have a 15-20% increased risk (Carbone 1992: 1A-13S). More than 80% of lung cancer

cases in the United States are believed to be the direct result of cigarette use (Carbone 1992: 1A-13S). The smoke from cigarettes introduces carcinogen-activating enzymes that result in alterations in an individual's oncogenes and tumour suppressor genes. Oncogenes are normal cellular genes that, when mutated or overexpressed, cause unregulated cell growth and tumour suppressor genes are cellular genes that control and regulate cell growth; it is the loss of these functions that results in unregulated, cancerous growths (Carbone 1992: 1A-15S).

The biological category of carcinogens includes infection from certain viruses, bacteria or parasites, dietary factors, moulds, certain drugs and toxins. The papillomavirus is the most commonly known viral carcinogen and is the most complex of human pathogenic viruses (zur Hausen 2000: 246). At least two variants, HPV-16 and HPV-18, have been associated with cancer development (zur Hausen 2000: 248). Cervical cancer is the most common carcinoma to be caused by infection from the papillomavirus, with over 95% of biopsied cervical cancers containing HPV-16 sequences (zur Hausen 2000: 248). The human papillomavirus is transmitted sexually through genital contact and in most cases will not lead to any health problems; however it is through continued exposure or infection that cancer results (Center for Disease Control). Certain foods have also been linked with carcinogenic effects. For instance, consumers of large amounts of Chinese-style salted fish have been noted to have an increased risk of nasopharyngeal cancer (Ning et al. 1990; Armstrong et al. 1998). Other more common foods have also been described as possibly carcinogenic, including pickled vegetables and coffee. The carcinogenicity of pickled vegetables is associated with the pickling process used mainly in Asia, which does not use salt or vinegar and instead relies on natural fermentation that can lead to

contamination by mould (Abnet 2007: 194). Studies have suggested that these vegetables might contain mutagens that could result in an increased risk of esophageal cancer (Cheng et al. 1980; Lu et al. 1981). Coffee has also been listed as possibly carcinogenic, leading to an increased risk of cancer of the lower urinary tract (Cole 1971), but a subsequent study suggested that the evidence for this was statistically insignificant (Viscolli et al. 1993: 1435).

Aside from carcinogens, it is also recognized that there is some genetic predisposition to the formation of cancers. Deleterious genetic mutations may exhibit a Mendelian inheritance and can accumulate in family members, leaving them open to a higher risk of cancer (Frank 2004: 65). To be considered at risk of developing cancer, an individual must be a carrier of at least one mutated allele, for instance breast cancer has been known to occur in women who carry a mutation in one of their tumour suppressor genes, BRCA1 (Frank 2004: 765). A genetic predisposition in such individuals will also result in cancer occurring more frequently and at a younger age (Frank 2004: 768). A genetic predisposition due to inherited, mutated genes has also been noted in lung cancer (Heighway et al., 1986) and colorectal cancer (De la Chapelle 2004).

Finally, maturity is another factor that contributes to cancer development as the risk of developing the disease rises with advanced age due to the tendency for cellular repair and replication mechanisms to be less effective as an individual grows older (World Health Organization). Throughout life, an individual's DNA undergoes self-replication, however occasionally this process may result in either DNA damage or mutation. Both DNA damages

and mutations will accumulate over an individual's life and lead to deleterious effects including cancer development.

Metastasis

While benign tumours remain localized, the main distinguishing feature of malignant cancers is their ability to spread throughout the body through a process called metastasis. This involves cancer cells detaching from the tumour, penetrating the lymphatic or circulatory system and spreading to either the surrounding lymph nodes or to other regions of the body (Galasko 1981: 49). Batson (1940) provided the most plausible explanation for metastasis through his experimentation with dye injections into the dorsal veins of the penis. With a radiograph Batson was able to track the dye's spread into other regions of the body including the pelvis, the lumbar spine, the thoracic cage and the base of the skull. Now dubbed the Batson venous plexus, many clinicians agree that this is one of the main processes by which cancer metastasizes to other regions of the body (Zindrick et al. 1982; Libson et al. 1987; Morgan et al. 1990; Anton 1988; Vinholes et al. 1996; Coleman 2006). As cancer cells travel throughout the body via haematological routes, the vast majority of metastases tend to occur in the axial skeleton due to the high presence of red bone marrow in this region (Coleman 2006: 6243s). Aside from the axial skeleton, other areas of the skeleton are also vulnerable but are less common and at times harder to diagnose. For instance the bones of the foot are much more infrequently affected however they may still occur in advanced cases such as lung cancer, though they are not generally recognized. This is partly because metastasis to this region occurs only in more advanced

cases and at this point the patient may no longer be ambulatory and thus little attention is paid to the feet (Gall et al. 1976: 1494).

Bone is the most common site for metastatic cancer with carcinoma of the breast, prostate and lungs being the sites of origin approximately 75% of the time. In comparison, thyroid and kidney cancer have a 30 to 40% chance of metastasis, while tumours in the gastrointestinal tract is less than 10% (Fig. 1) (Coleman 2006: 6243s). In areas rich in red bone marrow, tumour cells produce adhesive molecules that bind them to the marrow cells and the bone matrix; this causes the production of bone resorbing factors that further enhance a tumour's growth. The microenvironment of bone is ideal for tumour cells to grow and proliferate as it holds a large reservoir of immobilized growth factors, including transforming growth factor β, insulin-like growth factors I and II, fibroblast growth factors, platelet-derived growth factors, bone morphogenetic proteins and calcium; when these are released and activated by the body during bone resorption they provide an ideal environment for the growth of tumour cells (Roodman 2004: 1656).

Metastases can result in either lytic or blastic activity. Osteolytic activity results when an imbalance occurs in the remodelling process: bone resorption increases but fails to stimulate enough new bone formation. The only cancer that solely produces lytic bone lesions is multiple myeloma. In this cancer osteoclasts accumulate at bone resorbing surfaces adjacent to the myeloma cells and bone formation is thus suppressed (Roodman 2004: 1655). In blastic metastatic bone formation resorption is increased and new bone is deposited away from the sites of previous bone resorption; this is most typically found in cancer of the prostate. When viewed histologically metastases from prostate cancer show a

substantial number of osteoblasts adjacent to the tumour cells, whereas few or no osteoblasts are seen in normal bone or in skeletal metastases from other types of cancer (Logothetis and Lin 2005: 21). It has been suggested that prostate cancer cells might depend on osteoblasts for their growth as these cells produce biological factors that agitate the bone microenvironment and affects the normal balance between osteoblast and osteoclast activities, resulting in a blastic metastasis (Logothetis and Lin 2005: 22). Metastatic lesions can also be mixed in their character, meaning they can be lytic and blastic at the same time; this reflects the co-existence of both processes and is usually seen in breast cancer (Vinholes et al. 1996: 292). While breast cancer is known to predominantly produce lytic lesions, at least 15 to 20% of these can also be blastic. Contrary to prostate cancer and multiple myeloma, breast cancer cells produce biological factors that directly or indirectly induce osteoclastic activity, which results in a mixed skeletal reaction (Roodman 2004: 1659). It should also be noted that some cancers do not spread to the skeleton initially. For example colorectal cancer, the third most common soft tissue cancer among adults, has been observed to first spread to the liver and lungs much more frequently than to the skeleton. In fact skeletal metastasis of this type of cancer is usually indicative of the terminal phase (Roth et al. 2009: 2).

For many patients metastatic cancer is a chronic condition that produces further complications including hypercalcemia, a condition where there is an excess of calcium in the blood, which is a consequence of bone destruction due to lytic processes. Pathological fractures may also become a problem as the lytic destruction reduces the load bearing ability of bones; blastic activity on the other hand, produces bone that does not in any way lend to structural support. This causes painful microfractures, which can then lead to

macro-fractures (Coleman 2006: 6245s-6246s). Metastases in the skull may reach considerable size and lead to pressure on the sinuses and nerves resulting in discomfort and possible neurological problems (Stark et al. 2003: 221). Patient survival from metastatic complications varies among different tumour types and the time since the initial diagnosis; the median survival rate for metastatic prostate or breast cancers is measurable in years while that of lung cancer is typically measured in months (Coleman 2006: 6243s).

In pre-modern societies, metastases would mostly be undetectable without the aid of radiographic imaging. Treatment would have been aimed at alleviating the main symptoms of metastasis, namely pain and possible fractures of weakened weight bearing bones due to lytic activity.

Benign Primary Bone Tumours

Osteoblastic

Common primary osteoblastic benign bone tumours are osteoma, osteoid osteoma, enostosis and osteoblastoma. An osteoma is the most frequently reported neoplastic defect and is sometimes referred to as a 'button osteoma' due to its small, round appearance. It is generally characterized as a hard, smooth lump, less than two centimetres in diameter which grows for an extended period of time (Campanacci 1990: 349; Ortner and Putschar 1985: 368). Osteomas are more commonly seen in adult males and are found in one percent of all modern medical autopsies. They occur almost exclusively on the outer table of the skull, usually on the frontal and parietal bones, though at times they may also form in the frontal and maxillary sinuses. Due to their slow growth it is likely that an osteoma will manifest sometime in childhood and go unnoticed; some clinicians believe that that they

may be a response to a traumatic event (Campillo 2005: 94). An osteoma is often asymptomatic unless it alters the sinusal drainage, which could cause sinusitis; they can also deform the wall of the eye orbit (Kirkpatrick-Smith 2010: 732). In exceptional cases, osteomas may cause intracranial symptoms, eroding the wall of a sinus and placing it in contact with epidural space. Usually surgical intervention is not needed unless the osteoma becomes symptomatic (Campanacci 1990: 354).

Osteoid osteomas are normally found more in males than females and appear during late childhood, adolescence and young adult age. They are localized on the proximal femur, tibia and humerus and are small in size (Campanacci 1990: 371). They are characterized by chronic pain, which is so intense that many modern patients usually require an analgesic. The pain is independent of the function of the neoplastic site and so it does not worsen through usage or lessen during rest and is more intense during the night. (Campanacci 1990: 356). The pain is not always localized to the osteoid osteoma and may mislead the patient to think that it is a joint or nerve affliction, such as sciatica (Campanacci 1990: 356). As an ancient neoplasm an osteoid osteoma would have undoubtedly caused the individual, unbearable chronic pain. This would have been worsened by not having access to modern day analgesics, unless some kind of opiate was available to them.

A solitary enostosis, also known as a bone island is characterized as a growth of cortical bone within the trabecular bone. This tumour is typically asymptomatic and is usually found accidently when radiographs are taken for any other medical reason. Therefore, it would have had no implication on people in antiquity. It is most common in adults with no predilection for sex and is usually found on the pelvis, femora and other long

bones; it may be found anywhere on the skeleton, but it is rarely found on the spine.

Radiographically a solitary enostosis appears as ovoid, round or oblong in shape, uniformly

dense and has brush-like or feathered borders. This neoplasm could be easily confused as a

possible osteoid osteoma, a blastic metastasis or an osteoblastoma (Greenspan et al. 2007:

52).

Osteoblastoma is the last of the common primary benign neoplasms. Also known as

a giant osteoid osteoma, this is a rare kind of tumour that is most common in females under

the age of 20 years. Osteoblastomas are usually found in the spine; one third are located in

the thoracic and lumbar regions (Auferheide and Rodríguez-Martín 1998: 376). An

osteoblastoma causes expansion within the bone and radiographically show lesions of

either a lytic or blastic nature; however a diagnosis is difficult to make without a

radiograph because it does not have any specific characteristics when viewed normally

(Waldron 2009: 173).

Chondroblastic

The benign, primary chondroblastic neoplasms, which are those that arise from

cartilage, are osteochondroma, enchondroma and chondroblastoma.   Osteochondroma is

the most common of the benign bone tumours. Also known as an osteocartilaginous

exostosis, this neoplasm has no sex predilection and is usually diagnosed in individuals less

than 30 years of age (Ortner and Putschar 1985: 371; Greenspan et al. 2007: 184). It may

occur in any bone that develops by enchondral ossification and has a limited growth

period, most often in childhood; like other neoplasms it can arise spontaneously but it can

also occur after an injury (Ortner and Putschar 1985: 371; Waldron 2009: 175). Its final

13

shape is greatly influenced by the mechanical stress experienced by the bone, such as the pulling of the muscles and tendons; for example on the proximal humerus, an osteochondroma tends to be broad based and rather bulky (Ortner and Putschar 1985: 371). Symptoms for an osteochondroma include painless swelling and pressure on the adjacent muscles, nerves and blood vessels; in rare cases this neoplasm could become malignant in the form of a chondrosarcoma (Waldron 2009: 176).

An enchondroma can occur as either a single or multiple tumours. Single enchondromas most frequently occur in the hands, specifically in the proximal phalanges with a preference for the fifth, while the carpals are rarely involved. They manifest between the ages of 20 and 30 with no predilection for sex. These tumours are asymptomatic and have a characteristic radiographic appearance where the lesion is intramedullary (Waldron 2009: 174). Multiple enchondromas, also known as enchondromatosis, have traditionally been classified in two forms, Ollier disease and Maffucci's syndrome, but recently the distinction between them has become no longer justifiable and it is now thought that they are probably one in the same (Mellon et al. 1988). Multiple enchondromas are asymmetric, affecting the femur, tibia and hands. The bones become swollen and there is the possible complication of soft tissue haemangiomas (Waldron 2009: 174).

Chondroblastoma is a rare type of benign tumour that is found in the epiphyses of long bones, especially in the femur, humerus and tibia. It is twice as common in males and usually occurs in the second and third decades of life. A chondroblastoma can cause local pain, swelling, restriction of movement and can become malignant with widespread metastasis (Waldron 2009: 175).

Fibroblastic

The primary, benign, fibroblastic neoplasms include giant cell tumours and meningioma. Giant cell tumours, which are also known as osteoclastomas, commonly occur in individuals between 20 and 40 years of age, and are normally found in the long bones, specifically the distal femur, proximal tibia, distal radius and proximal humerus. This tumour destroys the pre-existing trabecular bone and original cortex and forms a thin new periosteal cortical shell with rounded perforations and reinforcing ridges on the inner surface (Ortner and Putschar 1985: 375 - 376). A giant cell tumour often causes pain, usually felt in the joint and also limits the function of the joint according to its proximity. Visible swelling can also occur if the tumour forms in the superficial bones or those with a small diameter such as the proximal tibia, distal radius and ulna, proximal fibula, metacarpals and phalanges (Campanacci 1990: 120). This tumour's growth is largely sporadic and unreliable as at times it will grow slowly and will remain self contained for years, while other cases have seen the tumour proliferate and become invasive in a few weeks (Campanacci 1990: 141).

A meningioma is a neoplasm that occurs in the dura matter of the brain and spinal cord; when the cancer invades the inner-table of the cranium there is a massive response of reactive bone in the form of radiating spicules projecting from the outer table of the skull (Ortner and Putschar: 378). This type of neoplasm represents approximately 20% of primary endocranial tumours and has a predilection for adult females; occasionally an osteoma can form the base of such tumours (Campillo 2005: 103).

Primary Malignant Bone Tumours

Malignant bone tumours often have a much greater impact on the quality of life and survival of patients. The first and most common of these is osteosarcoma, which originates within the bone and has a predilection for males (Campanacci 1990: 455). In modern classification systems ten major types of osteosarcoma are recognized based on a combination of histological, radiographic and clinical data (Dorfman and Czerniak 1994: 205). Osteosarcoma is most commonly found in the bones of the knee and shoulder and occurs between the ages of ten and thirty, although a case can arise in middle age from abnormal developing bone (Ortner and Putschar 1985: 384). In most cases an osteosarcoma originates at the metaphysis and progresses through the cortex, producing large soft tissue masses; however its shape and appearance is dependent on the location within the bone and the amount of bone being produced by the cancer cells (Waldron 2009: 179). From its onset, this neoplasm will induce mild, infrequent pain that can become worsened through movement or mechanical function. Over the course of a few weeks the pain will worsen and become chronic, swelling will also begin and the skin above the lesion will be warm to the touch. If the cancer metastasizes to the lungs, the patient will then lose body weight and become anaemic (Campanacci 1990: 459). An osteosarcoma is usually seen as a large mass of bone, often with spicules. On a radiograph the tumour will appear within the medullary cavity and the cortical bone; a sunburst appearance may be present but the absence of one should not rule out the possibility of its diagnosis. This type of bone cancer is the most highly resistant to treatment and would have been fatal in the past (Waldron 2009: 180).

A chondrosarcoma is a malignant tumour formed within the cartilage that may develop on its own or from an existing benign chondroma. Chondrosarcoma is most common in the long bones and pelvis and appears between the ages of 30 and 60 years, more often in males than in females. Usually these tumours originate in the medullary cavity and are thus called primary chondrosarcomas, but they may originate on the bone surface as well and are then referred to as a secondary chondrosarcoma (Waldron 2009: 181; Greenspan et al. 2007: 213). A primary chondrosarcoma is known for the severe pain that it causes but has no apparent mass, while a secondary chondrosarcoma is asymptomatic despite its large mass (Greenspan et al. 2007: 214). Whether it is primary or secondary, a chondrosarcoma can grow to considerable size and erode the cortex; survival rates are poor if it should metastasize to other organs. Finally, this neoplasm does not have any distinctive features and can be difficult to diagnose without the use of histology (Waldron 2009: 181).

A fibrosarcoma arises from the collagen and is a relatively rare malignant cancer. This neoplasm is predilected for males between the ages of 30 and 50 and is usually found in the knee or the pelvis (Waldron 2009: 181). A fibrosarcoma is characterized by interlacing bundles of collagen fibres and spindle shaped tumour cells; common symptoms include pain and swelling which range in duration from a few weeks to several months (Greenspan et al. 2007: 297).

Ewing's sarcoma is usually observed in children and adolescents with a predilection for males; interestingly it does not commonly occur in people of African descent (Waldron 2009: 181; Greenspan et al. 2007: 325). Ewing's sarcoma is an aggressive, lytic neoplasm

that occurs most frequently in the ribs, flat bones and the diaphyses of long bones. In most cases it has a poor survival rate and is believed to arise from a chromosomal abnormality affecting chromosomes 22q12 and 11q24 (Waldron 2009: 181). On occasion it may metastasize to other bones and presents symptoms such as fever, malaise and weight loss, along with a localized, painless mass (Greenspan et al. 2007: 325).

Another primary bone tumour is multiple myeloma, which results from the accelerated growth of plasma cells in the blood-forming tissue of bone marrow and is therefore most commonly found in the axial skeleton, though this is not exclusive (Roberts and Manchester 2005: 258; Greenspan et al. 2007: 346). Multiple myeloma usually occurs in males between the ages of 50 and 60 and the initial symptom is pain, which worsens during the day and is enhanced by activity and can be initially mistaken for sciatica before a clinical diagnosis is made. Other symptoms include malaise, fatigue, weight loss, fever and bone pain (Greenspan et al. 2007: 347). Skeletally, lesions created by multiple myeloma are characteristic as circular perforations, usually in the skull, of various sizes (Roberts and Manchester 2005: 259).

Leukemia is a disease, which affects the white blood cells and arises in the bone marrow, replacing it with neoplastic cells (Levesque et al. 1998: 253). Leukemia is classified as either acute or chronic, the latter of which is only present in adults; however acute leukemia can occur at any age with a small peak of incidence in children under the age of five (Waldron 2009: 183). Skeletal changes due to this disease are more extensive in acute leukemia than in the chronic variant and are therefore more often seen in children than in adults. These skeletal changes include osteopania, lytic lesions with new periosteal

bone formation as well as transverse metaphyseal bands of diminished bone density and dense transverse metaphyseal lines caused by growth arrest, while blastic changes are unusual (Waldron 2009: 183; Rubens and Mundy 2000: 128).

CHAPTER 3: PALEOPATHOLOGY OF CANCER

In the early years of paleopathology, the search for examples of ancient neoplasms was undertaken by notable figures such as Aleš Hrdlička (1927: 7), Roy Moodie (1923: 402-403) and Marc Ruffer and J. Willmore (1913), however they found few examples and concluded that cancer and other neoplasms were uncommon in the past (Sigerist 1951: 59; Putschar 1966: 62).

Today neoplastic disease has begun to garner more discussion among paleopathologists regarding cancer's prevalence in the past (Capasso 2005; Waldron 1996; David and Zimmerman 2010; Weiss 2000; Ricci et al. 1995, Nerlich et al. 2006) and in constructing surveys of past archaeological cases of the disease (Capasso and Di Tota 1996; Fornaciari and Giuffra 2012; Strouhal 1998; Bourbou 2003; Brothwell 1967; Campillo 1998). However, topics such as the paleoepidemiology and biocultural aspects of cancer have only begun to be touched upon and explored (Halperin 2004) and these are still far from being understood (Marques et al. 2011).

Possible Reasons For the Lack of Archaeological Cancer

The main reason attributed for the lack of archaeological cancer cases is the lower average life expectancy of the past. Early paleodemographic research showed through the use of mortality tables that on average, ancient populations did not live as long as today and thus the social and medical problems associated with old age did not arise (Angel 1947:24). For instance, mortality tables such as those by Russell (1958: 26) indicate that in ancient Rome mortality was most high during early childhood and few lived to an age where there is a higher risk of developing a carcinoma. More recent research on skeletal

evidence indicates that life expectancy for the wealthy was between 40 and 50 years and this was most likely lower for those of lower socioeconomic status (David and Zimmerman 2010: 731). Since people in the past had a lower average life expectancy than is seen today, it has been assumed that they simply did not live long enough to develop cancer (Weiss 2000: 194). Others have noted that since primary malignancies of bone usually occur during the growth periods and in the young, these should be seen in the ancient remains (Ortner 1981: 733; David and Zimmerman 2010: 731). Though this is a reasonable observation, juvenile skeletons are not often preserved as well as adults and pathologic processes, such as lytic activity, could have left the bones more susceptible to damage and decay.

The other reason often given for the lack of ancient cancer evidence is the assumption that there were lower levels of man-made environmental carcinogens. However, this has been been contested by researchers (Capasso 2005; Marques et al. 2011; Weiss 2000). For instance it has been assumed that antiquity was free of pollution due to the lack of heavy industrialization that has been present since the late 19th century. However humans have been polluting the air since they learned to control fire, as the burning of firewood releases small amounts of trace metals. Research has shown that smelting large quantities of ores in open fires results in the release of trace element emissions into the atmosphere (Nriagu 1996: 223). It has been shown that the lead content of ice layers deposited in Greenland between 500 BCE and CE 300 was approximately four times that of background levels, which implies widespread pollution of the Northern hemisphere. In societies that had the technological advancement to process metals, such as in ancient Greece and Rome, vast amounts of material were produced; this has been estimated to include one hundred

thousand metric tonnes of lead, fifteen thousand metric tonnes of copper and ten thousand

metric tonnes of zinc (Nriagu 1996: 223).

"Indoor pollution" from domestic activities would also have been a risk from the use

of hearths for heating and cooking, as well as oil lamps used for light; the constant use of

these would have been a source of dangerous quantities of carbon and other toxic gases

(Capasso 2000: 1774). An example of the carcinogenic effects of "indoor pollution" is seen

in the Grottarossa mummy. Discovered in 1956 in Grottarossa, a district on the outskirts of

Rome, this mummy of an eight-year-old girl from the CE 2nd century exhibited signs of

bilateral pleural effusion. This resulted as a secondary infection from pneumonia and was

determined to be the cause of death (Ascenzi et al. 1996: 214). However, during their

investigation researchers also noted the child's lungs had severe anthracotic pigmentation

caused by the accumulation of carbon that had been inhaled during life (Ascenzi et al. 1996:

214). The high amount of carbon present in the girl's lungs, despite her young age at the

time of death, gives evidence that indoor pollution was a significant risk for people of

antiquity. If the child had not contracted pneumonia, lung cancer could have developed

later in life due to the high amount of carbon in her lungs, as studies have shown that this

substance is carcinogenic and repeated inhalation and exposure could ultimately lead to

cancer (Baan 2006: 295). Aside from pollution, other natural carcinogens were present in

antiquity such as infectious diseases, natural outcroppings of carcinogenic minerals and

exposure to UV rays (Aufderheide and Rodrígues-Martin 1998: 374). Social customs such

as betel nut chewing and tobacco use would have also promoted cancer in some

individuals. Genetics were also a factor, as endogamous mating in small populations would

favour the transmission of harmful mutations (Marques et al. 2011). However, a recent

paleoepidemiological study gave further evidence for this through an examination of three skeletal populations recovered from the two Egyptian necropoles of Thebes-West and Abydos, which encompasses a time period between 3200 and 500 BCE; a third population, an ossuary, was included from from Southern Germany dating between CE 1400 to 1800 (Nerlich et al. 2006: 197-198). With the data they collected, the researchers employed a mathematical model for skeletal involvement of malignant tumours, developed by Waldron (1996) through the use of an English population dating from CE 1901 to 1905 (Nerlich et al. 2006: 199). Their results indicated that tumour rates were not statistically different between the ancient Egyptian, the historical Southern German and the recent English reference population, which signify that cancer was present in spatially and temporarily different populations over the last 4000 years. This study concluded that the rise in tumour frequencies in present populations was more related to higher life expectancy than environmental or genetic factors (Nerlich et al. 2006: 197).

Scholars have also proposed that tumours are not commonly found in archaeological contexts for other reasons that include issues of preservation, identification and diagnosis. To begin with, since taphonomic processes can destroy lesions, the ability to discover tumours is dependent on their state of preservation (Marques et al. 2011). Bone density is a factor in preservation, as lesions of extreme osteolytic activity would be much more likely to be destroyed than those of osteoblastic activity (Weiss 2000: 195); however much of the osteoblastic bone formed by metastasis consists of woven bone that is quite fragile and could be destroyed as easily as a highly lytic bone lesion. A paleopathological study on the benefits of radiographic imaging in identifying cancer lesions showed a detection rate three times that of a visual examination (Rothschild and Rothschild 1995:

23

358). However, since there must be a 30-50% increase of bone density for a lesion to be recognized on a radiograph, some visually detected lesions may not be seen in this manner. Without a radiograph, osteoblastic lesions could be overlooked because most form and are isolated in the trabecular bone (Rothschild and Rothschild 1995: 361). Moreover, as many cancers originate in the soft tissue it is unlikely that they would commonly be seen in archaeological contexts unless mummification had occurred; for instance, Zimmerman (1977) has shown that soft tissue tumours can be preserved well through mummification and be accurately diagnosed.

Another problem is that cancers can often be confused with each other or other pathologies. For instance, multiple myeloma can be easily mistaken for metastatic cancer (Capasso 2005: 2) and on a radiograph a haemangioma may look like an osteosarcoma, due to the similar sunburst appearance of new bone (Brothwell 2012: 423). In other cases, lesions were diagnosed as an osteosarcoma by some investigators, but were diagnosed as an infection by others (Weiss 2000: 198). For instance, Brothwell (1961: 321) identified a lesion on the neck of a humerus as neoplastic but Wells (1960)[2] thought it to be an abscess resulting from a wound. Since cancers are deemed rare or uncommon, some paleopathologists might not consider them a possibility in their diagnosis or simply not expect to come across them, especially in certain anatomical regions. For instance, Carrascal et al. (2013) report on a Medieval aged mandible found in Spain that exhibited a large, lytic lesion. Normally, lesions in the mandible are usually attributed to oral pathologies and thus ante-mortem tooth loss, calculus, caries and alveolar resorption are considered more likely in the differential diagnosis. However, the lesion had margins

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[2] As cited in Brothwell (1961: 321)

indistinguishable from the rest of the bone and when x-rayed, showed radiolucent lines

and opacities. Due to this and the size and shape of the lesion, inflammatory, traumatic,

infectious and pseudotumoural injuries were ruled out as possibilities, leaving a neoplasm

as the most likely cause (Carrascal et al. 2013: 320).

Finally the last reason for the perceived rarity of archaeological cancer is that the

disease may have led to death sooner than it does today. Before the 20th century, the

primary treatment for cancer was surgery and that was only done when the tumour

became visible at the body's surface; deep-seated tumours would have been unseen and

thus evaded medical intervention. Without any attempt of treatment the cancer would

interfere with the function of vital organs and thus kill the individual before metastasis to

the skeleton could occur (Weiss 2000: 194; Capasso 2005: 10; Ortner 1981: 733).

The Most Common of the Uncommon

Though almost all types of modern neoplasms have been documented in ancient

human remains (Capasso 2005: 4) the most common to be found tend to be osteomas,

nasopharyngeal cancer and multiply myeloma. Many examples of osteomas have been

found in skeletal collections, such as that of the National Museum of Naturally History in

Washington D.C., as well as in ancient human populations (Ortner 1981: 733). In some

areas and time periods its prevalence has been more frequent than in modern times. For

instance, though 1% of all modern autopsies exhibit a cranial osteoma, 2.5% of Egyptian

skulls dating from pre-dynastic times to the Roman conquest also display osteomas

(Capasso 2005: 8). Nasopharyngeal carcinoma seems to be more common in ancient

societies than in modern times, where this type accounts for only 0.25% of cancers

worldwide (Capasso 2005: 9). It is only in parts of Africa, such as Tunisia, Algeria, Morocco

and Sudan, where nasopharyngeal carcinoma comprises 7% of all malignancies. In these

areas, nasopharyngeal carcinoma has been associated with high infection rates of the

Epstein-Barr virus and exposure of the nasopharygneal mucosa to chemical carcinogens

from local flora including: *Croton tiglium, C. megalocarpus, C. macrostachyus, Euphorbia*

lathyris, E. tirucalli, E. antiquorium, E. milli, E. pekinensis, E. kansui, Aleuritis fordii, and

Daphne odoro; many of which are used in Sothern China in folk remedies and commercial

products such as oil paints and varnish (Ito 1983: 324). Nasopharyngeal cancers are well

documented through the vast destruction of the facial bones, the sphenoid and the cranial

base. Many ancient Egyptian cases have been documented through histological analyses

and it has been calculated that 15% of all malignancies in ancient Egypt were

nasopharyngeal cancer (Capasso 2005: 9). In regard to multiple myeloma, the high rate

could be related to high frequencies of chronic infections as these conditions can

excessively stimulate the immune system, encouraging the emergence of transformed

plasmacellular cells (Capasso 2005: 10).

Cases of Cancer in the Paleopathological Literature

Osteoma

In Greece, a large number have been found in several skeletons of both sexes in

Thasos (Agelarakis 2002: 19), as well as Thrace and other Aegean islands (Bourbou 2003:

183). Bourbou (2003) also mentions an osteoma found on the frontal bone of a young

adult male from Eleutherna, an adult of unknown sex from Messene and an adult female

from Sourtara. More recently, Kirkpatrick-Smith (2010) reported a large nasal neoplasm,

most likely being an osteoma, found in an adult male from the Athenian Agora, dating back to the late Bronze Age. A very large example of an osteoma was also found on an Egyptian skull from the Roman period (Brothwell 1967: 323). Another example of a probable osteoma is that of a 20-25 year old female from an ossuary at Křtiny, in the Czech Republic, which was dated between the late 13th and mid 18th century CE (Strouhal et al. 1996: 298).

Osteoid Osteoma

Osteoid osteomas seem to not be as common as the osteomas, this is probably due to their small size and their propensity for originating within the bone; if they do not expand outward through the cortex they may go unnoticed. In Medieval Corinth, there was a case of osteoid osteoma in the distal femur of an adolescent male (Bourbou 2003: 183). Aufderheide and Rodrígues – Martín (1998: 376) mention only three cases of osteoid osteoma in the paleopathological record, one of which, found on the tibia of a Saxon as described by Brothwell (1967: 325), is now thought to be a chronic abscess. The other two examples include an Anglo-Saxon femur (Wells 1965: 393) and the right tibia of an adult male from Czechoslovakia (Aufderheide and Rodrígues – Martín 1998: 376). In Szeczin, Poland Gładykowska-Rzeczycka and Myśliwski (1986) report of an osteoid osteoma on the tibia of an adult male dated between the 14th and 15th centuries.

Osteochondroma

This benign cartilage-originated neoplasm has been described in two examples from Ancient Egypt. The first was a femur from the 5th Dynasty (Brothwell 1967: 323) and the second is a right innominate from a 12th Dynasty adult female (Ortner and Putschar 1985: 380). Another example was found in the right femur of an adult female from Ostrów

Lednicki in the Polish district of Poznań (Gładykowska-Rzeczycka 1997). Ortner (1981:

734) also reports an example of a juvenile osteochondroma from the Winchester-Saxon

skeletal pathology collection of the British Museum in London. Though sex was unknown,

the individual was aged to approximately four years and had prominent bony projections

in the distal metaphyses of the left humerus and both femora. As this neoplasm is benign, it

is unlikely that it would have been the cause of death in any of these cases.

Meningioma

Meningioma involves a bony reaction to tumour cells lining the dura matter of the

brain and spinal cord. Archaeologically, two Egyptian examples were found on the calvaria

from an individual at Helouan from the 1st Dynasty and the other at Meydum from the 20th

Dynasty (Rogers 1949: 423). Another example was found in Peru that exhibited a lesion

located on the cranial vault and consisted of fused spicules of bone that radiated out

towards the surface (Abbot and Courville 1939: 103). Abbot and Courville (1939: 105) also

tell of a similar meningioma case from San Nicholas Island, located off the coast of Southern

California. Jónsdóttir et al. (2003) report a meningioma found an adult male from Alaska

dated CE 1000-1800.

Other Benign Neoplasms

Two cases of ameloblastoma have been reported in the paleopathological literature,

the first of which was found at 'Accés Est Casserres', a necropolis near Barcelona, Spain.

The individual was that of an adult male, aged 45 to 55 years of age and dated between the

fifth and ninth centuries; the lesion was located on the right gonion of the mandible

(Carrascal et al. 2013). The other case of ameloblastoma was found in Czersk, Poland,

again on the mandible of an adult male (Gładykowska-Rzeczycka 1978). In the Czech

Republic, Strouhal et al. (1996) report on a benign tumour, possibly a fibroma, found on the

skull of an adult male from a late 13th to mid 18th century CE ossuary in Moravia. The

lesion in question was described as a horseshoe-shaped groove in the posterior aspect of

both palatine processes of the maxilla (Strouhal et al. 1996: 295). More recently a teratoma

was found in an individual from Eten, Peru. A teratoma is a germ cell neoplasm that

develops and differentiates to varying degrees toward mature epithelial tissue types

including bone, teeth, hair, gut mucosa, lung and cerebral tissue (Klaus and Ericksen 2013:

1). The individual with this neoplasm was a female, aged between fifteen and twenty years;

the neoplasm itself was first observed to be an abdominal mass consisting of 83 bones and

38 dental elements, all of which were malformed and unclassifiable. Upon further

investigation, Klaus and Ericksen (2013: 5) diagnosed the neoplasm as an ovarian

teratoma.

Osteosarcoma

In Minoan Crete, McGeorge (1988: 50) identified a case of osteoblastic sarcoma, as

well as an unspecified case of metastatic cancer, though she does not give any specific

information to either case. Other cases of osteosarcoma include two femora from a

Pompeian sample, but there is no further information given regarding them (Henneberg

and Henneberg 2006: 32). From Egypt two cases have been thought to been found in

graves from the 5th Dynasty in Gizeh, however like the Pompeian example, there are no

illustrations or morphological descriptions given and might be a misdiagnosis (Micozzi

1991: 841). Another Egyptian example was observed on the pelvis of an individual dated

to CE 250. This tumour was observed to have originated in the trabecular bone, which then expanded to produce a deformation of the obturator foramen and began to encroach on the acetabulum (Ruffer and Willmore 1913: 483). A Polish example from Skrwilno was reported by Gładykowska-Rzeczycka (1997). This individual was an adult female dated to the medieval era and exhibited a tumour on the anterior surface of the distal metaphysis of the humerus; as this specimen was badly preserved a radiograph was taken to confirm the diagnosis (Gładykowska-Rzeczycka 1997: 47-48). The skull of an adult male from Paucarcancha, Peru, was observed to have a large tumour on the left parietal and frontal bones that had destroyed the inner table of the cranial vault and extended 4.5cm outwards from the skull (MacCurdy 1923: 264). Though the original author attributed this to an osteosarcoma, Ortner (1981: 735) speculated that this could instead be a meningioma. Finally Suzuki (1987) reports on a case of osteosarcoma in a pre contact – Hawaiian, young adult female from the island of Oahu. This tumour was located on the distal metaphysis of the left femur and was described to have a course, coral-like appearance. The diagnosis was based on the sunburst pattern that became apparent when viewed on a radiograph, however this characteristic should not be seen as an absolute indication for this type of malignancy (Waldron 2009: 179-180).

A case of periosteal osteosarcoma, a much less common variant of osteosarcoma, has also been identified archaeologically in the lower leg of a young woman from Medieval Corinth Bourbou (2003: 183) and another possible case was identified by Fox Leonard (1997: 451) on the shaft of a right humerus from Paphos. Periosteal osteosarcoma occurs in childhood and is generally located in the diaphysis of the long bones, but mainly in the femur and tibia; it has a low rate of metastasis (Campanacci 1990: 498). Evidence for this

condition is rare as it only occurs in approximately one percent of all osteosarcomas (Aufderheide and Rodrígues – Martín 1998: 379).

Multiple Myeloma

Multiple myeloma was observed in Egypt, on the skull of a male, aged 30 to 35 years old from between the 3rd and 5th Dynasties. The lesions consisted of eleven circular holes on the outer table of cranial vault, with no signs of ante-mortem or peri-mortem healing (Wells 1963: 261-262). As it is rarely found in individuals below the age of forty years (Roberts and Manchester 2005: 258), it is unknown if Wells' (1963) diagnosis was correct. Two cases of multiple myeloma were found in Florida the first of which dated from CE 500 to 1200 (Morse et al. 1974: 449) and the second was from CE 200 to 900 (Morse et al. 1974: 451). The first specimen was estimated to be a male aged 45 and exhibited a large opening on the occipital, frontal and parietal, penetrating both the inner and outer tables and additional lesions were revealed upon radiographic examination (Morse et al. 1974: 451). The second individual was a fragmented female skeleton that was approximately 25 years old at the time of death; this specimen also had punched-out lesions, characteristic of multiple myeloma (Morse et al. 1974: 452-453). Another case was found in a in a pre-Columbian male, dating to the late 9th century CE, excavated five miles west of Binghampton, New York (Ritchie and Warren 1932: 622). An additional pre-Columbian specimen, dating to the 13th century CE, exhibiting multiple myeloma was reported by Brooks and Melbye (1967). This was a female, aged 40 years and was excavated from the burial areas of the Kane Mounds near St. Louis, Missouri (Brooks and Melbye 1967: 23). A more recent example was uncovered in a medieval cemetery in the United Kingdom; the

skeleton was that of an elderly individual, probably male, who displayed multiple round, lytic lesions with smooth margins (Wakely et al. 1998: 950).

Metastasis

In Europe, Angel (1984: 68) mentions a Greek case of metastatic cancer in a skeleton from the Late Bronze Age, but unfortunately does not say where it was found or give any other pertinent information. Šefčáková et al. (2001) report on a case of metastasis, which they claim to be the oldest example from Slovakia dated from the 8th to 12th centuries CE. The individual is a male, aged between 50 and 60 years that showed observable lytic lesions on the skull and axial skeleton that were circular or ovular with irregular edges. In Northern Germany, Grupe (1988) tells of a male skeleton, aged between 40-50 years and dated from the 11th to 12th century. The skeleton was observed to have lesions on the os coxae, the hands, the lumbar vertebrae and the manubrium. Multiple myeloma was also considered but was then rejected, as the lesions were not uniform in size and not present in the skull. Assis and Codinha (2010) report on a probable case of metastatic carcinoma in the skeleton of an adult female that was excavated at the ancient necropolis of Constância, Portugal which is dated from the 14th to 19th century. The skeleton was observed to have lytic lesions on the skull and axial skeleton as well as the upper limbs and femora. These lesions were diagnosed as metastatic cancer due to their asymmetric pattern, their irregular shape and the presence of some mixed lesions consisting of both lytic and blastic activity, evidenced by fine woven bone (Assis and Codinha 2010: 607). In a Polish example, Kornafel et al. (2000) discuss a female skull, aged 30 to 40 years from sometime between the 15th and 16th centuries. This specimen was

noted to have a circular lesion in the parietal with wavy edges that widened towards the outer edge of the bone, creating a sort of crater; no other lesions were found on the cranium or post-cranially. Based on the lesion's location and the individual's age it was differentially diagnosed as a possible meningioma or metastatic brain cancer (Kornafel et al. 2000: 34-35).

In Asia, Suzuki (1989) mentions a Japanese adult, fragmented skull found on Honshu Island from the Jomon period dated from the 2nd to 1st millennia BCE. In South America, Luna et al. (2008) reports an Argentinian specimen of an adult male, aged 40-50 years, which was excavated from a prehistoric cemetery in Lihué Calel National Park. This individual was dated from between 1030 and 370 BCE (Luna et al. 2008: 493). In Chile, Allison et al. (1980) notes a female mummy bundle, dated to the eighth century CE, which exhibited three large cranial lesions on the parietals suspected to be metastatic. From North America, an Alaskan cranial fragment of an adult male Paleo-Eskimo was observed to have rounded lytic lesions with grooved borders. A radiographic examination revealed more areas of bone loss within the bone, further implying a metastasis (Lagier et al. 1982: 242). Other examples of metastasis have also been reported in the paleopathological literature (Tashiro 1982; Smith 2002; Ortner et al. 1991; Møller and Møller 1952; Mays et al. 1996; Manchester 1983, Marks and Hamilton 2007; Baraybar and Shimada 1993).

Metastatic prostate cancer seems to be more easily recognized in the archaeological record compared to other soft tissue carcinomas such that of the breast or lung due to its characteristic formation of osteblastic lesions. For example, Prates et al. (2011) employed Multi Detector Computerized Tomography (MDCT) to detect several dense bone lesions

located on the spine, pelvis and proximal extremities of a male Ptolemaic Egyptian mummy, from the Museu Nacional de Arqueologia in Lisbon. Tkocz and Bierring (1984) report on a possible case of secondary prostate cancer in the remains of an adult male dating back to the Middle Ages in Denmark based on the presence of osteoblastic lesions on the axial skeleton. In a male aged 45-55 years and dating to the 14th century CE from Canterbury, England, Anderson et al. (1992) also diagnosed metastatic prostate cancer based on the osteoblastic deposits on the pelvis, ribs and skull, as well as the age and sex of the individual. Finally Waldron (1997) identifies a case of secondary prostate cancer in a male from the 19th century that exhibited widespread periosteal new bone on the base of the skull, the vertebrae and the right scapula. Interestingly, Waldron (1997: 244) also notes that in Europe there appears to be a positive gradient in the incidence rates of prostate cancer among religious groups (Protestants>Catholics>Jews) and higher social class; from this it could be that socio-cultural factors might also have a role in the aetiology and incidence of this disease.

CHAPTER 4: METHODS AND MATERIALS

Methods

My methodology consisted of first reviewing the cases of neoplastic disease found in the Athens Collection using macroscopic and microscopic observations, and then comparing those observations to the suspected neoplastic lesions in the archaeological material. The Athens Collection was of use for this research due to the high amount and variety of secondary neoplasms that were represented; unfortunately there were no primary bone cancers within this collection, other than leukemia, a cancer of the blood that originates in the bone marrow. The goals of examining the Athens Collection were to methodically and rigorously review the appearance of neoplastic-derived lytic and blastic lesions and then to see if metastatic lesions from different types of cancer were in any way characteristic in their appearance or destruction across the skeleton.

I had complete access to all the neoplastic cases in the collection and with each case I began my investigation by examining the components of the axial skeleton, namely the skull, pelvis, ribs and vertebrae. This is where 90% of bone metastases occur due to the high presence of red bone marrow and distribution of cancer cells through the Batson venous plexus (Coleman 2006: 6243s; Batson 1940). I also included the scapulae in the initial investigation as I noticed that more than one of the cases exhibited clear scapular lesions. I then macroscopically examined each bone from all aspects for signs of lytic or blastic activity that consistent with cancer. Lytic lesions were those created through destruction of bone. Blastic lesions were those that appeared to be proliferative or extra growth of new bone; this included both cortical and periosteal bone. I limited my

investigation to the axial skeleton due to the predilection of metastases spreading to this region and time constraints. However, if a cursory examination of the appendicular bones indicated the presence of lesions, these too were recorded. After the initial macroscopic review of the axial skeleton I recorded the specific nature of each lesion observed.

To facilitate the documentation, I created data forms designed for recording neoplastic lesions. I used the style and organization from the recording forms found in Buikstra and Ubelaker (1994); their design was aimed to incorporate measurements, descriptions and neoplastic-specific categories. These forms were necessary as there is no standardized form of recording for this disease category. The first form (Appendix A) was used as a summary for each skeleton, indicating the distribution of neoplastic lesions, as well as other biographic information such as the age and sex of the individual.

The second or form (Appendix B) was used to record the individual lesions on each individual bone. Using this, I recorded the total number of lesions that were observed on each bone. Each form allowed for detailed observations to be made for a maximum of six lesions. For simplicity and to avoid confusion, each lesion was assigned a number between one and six to be used as a descriptor in the form. Measurements were taken of the maximum length, maximum width and, if applicable, the maximum height and/or depth with Standard Gage metric digital callipers; a soft measuring tape was used for lesions that were either fragile or too difficult to access with the callipers. Measurements were not taken for lesions that occupied the entire surface of the bone, as this seemed redundant; I simply noted that the lesion extended over the entire surface. I also noted whether the lesion affected the cortical, trabecular or subchondral bone. I classified the lesion as

benign, malignant or unknown; and blastic, lytic or mixed. Here "lytic" was used for lesions that had destroyed bone, "blastic" was used for lesions that built up bone and "mixed" was for lesions that exhibited a combination of building and resorbing bone. The designation of "benign" was given to nonaggressive lesions that were not invasive or destructive, while "malignant" was used for lesions that were aggressive and destructive. When these designations were established I further distinguished the lesions as either primary, metastatic or unknown. I also noted whether there were other pathologies present, the condition of the bone and what kind of documentation I had for each specimen including: photographs, microscopic photographs, radiographs and drawings.

Microscopic observations were accomplished through the use of a Dino-Lite digital microscope and were primarily used to distinguish between pathological lesions and post mortem damage. This was done by microscopically examining the edges of lesions; those that appeared ragged or brittle and displayed a different colour then the surface of the bone were determined to be post-mortem damage, while edges that appeared smooth, scalloped, or moth-eaten were considered pathological.

After reviewing the cases in the Athens Collection, I examined the archaeological material in the Athenian Agora and Corinth, as well as modern skeletons in the Wiener Laboratory and University of Waterloo with the same methodology used on the modern skeletal material. For the archaeological material my goal was to re-examine the previous diagnoses offered by other researchers. For the newly discovered cases in the Wiener Laboratory and Waterloo collections, my goal was to establish a differential diagnosis that

considered cancer as an option. During this time I continued to make use of the Athens collection as a comparative reference.

Materials

This project required examining both known, identified cancer cases and undocumented lesions in archaeological and modern remains. To accomplish this I looked at five skeletal collections, examining a total of 37 specimens. This consisted of 23 specimens with neoplastic lesions from the Athens Collection (Appendix C) and seven archaeological specimens that were identified as displaying evidence of neoplastic activity. The archaeological material in this study was comprised of previously excavated skeletons in Greece from the Athenian Agora (Bourbou 2003; Little 1997)[3] as well as from Ancient Corinth (Fox Leonard 1997; Zervos et al. 2009) (Appendix D). While these examples were previously published, my intention was to reassess the differential diagnoses after reviewing other known cases from the University of Athens Collection. I also identified seven specimens from the comparative skeletal collection in the Wiener Laboratory at the American School of Classical Studies in Athens and from the osteology laboratory in the Anthropology Department at the University of Waterloo (Appendix E). These are unpublished, previously unidentified specimens for which I conducted the first differential diagnoses.

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[3] As cited in Bourbou (2003: 183).

Materials Catalogue

The Athens Collection

A key component to my research was being able to examine the University of Athens Human Skeletal Reference Collection. The collection consists of over 200 skeletons with documented age, sex, occupation, place of birth and death, and cause of death. The collection was first developed in the Wiener Laboratory at the American School of Classical Studies at Athens between 1996 and 1997. Skeletons with inventory numbers beginning with WLH are part of this original collection. It was later donated to the Department of Animal and Human Physiology at the University of Athens and was further expanded during 2001 and 2003 (Eliopoulos et al. 2007: 222). Skeletons with inventory numbers beginning with ABH are the new additions the collection, since its move to the University of Athens. All of the remains come from unclaimed exhumations from Greek cemeteries. Greek cultural funerary customs include reburial three to five years after the funeral but if family members are unable to pay the rent on cemetery space then the remains are placed in an ossuary and then into a large underground pit. As these unclaimed skeletons present an opportunity for anthropological research, the remains were added to the Athens collection, instead of being placed in the underground pits (Eliopoulos et al. 2007: 222).

When this collection was being amassed the specimens were initially selected for the visible presence of pathologies and cancer was well presented. In the Athens Collection, 54 specimens are listed as having cancer as their cause of death and include primary and secondary carcinomas of sift tissue. All of the specimens were well preserved and were complete except for a few small bones, such as from the hands and feet, that were not

39

recovered during the exhumation. Due to time constraints I was only able to examine 23 of

the 54 specimens. I chose to examine representation from each type of cancer listed in the

catalogue, focusing on those that hare often cited in the medical literature in regards to

metastasis, namely lung, breast and prostate cancers. I also reviewed other types that are

not often cited such as ovarian and pancreatic cancer. In total I examined skeletal lesions

associated with 10 types of soft tissue cancer. The specimens I studied included the

following: (see also Appendix C).

WLH 4

WLH 4 was a 68-year-old housewife who died in 1964. Her cause of death was

listed as cancer with widespread metastasis and wasting. Metastatic lesions were observed

on the skull, pelvis, femora, humerii, scapulae, tibiae, ulnae and radii (Fig. 2). These

consisted of mixed lytic and blastic lesions. The lesions were not bilateral, as the left femur

had substantial blastic reactions on the cortical bone alone the diaphysis.

WLH 13

This was a 49-year-old housewife who died in 1965 of lung cancer with multiple

metastases (Fig 3). The skull exhibited a large, lesion on the left frontal, near the coronal

suture. The centre of the lesion had lytic holes penetrating the cranium and the outer

margins of the lesions consisted of lytic porosity of the cortical bone. This porosity

consisted of holes of varying size and it extended past the suture onto the left parietal (Fig.

4). Both femora had a pathological fracture at the proximal diaphysis. The epiphyses were

normal in both bones, but the diaphyses had extensive periosteal reactions along the entire

surface of the bone, culminating in striations at the distal end (Fig. 5). Her ribs exhibited lytic porosity, which also resulted in a pathological fracture.

WLH 14

This was a male, aged 65-years-old and died in 1985, with cause of death listed as cancer with metastasis to the brain. In general, most of the lesions throughout the skeleton were lytic, round in shape and roughly the same size (Fig. 6). The sphenoid was destroyed and lytic lesions, measuring approximately 5-10mm in diameter, were observed endocranially. On the long bones, there were proliferative lytic lesions that appeared punched out; conversely the proximal femur had blastic growth. The pelvis had widespread destruction, with space occupying lesions in the trabecular bone. The sternum had a large, round lytic lesion as well. In the vertebrae, the lumbar bodies were half destroyed, giving the appearance of having been carved out.

WLH 15

This specimen was a 5-year-old juvenile female who died of leukemia in 1968. Fine porotic lesions were observed on the pelvis, scapulae, vertebrae, maxilla, mandible, temporals, parietals and cranial base (Fig. 7).

WLH 29

WLH 29 is the only identified example of prostate cancer in the Athens Collection. The specimen is that of a male, aged 96 years old, who had died in 1986; he was a lawyer. On the ischium there was blastic activity consisting of smooth, bony islands. On the sternum, there were thin sheets of new periosteal bone as well as on the sacrum, iliac crest,

pubis and the posterior of the ilium (Fig. 8). This individual also had a severe case of DISH, with fusion of 12 consecutive vertebrae from the thoracic and lumbar regions. With this individual, some of the lesions observed could be attributed to his advanced age.

WLH 32

This 44-year-old housewife died in 1988 due to brain cancer (Fig. 9). The sella turcica of the sphenoid had been completely destroyed and there was a marked roughness at the endocranial spheno-occipital synchondrosis. There also appeared to be lytic activity on both lacrimals and the surrounding area.

WLH 46

This was a male aged 27 years old who died of pancreatic cancer. Apart from lytic lesions along the sacrum, there was no other observable skeletal involvement.

WLH 50

This was a male, aged 50 years old who died of brain cancer in 1966. On the frontal and occipital was a possible hyperostosis but without a radiograph this could not be confirmed. On the endocranial surface of the parietal were large lytic lesions and the diplöe was thin in some areas, lacking trabeculae. On the sphenoid, lytic lesions were observed on the greater wings and sella turcica; the lesser wings appeared to be moth eaten.

WLH 62

This was a male, aged 41 years old who also died of brain cancer. Blastic activity in the form of an osteophyte was present on the sphenoid at the sella turcica. On the endocranial surface of the frontal bone there was a large lytic lesion measuring approximately 1cm in length. Porosity was also observed around the auditory meatus. Interestingly, this specimen had a large, round trephination on the posterior, right parietal, the edges of which had signs of healing (Fig. 10). This suggests that surgery was performed on this individual for his brain cancer.

WLH 72

This specimen was a male pilot, aged 60 years old who died in 1981 of pancreatic cancer. Like the previous pancreatic cancer case, WLH 46, there was little skeletal involvement. There were bony crenulations on the iliac crest, which could be a roughened muscle attachment. The sacroiliac joint was fused as well, but this could be due to age, as evidenced by signs of joint disease in the spine.

ABH 84

This was a 65-year-old female, whose cause of death was listed as generalized carcinomatosis and heart and respiratory failure. Small lytic lesions were observed on all of the vertebrae, primarily on the lumbar vertebrae (Fig. 11).

ABH 88

This breast cancer case was a female aged 35 years old at time of death (Fig. 12). There were localized swellings on the shafts of both the left and right fourth to eighth ribs that appeared to be blastic in nature. As some were broken in half at the site of the lesion,

it appears that the rib shafts had expanded outward to accommodate a tumour until they split in half; this is evidence of a space-occupying lesion.

ABH 91

This specimen was a female aged 51 years old, who also had died of breast cancer (Fig. 13). Small metastatic lesions were seen on the iliac crests that were circular in shape, with a mix of smooth and ragged edges. There was also minor lytic activity on the scapula, consisting of very small lesions that were irregular in shape. The ribs had sporadic lytic holes throughout the shafts that were circular in shape and relatively similar in size.

ABH 92

This was a female aged 54 years old who died of ovarian cancer. In this specimen possible lytic lesions were observed on the posterior-medial ilium.

ABH 93

The other case of ovarian cancer was in a woman aged 47 years old. Apart from minor lytic activity at the iliac crest and sacrum this specimen showed very few skeletal lesions.

ABH 95

This was a female, aged 37 years old, whose cause of death was listed as nasal cancer. There was widespread destruction in the nasal cavity; the vomer, sphenoid, lesser conchae and lacrimals were all affected. This specimen had some lytic lesions on the ilium.

ABH 96

ABH 96 was a female, aged 33 years old who had died of a brain tumour. The spheno-occipital synchondrosis was destroyed through lytic activity, resulting in large gaps at the cranial base. There was also some destruction of the dorsum sellea of the sphenoid and the endocranial surface of the frontal. Post-cranially there were no observable lesions.

ABH 101

This specimen was a 2 year old, juvenile female who died of leukemia. Fine porotic lesions were observed on the pelvis, scapulae, maxilla, mandible, and temporals (Fig. 14).

ABH 111

This was a 44-year-old male whose cause of death was lung cancer. Here the ribs have some trabecular bone loss and only one had a noticeable blastic lesion, which consisted of a round growth on the distal end of the shaft; its appearance was reminiscent of a cortical shell due to its hollow cavity.

ABH 112

This was a female aged 56 years old, who died of buccal cancer. The most noticeable observation was the destruction of the lower facial bones, specifically in the maxilla and mandible (Fig. 15). The lesions were only on one side, suggesting that the cancer was unilateral. On the mandible there was blastic activity around the mental foramina and lytic deterioration of the mental eminence, both anteriorly and posteriorly. The lytic activity extends up into the eye orbit, temporal, lateral aspect of the frontal, the sphenoid and the inferior zygomatic; however, these bones were not as greatly affected as the maxilla and mandible.

ABH 147

This specimen was an 84-year-old male who died of lung cancer. Metastatic lesions were observed on the pelvis, with a focus at the iliac crest and near the auricular surface. On both of the scapulae, the inferior portion of the blades exhibited lytic lesions. The sacral bodies had round lytic lesions as well. In the spine, there was progressive destruction towards the lumbar region. The ribs were badly damaged by lytic activity, leaving them hollow, and the remaining cortical bone at the sternal ends was twisted in various directions (Fig. 16).

ABH 187

This specimen was a 9-year-old, juvenile female who died of leukemia. Fine porotic lesions were observed on the scapulae, vertebrae, femoral metaphyses, maxilla, sphenoid, mandible, temporals, parietals and cranial base (Fig. 17).

ABH 202

This specimen was a 25-year-old female who died of leukemia. There was very little skeletal involvement apart from minor porosity on the right ischium and ilium as well as both scapulae at the inferior and superior margins (Fig. 18).

The Athenian Agora

The Athenian Agora has been undergoing excavations by the American School of Classical Studies since 1931. Located at the base of the north side of the Acropolis, the Agora was the market place and civic centre of public life in ancient Athens (Camp 2003: 4).

The skeletons I examined were from two wells, dated to the Neolithic and late antique periods, and a Christian grave.

AA 13

The first specimen from the Athenian Agora was AA 13, a female, aged 30-39 based on the morphology of the auricular surface (Lovejoy et al. 1985), from a Roman era well that was excavated in 1936. The body was deposited in the well following the Herulian Sack of Athens in AD 267, and is believed to be a victim of this attack (M. Liston, personal communication.) This specimen was well preserved and the skull had severe blunt force trauma on the face and right parietal. A lytic lesion was observed on the left aspect of the occipital, inferior to the lambdoidal suture (Fig. 19). This lesion had penetrated both tables, leaving an irregular shape and bevelling at the upper margin. Angel (1945: 316) initially diagnosed this lesion as post-mortem damage.

AA 32

Specimen AA 32 dates to the Neolithic Period and was one of two individuals recovered from a well in the Agora (Angel 1945: 291-292; Shear 1940: 298). According to Angel (1945: 293) this specimen was a young adult male. AA 32 was fragmented, consisting of only the calvarium. A large benign growth projected from the left aspect of the occipital squama (Fig. 20) (Angel 1945: 293).

AA 83b

The last skeleton, specimen AA 83b, is that of a male aged 35-39 based on the auricular surface (Lovejoy et al. 1985), from a Byzantine grave found under the floors of the Temple

of Hephaestus, which was converted to a Christian church in the seventh century CE (Camp 2003: 12). After death this individual was originally placed in a small wooden box, buried in a simple cut grave and was excavated in 1939 (Agora Notebooks, Section Alpha Alpha: 1704). These remains were comingled with another individual while kept in storage at the Agora. With help from M. Liston, I attempted to differentiate the two individuals, however it is possible that some skeletal elements might have been confused for the other. This specimen was well preserved and had observable lytic and blastic lesions on the skull, the pelvis, the vertebrae, the thoracic cage and the long bones (Fig. 21).

Ancient Corinth

The site of Ancient Corinth has been occupied since the Early Neolithic and has been undergoing excavation by the American School of Classical Studies since 1896 (Leekley and Noyes 1976: 75). For my research I included four specimens from this site, which ranged from different time periods including the Late Classical (fifth century BCE), Late Roman (fourth century CE) and Ottoman rulings (17th century). Of these specimens, two were individuals within comingled burials (Fox Leonard 1997), while the last two were excavated recently from an early Ottoman cemetery in the Panayia Field (Zervos et al. 2009). All of the specimens were weathered, bleached white, fragmented and not well preserved. The skeletal material at this site was comingled while in storage and with help from M. Liston, I attempted to locate the previously identified lesions that were reported by Fox Leonard (1997) and Zervos et al. (2009).

61-10

Of the two individuals with neoplasms reported by Fox Leonard (1997) the first of these skeletons was an individual from burial 61-10 which was excavated in 1961. This burial dates to the second century CE of the Roman Period and included the remains of a subadult aged eight to nine years of age. Sex was not determined due the individual's young age and that sexing solely long bone can be problematic. Of interest in this burial was a tibia that exhibited a swelling at the proximal diaphysis (Fig. 22). Fox Leonard diagnosed this as a giant cell tumour (1997: 306).

62-31

The other specimen from this series was in burial 62-31. This burial consisted of an inverted limestone sarcophagus, which dates to the third century CE of the Roman period and was also excavated in 1962. The skeleton is that of an adult female, but could not be more precisely aged, as there were no epiphyses present or evidence of incomplete tooth root formation (Fox Leonard 1997: 354). On the frontal there was a very small osteoma, ovular in shape, measuring 2.45mm long and 1.36mm wide (Fig. 23).

2000-09

From the Ottoman cemetery, specimen 2000-09 dates to the seventeenth century CE and is a female aged 25-27 years old at time of death (Zervos et al. 2009: 560). This individual had an irregular lytic lesion on the left frontal that penetrated both the inner and outer table, with porosity around the edges; the lesion appeared bevelled on the inner table (Fig. 24). The skull was well preserved but was very fragile and no longer held together by

the sutures. A fragment of the scapula had possible lytic lesions and two thoracic vertebrae had lytic lesions on the vertebral body and spinous process.

2002-1b

Specimen 2002-1b was a male aged 39-44 years old (Zervos et al. 2009: 596). On the right innominate there was lytic activity along the posterior iliac crest, which consisted of small porosities (Fig. 25). However as this lesion was obscured by dirt and it was not possible to properly wash the bone in the time available, no other observations could be made. The occipital also had an irregular shaped impression on the endocranial surface, which measured 67 x 20mm (Zervos et al. 2009: 596).

The Wiener Laboratory at the American School of Classical Studies in Athens

Skeletal material from the Wiener Laboratory's Comparative Specimen Collection was also utilized. Though the origin of these specimens is unknown, Dr. Sherry Fox, the director of the Wiener Laboratory at the American School of Classical Studies, suggests that they are all pre-modern dating to around the 19th century CE and are possibly from the Athenian Agora (personal communication).

L 1

Specimen L 1 was the remains of an adult male, aged 35 to 39 according to the morphology of the pubic symphysis (Brooks and Suchey 1990; Suchey and Katz 1986). The skeleton was incomplete and possibly comingled with other specimens in the comparative collection. Both innominates of this specimen displayed similar lytic activity in the iliac

crest (Fig. 26). There was also post mortem damage in this area exposing much of the trabecular bone, which appeared normal.

WL 1

This specimen was that of a juvenile aged one year based on dental formation and eruption (Ubelaker 1989: 47); due to this very young age sex was not determined. Porous lesions were observed on the skull, including the frontal, temporals, occipital, sphenoid, maxilla, and mandible, as well as the left and right scapula, the humerus, ulna, femur and tibia (Fig. 27). The majority of these lesions consisted of a fine porosity in the cortical bone. Small lesions of periosteal new bone were also seen on the endocranial surface of the frontal around the frontal crest. In this specimen the pelvis was not present.

WLCS

WLCS was composed of four bone fragments (Fig. 28). It is unknown if any of these fragments are from the same individual, however the minimum number of individuals is one and the degree of preservation and bone colour were consistent with a single individual. These fragments consist of WLCS 1, a proximal diaphysis of the right ulna, which had a possible space-occupying lesion; the interior of the bone appeared to be hollowed out and the surrounding trabeculae did not appear damaged. WLCS 2 was a right femoral head that exhibited a lot of post-mortem damage akin to lytic pathologies; with the use of microscopy post-mortem damage was confirmed. WLCS 3 and WLCS 4 were both distal ends of the left femora. Very small lesions were observed at the lateral edge of the femoral condyles, however these may not be cancerous and instead may be either joint related or post-mortem damage.

Anthropology Department, University of Waterloo

Finally, the last four specimens to be included in this study consisted of skeletal material from the osteology laboratory in the University of Waterloo. As most teaching skeletons in North American universities were bought from India, the largest supplier until the country banned the practice in 1987 (Corrales 1987), it is probable that this material came from that region and a pre-modern date. All of these specimens were well preserved.

UW 8

The first of these specimens was UW 8, an adult male, aged 25 to 35 based on the pubic symphysis and auricular surface (Brooks and Suchey 1990; Suchey and Katz 1986; Lovejoy et al. 1985). This was an articulated teaching skeleton in the Anthropology Department's osteology laboratory and was disarticulated at the beginning of 2013. Upon disarticulation it was observed that all of the left ribs and two of the right ribs had a mix of blastic and lytic activity on the pleural side of the shafts. Lytic porosity was also observed on the spinous processes of the fifth and sixth thoracic vertebrae, the iliac crest of the left innominate, the mandible, femora and the endocrainal surface of the frontal and parietals. In the sphenoid, the sella turcica had also undergone lytic destruction. Radiographs were taken of the axial skeleton and the proximal femora, revealing more lesions in the bone that were unobservable before, notably in the sternum and the innominates (Fig. 29).

M 1

The second specimen was the mandible of an adult female based on the presence of the third molar (which is missing due to post-mortem loss) and a visual, macroscopic analysis

of the cranium, which included gracile features and the absence of an occipital

protuberance. This specimen had a large osteoblastic growth on the right gonial angle that

was smooth and ovular in shape (Fig. 30). A radiograph showed that this lesion was

composed of cortical bone.

CA 1

The third specimen from the University of Waterloo was CA 1, which consisted of the

skull of an adult male aged 30 to 45 years old based on cranial suture closure (Buikstra and

Ubelaker 1994: 32-38). A small osteoma was observed on the left frontal above the

supraorbital margin (Fig. 31).

UW 23

The final specimen was UW 23, a recently acquired skull of a female, aged 7-12 years

based on the infusion of the spheno-occipital synchondrosis and the recent fusion of the

occipital condyles. Fine, porous lesions were observed on the frontal, temporals, occipital

and maxilla (Figs. 32).

CHAPTER 5: RESULTS

The skeletal lesions observed in this study are outlined in this chapter. Beginning with the medically identified cancers cases in the Athens Collection, I will review the lesions among specific types of cancer as well as the non-specific cases of metastasis. From this I will proceed to the suspected cases of cancer from four different sites, two archaeological and two pre-modern. From examining all of these specimens, I noticed similarities among the lesions' appearance and distribution.

The Medically Diagnosed Cases in The Athens Collection

In the Athens Collection, cases specifically catalogued as metastatic exhibited a variety of lesions with similar appearances. The individuals with metastasized cancers had the most clearly diagnostic lesions. Some individuals had primarily lytic or blastic lesions; others had mixed lytic and blastic skeletal responses. The primarily lytic lesions were seen in cases of brain cancer and leukemia (WLH 15, WLH 32, WLH 50, ABH 96, ABH 101, ABH 187). Primarily blastic lesions were seen in prostate cancer (WLH 29). Mixed lytic and blastic lesions were found in breast and lung cancer and non-specified metastasis (WLH 4, WLH 13,WLH 14, WLH 33, WLH 42, WLH 55, ABH 88, ABH 91,ABH 111, ABH 147).

Cases of Unspecified Metastasis

WLH 4, a case of cancer with widespread metastasis and wasting, exhibited diffuse lesions on the skull, pelvis, femora, humerii, scapulae, tibia, ulnae and radii. These lesions consisted of a mix of lytic and blastic activity that were observed throughout the skeleton and were not symmetrical. On the skull, periosteal lesions were seen on the frontal and the

parietals. On the frontal a large lesion was located along the midline, superior to glabella, a smaller lesion was on the right portion of the sqauma close to the coronal suture and in between these was a third, smaller lesion (Fig. 33). These lesions consisted of a mixed periosteal reaction where the bone had been destroyed and developed in a number of areas. Lytic porosity could be seen along the margins and overall these lesions were round and irregular in shape. At the back of the skull on both parietals, there was a similar lesion. Here it extended over the sagittal suture and down toward the occipital. On the parietal a large hole had formed penetrating both tables, the edges of which were ragged and moth-eaten (Fig. 34). The left innominate had a cluster of blastic lesions on the ilium and auricular surface. The lesions on the ilium were irregular in shape and consisted of rough bone laid over the cortex; on the auricular surface these lesions consisted of small bony globules of cortical bone. A small blastic lesion of irregular, rough bone was also observed between the auricular surface and the retro-auricular area (Figs. 35, 36). On the left scapula, four blastic lesions were noticed on the anterior scapular blade and two on the posterior, inferior to the scapular spine (Figs. 37, 38). The left femur exhibited osteoblastic activity along the mid diaphysis that was not as extensive on the right femur. This lesion had altered the cortical bone, making it appear rugged and misshapen. The same was seen on the right humerus and in both long bones the epiphyses and joint surfaces were spared. Osteoblastic lesions were round in shape and varied in size, however on the long bones they were ovular in shape.

For WLH 14 the cause of death was attributed to metastasis to the brain. There were mixed lytic and blastic lesions. Lesions were also observed on the skull, pelvis, vertebrae and thoracic cage. The majority of these lesions were round and roughly the same size,

with edges that appeared chewed due to their small irregular points and they looked to radiate outward form a central point, expanding and destroying more bone in the process. At the cranial base, the basilar of the occipital and body of the sphenoid is completely destroyed (Fig. 39). Lytic lesions were also present on the inner table of the cranium that ranged between 5 and 10mm in diameter. Widespread destruction was seen in the pelvis with space-occupying lesions found in the trabecular bone of the ilium (Figs. 40, 41). This is where a soft tissue tumour has infiltrated the bone and, after death, had decayed leaving a negative impression of its shape. In the spine there were lytic lesions in the vertebral bodies, similar to those seen in the pelvis, characterized as round and of various size; the lumbar bodies had greater destruction with the appearance of having been carved out by the tumour (Fig. 42). In the thoracic cage, the sternum had a solitary lytic lesion on the superior body that had completely destroyed the bone, leaving a large opening (Fig. 43). The edges of this lesion were ragged and there was no reactive bone at the margins. Lytic metastatic lesions do not follow bone geography, but appears to expand in a roughly circular shape, and do not differentiate between the contours or features of the bone as it continues to expand. For example, in WLH 14, the left scapula has a round metastatic lesion on blade that extended through the bone into the base of the spine leaving a large opening approximately 15mm in length. Though the scapular spine is much thicker than the blade, the cancer continued to progress through the bone. The ribs also had round destructive lesions that caused many to break in half. The long bones of WLH 14 had a mix of lytic and blastic lesions at the diaphyses, with no complications at the epiphyses or metaphyses. The lytic lesions were round and appeared punched out indicating that they were quickly destroyed and there was no attempt to build new bone in these areas (Fig.

44). Lytic activity in the left femur had caused the proximal end to break away from the rest of the bone; this allowed for viewing of the femoral epiphysis, which was devoid of trabecular bone (Fig. 45). With this loss of bone and lytic destruction, the individual would not have been able to support their weight and walking would have been difficult.

Breast Cancer

In ABH 88, the cause of death was attributed to the breast cancer metastasis to the lungs. In three of the ribs, I noticed that pathological fractures had occurred. These were located on different regions of the shaft of each rib and in the interior of the bone, new bone formation could be seen. Moreover, there were signs of healing as evidenced by a bulbous growth of bone around the edges (Fig. 46). The other breast cancer case, ABH 91, displayed small metastatic lesions at the iliac crest (Fig. 47). These were circular in shape and had a mix of smooth and ragged edges; the underlying trabecular bone was completely destroyed, leaving only the cortical bone on the opposite side; similar lesions were seen on the rib shafts, though these were smaller.

A surprising find among the breast cancer cases was an osteoblastic lesion on the posterior left parietal of WLH 91(Fig. 48). This lesion was flat and round with a clear demarcated border. Ortner identified a similar lesion in an individual from Peru as an osteoma (2003: 517, figure 20-21). In this case, the tumour was also on the parietal and was also flat and round with a clear border.

From the breast cancer cases, lesions appeared predominantly on the ribs and pelvis. These consisted of a mix of blastic and lytic lesions. In the ribs, pathological fractures

occurred and there was evidence of healing. The same was not observed in the lung cancer cases where rib lesions were also observed.

Lung Cancer

Three of the lung cancer cases, WLH 13, ABH 147 and ABH 111, had similar lesions on the ribs, though in ABH 111 this was seen to a lesser extent. In these cases, the ribs displayed a mix of lytic and blastic lesions. The ribs of ABH 147 were damaged by lytic activity, leaving them hollow, and the remaining cortical bone at the sternal ends was twisted in various directions. In ABH 111 the ribs were in better condition but there was a noticeable osteoblastic lesion in the form of a round growth at the distal shaft, which appeared as a hollow, cortical shell. In WLH 13, one rib had a pathological fracture resulting form lytic destruction (Fig. 49). Unlike in the breast cancer cases, there was no evidence of attempted healing. Round, lytic lesions in ABH 147 were also on the pelvis and bilaterally on the inferior scapular blades; these were similar to the scapular lesions in WLH 14 as they progressed through the blade and into the scapular spine. In comparison to the breast cancer cases, lung cancer is similar in its lesion distribution to the rib that can result in a pathological fracture. However in breast cancer there was an attempt to repair the damage, while in lung cancer there was not. Apart from this distinction, it is difficult to discern between the two cancers.

Brain Cancer

The brain cancer cases, WLH 32, WLH 50 and ABH 96 had lesions on the sphenoid. This consisted of lytic destruction of the sella turcica and greater wings. In WLH 32, the clinoid processes of the sphenoid were destroyed and lytic lesions on the greater wings were

apparent in the eye orbits (Figs. 50, 51). In WLH 50, the clinoid processes were also destroyed and the damage extended the sella turcica, where through lytic destruction, the trabecular bone had been exposed. The left greater wing had a lytic lesion near the sphenoidal body. The edges were moth-eaten and the trabecular bone was exposed (Fig. 52). Damage was seen on the cranial base of ABH 96 where there was a large gap between the sphenoid and occipital, caused by lytic destruction. In summary, brain cancer seems to affect the sphenoid causing destruction at the sella turcica and the greater wings. In these cases there were no post-cranial lesions and this could be due to the low survival rate of brain cancer, which has been reported to be approximately 18% (Sant et al. 2003: v108).

Prostate Cancer

WLH 29 was the only identified case of prostate cancer in the Athens Collection and osteoblastic lesions were distributed throughout the skeleton. The majority of these were characterized as thin sheets of periosteal new bone laid down on the sternum, ribs, sacrum, scapulae, pubis and ilium. There were larger bilateral, boney growths on the ischium that consisted of smooth boney islands that were irregular in shape; more of these lesions were seen on the left ischium than on the right. On the iliac crest of both innominates, there were boney growths creating an extra shelf of bone with crenelated edges but I was unable to find similar descriptions of such lesions in the paleopathological or medical literature regarding prostate cancer. However, two other cases from the Athens Collection, WLH 33, brain cancer, and WLH 50, breast cancer, displayed similar a pelvic lesion (Fig. 53). As descriptions of this could not be found in the medical literature it is unknown if this bony development is due to cancer or another cause. For instance, since the iliac crest is an

attachment site for three layers of abdominal muscles including the obliquus externus abdominus and obliquus internus abdominus, which are used for actions such as digging and raking (Jarmey 2004: 242-244), these growths could be the result of repeated, strenuous activity.

Leukemia

Of the four leukemia cases, the three juveniles, WLH 15, ABH 101 and ABH 187, exhibited similar distribution of porous lesions on the cortical bone of the pelvis, vertebrae and skull. The fourth individual, ABH 202, an adult female, did not display any lesions. The skull that had the most porosity in all of the specimens and these lesions were located on the parietals, the temporals, the maxilla and the mandible. WLH 15 and ABH 187 were more similar in their distribution pattern because they also had lesions on the base of the skull around the basilar suture.

Among the juveniles, pitting was observed in the maxillae and mandibles along the alveolar processes. Given the ages of these individuals, which range from 2 to 9 years, this pitting could be due to dental eruption as this bone is highly reactive. However I discounted this because the pitting continued from the alveolar processes up towards the nasal aperture and the inferior orbital margins in WLH 15 and ABH 187. In the same specimens, the pitting also extended to the zygomatics along the frontal processes, while in ABH 101 and ABH 187 bilateral porosity was noted at the coronoid processes (Fig 54). At the temporals all three individuals exhibited fine porosity superior to the external auditory meatus; ABH 187 also had porous lesions on the zygomatic process and the right temporal squama. On the neurocranium there was much less porosity in all three cases. The only

similar location was in ABH 187 and WLH 15 with porosity at glabella. In ABH 187 some

porosity was also observed along both parietals that was characterized by slight pitting on

the outer table. Endocranially, ABH 101 exhibited porosity on the occipital at the internal

protuberance. This porosity was concentrated at the centre of the feature and radiated

superiorly.

Postcranially, thee three juvenile cases had porous pelvic lesions on the pubis and the

ilia; in ABH 101 and WLH 15 this was extended to the ischium as well. These lesions

consisted of fine porosities in the cortical bone, which were not bigger than 1mm in

diameter. Similar porosity was also seen among all three cases at the axial borders of the

scapulae and along the scapular spines. Here the porosity was more pronounced and

rugged, with larger porosities than was seen in the pelvis. In the scapulae, there was

porosity on the scapular spine, the inferior angle and margins of the body (Fig. 55). The

vertebral bodies of ABH 187 and WLH 15 also exhibited porosity in the thoracic and

lumbar regions.

From these individuals, it appears that leukemia causes lytic pitting of the cortical bone

and the lesions tend to be seen on the pelvis, scapulae and spine, with a high concentration

on the facial bones.

**Previously Identified Archaeological Cases from the Athenian Agora and the Corinth
Excavations**

I examined skeletons with neoplastic lesions that had been previously identified

from two different archaeological excavations in Greece: the Athenian Agora and Ancient

Corinth.

The Athenian Agora

Of the three specimens from the Athenian Agora, AA 32 was diagnosed as a primary benign tumour (Angel 1945: 293) and AA 83b was diagnosed as metastatic cancer (Little 1997).[4] The lesion on individual AA 13 was originally diagnosed as post-mortem damage (Angel 1945: 316), but this has since been diagnosed as a metastatic lesion (M. Liston, personal communication).

AA 32

AA 32, a young adult male, had a large boney projection emanating from the lateral aspect of the occipital squama near the lambdoidal suture (Fig. 56). It was 20.13mm in length and 19.47mm in width. Although it was not possible to obtain radiographs, the tumour appeared to consist of solid cortical bone and is most likely an osteoma. Its position on the skull would have been above the hairline and aside from the occipitalis part of the occipitofrontalis muscle located along the superior nuchal lines, there are no major muscle attachments or soft tissues in this region, therefore there would not have been any negative physical consequences from this tumour (Jarmey 2004: 151).

AA 13

AA 13, an adult female in her 30's who was killed in the Herulian sack of Athens in CE 267, had severe blunt force trauma on the facial bones and the right parietal. At the time of her death she was also suffering from cancer, probably a metastatic disease that had spread to the skeleton from another primary site. The most obvious lytic lesion was on the

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[4] As cited in Bourbou (2003: 183).

occipital squama, inferior to the lambdoidal suture at lambda, measuring 23.57 x 16.93mm (Fig. 57). The lesion had penetrated both the inner and outer tables and the lower margins showed irregular, chewed edges. On the inner table the lesion margins were irregular and there was bevelling toward the outer table. A negative space between the inner and outer tables indicates that the diplöe had been destroyed as the cancer spread outward. Porosity was observed around the margins of the lesion and was characterized as sparse pitting in the cortical bone. Although primarily lytic, there is some blastic activity on the inner margins of the lesion involving the diploe. The skull is intact, and it was not possible to observe the endocranial appearance of the sphenoid, nor was it possible to obtain radiographs of this specimen. This lesion was similar in character and location to a lytic lesion observed in WLH 04, where the lesion also exhibited pitting at the margins, chewed edges and destruction of the diplöe (Fig. 37). Based on the sex and age of the individual, this could be a result of breast cancer as this type of carcinoma has a 20% of metastases spread to the skull, where as in lung or other miscellaneous cancers, this percentage is much lower (Krishnaumurthy et al. 1997: 2505).

AA 83b

AA 83b was an adult male, buried beneath the floor of the temple of Hephaestus during the Byzantine or Turkish period, when the temple was used as a church. He had the most extensive cancerous lesions of any of the archaeological cases I reviewed and was

previously diagnosed as a case of metastatic prostate cancer (Little 1997)[5]. The lesions on this specimen were a mix of lytic and blastic lesions distributed throughout the skeleton.

In the skull the right temporal had an endocranial lytic lesion, measuring 15 x 11.51mm, superior to the petrous portion and was irregular in shape, not penetrating into the outer table (Fig. 58). In the axial skeleton, on the body of the right scapula there was a lesion that measured 33.46 x 22.43mm. It was round, radiating outwards throughout the body, with the edges appearing as if they were chewed due to small irregular points of various size. It was similar to what was seen in the Athens Collection in specimen WLH 14, in the scapulae (Fig. 59), as well as the femora, pelvis, humerus, vertebrae and sternum. These bones also exhibited round, metastatic lesions of various size that appeared chewed at the edges and radiated outward. Rib fragments displayed lytic activity on the pleural aspect of the shaft and had no activity on the anterior side; this indicates that if cancer was present in this individual, then it metastasized to his ribs. Finally, two thoracic vertebrae showed lytic activity at the vertebral bodies. The first consisted of a hole through the centrum measuring 15.93 x 11.6 x 22.52mm. The other vertebra had a possible space-occupying lesion in the vertebral body, which was characterized by two openings, each measuring approximately 6mm wide that reached 6.21mm into the trabecular bone. The openings were separated by a column of trabecular bone and were visible due to the destroyed cortex from post-mortem damage (Fig. 60).

Blastic and lytic activity was observed on the fragmented, left innominate, especially on the ischium and lateral aspect of the body. The opposite side of the innominate showed

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[5] As cited in Bourbou (2003: 183).

blastic growth, which was more widespread and extended inferiorly toward the ischial tuberosity. The lunate surface of the acetabulum showed mixed blastic and lytic activity; the subchondral bone was almost completely destroyed in some areas, while developed in others (Fig. 61). The remainder of the acetabulum displayed lytic destruction. By comparison, in WLH 14, where there were multiple lytic lesions, the lunate surface was unaffected. Directly beside the acetabulum, superior to the ischial tuberosity, there was proliferative blastic activity, with two bony spicules projecting from the bone. A fragment of the iliac blade had a large blastic growth measuring 25 x 20.25 x 1.48mm; it was of irregular shape and consisted of woven bone laid down over the cortex (Fig. 62). The ischiopubic ramus had the same blastic activity as was seen on the ischium and the femur.

The most severe lesions were observed on the left femur. It was missing both epiphyses due to post-mortem damage and had a large amount of blastic activity at the posterior proximal metaphysis, measuring 145mm in length (Fig. 63). This activity was most drastic inferior to the lesser trochanter where there were two large bony spicules projecting downwards; additional spicules were also observed medially and inferior to the greater trochanter. The femoral neck had a mix of lytic and blastic lesions, which culminated in a large boney growth at its base. Along the posterior-lateral diaphysis, lytic activity could be seen becoming more prominent towards the distal end. Similar femoral lesions were previously observed among specimens from the Athens Collection, including WLH 4, WLH 13 and WLH 14 (Fig. 64). In each of these specimens, the femora had blastic activity, but this was limited to the diaphysis, whereas in AA 83b, the metaphysis was also affected.

Among the other long bones, the right femur consisted of only the proximal

metaphysis and diaphysis; it did not display lesions to the extent that was seen on the left

femur. Instead, lytic striations were observed along the diaphysis, though this could be a

periosteal reaction (Fig. 65). The left tibia, which was broken in half post-mortem, had two

lesions observed on the medial malleolus and the anterior distal metaphysis, both of which

were lytic with diffused borders. The lesion at the medial malleolus was circular in shape,

measuring 24 x 21.63mm, with irregular edges and exposed the absence of trabecular bone

(Fig 66). The anterior distal metaphysis was also lytic with destroyed cortical bone. The

left proximal fibula exhibited two small faint, lytic lesions at the metaphysis measuring 8.52

x 4.88mm and 6 x 6.08mm. At the lateral aspect of the right calcaneus, there was a

pronounced lytic activity measuring 33.5 x 24.66mm (Fig. 67). The lesion had destroyed

the cortex and left only a thin lattice of trabecular bone. Looking inside, it could be seen

that the calcaneus had been hollowed out at least 24.59mm into the bone. As there are no

muscle attachments on the lateral aspect of the calcaneus it is unknown to what extent the

individual's ambulatory abilities would have been affected; though keeping in mind the

blastic activity in the left, proximal femur and innominate, it is very likely that walking

would have been limited. A differential diagnosis of AA 83b will be given in the next

chapter.

The Corinth Excavations

Of the four specimens examined from the Corinth excavations two were previously

diagnosed as primary benign cancers (Fox Leonard 1997) and two were classified as

secondary malignancies (Zervos et al. 2009).

62-31

In specimen 62-31, the calvarium of an adult female, there was a very small osteoma on the left aspect of the frontal bone above the supraorbital ridge and was first identified by Fox Leonard (1997: 357). It was oval in shape, measuring 2.45mm long and 1.36mm wide (Fig. 68). In life, this osteoma was probably unnoticed by the individual.

61-10

The other primary tumour from Corinth was in specimen 61-10. This was a tibia from a juvenile, measuring 193mm in length and was aged eight to nine years old (Fox Leonard 1997: 306). This bone was distinguished by its swollen appearance at the proximal end, which measured 71.93mm in length (Fig. 69) and was diagnosed as a giant cell tumour (Fox Leonard 1997: 306). The surface of the tibia had a mix of lytic and blastic activity and the entire circumference of the bone was peppered with holes. Two small, post-mortem holes in the middle of the affected area allowed for the viewing of the interior of the bone and it appeared to be hollow. A radiograph provided by S. Fox (personal communication), showed an ovular space within the medullar cavity, with clear sclerotic borders. It extends outward from the bone causing the swelled appearance. On the opposite side there was an increase in periosteal bone formation, causing a thickening of the cortical bone (Fig. 70). A differential diagnosis of 61-10 will be given in the next chapter.

2002-1b

Specimen 2002-1b was a male aged 39-44 years and was from the Ottoman period (Zervos et al. 2009: 596). He had an impression on the endocranial surface of the occipital that was attributed to a tumour pressing against the bone (Zervos et al. 2009: 596). Due to the fragility of the skull I was unable to properly measure the impression, but Zervos et al. approximated the measurement to be 67 x 20mm (2009: 596). The impression was almost rectangular in shape with smooth, rounded edges and the ectocranial surface showed no signs of activity (Fig. 71). This impression would have been caused by a benign tumour because there was no evidence of invasion into the bone, as would be expected from a malignant cancer. In life, this individual may have exhibited neurological symptoms depending on the tumour's location on the brain (Taphoorn and Klein 2004: 160). On the right innominate I observed another lesion that were not reported by Zervos et al. (2009). These lesions consisted of porotic holes of various sizes at the posterior iliac crest (Fig. 72). The lesion was 34.05 x 22.62mm and had diffused margins.

2000-09

Specimen 2000-09, a 25-27 year old female, had a lytic lesion on the left frontal, which was originally diagnosed as a metastatic cancer lesion (Fig. 73) (Zervos et al. 2009: 560). It was 19.62 x 15.28mm and irregular in shape, completely penetrating through the cranium. There was porosity around the edges and bevelling on the inner table. This lesion was similar in appearance to the one observed in AA 13; both displayed porosity around the margins and bevelling at the inner table. As this was also a female, this lesion could be a result of metastatic breast cancer. However the individual's young age does not

support this as breast cancer normally manifests at an older age; the risk of developing

breast between the ages of 20 and 40 years is 0.49% (Bilimoria and Morrow 1995: 264). In

this individual I found other lesions that were not previously reported by Zervos et al.

(2009). A fragment of the right scapular body showed two possible lytic lesions measuring

6.09 x 4.09mm and 14.77 x 5.94mm. Two thoracic vertebrae also exhibited lytic lesions.

The first had a lytic opening on the inferior surface of the vertebral body that completely

penetrated the bone. It was round in shape with a pinch in the middle and was 6.24mm in

length, 5.16mm at the maximum width and 2.51mm at the minimum width; the edges were

smooth. The other vertebra had large porous holes on the spinous process and the lesion

measured 14.49 x 7.37mm (Fig. 74).

Previously Unidentified Cases

Modern skeletons with possibly neoplastic lesions were examined at the Wiener

Laboratory and the University of Waterloo Anthropology department..

The Wiener Laboratory

Of the specimens in the Wiener Laboratory one was suspected of having a primary

cancer and the rest were classified as metastatic.

WL 1

In WL1, a one-year-old juvenile of unknown sex, porotic lesions were observed on

almost all of the cranial bones. On the frontal, this was seen at glabella and bregma, along

with remnants of the metopic suture (Fig. 75). Due to the individual's young age this

porosity could be the result of fusion of the frontal bone. On the endocranial surface of this

bone, a cluster of nine osteoblastic lesions consisting of woven bone was present around

the frontal crest (Fig. 76). The largest lesion measured 8.59 x 4.35mm and the smallest was

3.61 x 2.73mm. In the occipital fine porosity was observed on the occipital at the basilar,

the lateral portions (Fig. 87) and the endocranial aspect of the squama along the internal

occipital protuberance. Both of the temporals had porosity superior to the external

auditory meatus that extended to the tympanic ring, giving it a moth eaten appearance. In

the sphenoid, porosity was observed on the cranial and orbital surfaces of the greater

wings and on the inferior body (Fig. 78). The maxilla also had porosity at the posterior

alveolar processes, though this could be due to dental eruption as none of the teeth were

present. On the mandible, both the left and right medial condyles had porosity ranging 16

to 17mm in length and 8mm in width. At the mental eminence there was also porosity

extending to the inferior surface, measuring 70 x 6.08mm. (Fig. 79)

The scapulae and long bones also had porosities. In the scapulae this was localized

to the scapular spines; the lesion extended the entire length of the feature and was

bilateral. The long bones displaying lesions were the left ulna and humerus. In the ulna

this lesion was located inferior to the coronoid process and was 8.93 x 6.82mm. The lesion

was porotic with non-demarcated borders and faintly extended down to the mid-diaphysis.

In the humerus, porosity was observed in the posterior diaphysis (Fig. 80). The porosity

appeared lytic with some periosteal response and was 16.79 x 5.79mm. A differential

diagnosis of WL 1 is given in the next chapter.

L 1

Specimen L 1 displayed lytic lesions on both innominates anteriorly and posteriorly

(Fig. 81). These lesions consisted of small porosities of various sizes not larger than 1mm in

diameter. They were clustered into small groups on the blade of the left ilium and under

the iliac crest of the right innominate. Under microscopy the edges appeared scalloped and

smooth. The lesions were accompanied by post-mortem damage exposing much of the

trabecular bone, which appeared normal. The lesions on L 1 are similar to that of 2002-1b

from Corinth in size, pattern and anatomical position indicating that these individuals

might have had the same kind of cancer.

WLCS

WLCS 1, a proximal ulnar head, had a space-occupying lesion. This bone fragment

appeared as if it had been hollowed out from within (Fig. 82). The lesion was 9.83mm deep

and spherical in shape. With microscopy, it was seen that the trabeculae were not

destroyed post-mortem, as they did not end abruptly but instead appeared smooth and

melted away. In WLCS 3, a fragment of a left distal femur, a small lesion was observed

superior to the medial condyle (Fig. 83). It was round in shape measuring 10.49 x 9.74mm.

The lesion is surrounded by large foramina that are normal found in the distal femur. If

these fragments are from the same individual then it is possible that metastasis had spread

to the elbow and knee. However it is very difficult to determine the type of cancer from

only two bone fragments.

WLCS 2, a right femoral head (Fig. 84), and WLCS 4, the distal end of a left femur

(Fig. 85), were determined to be post-mortem damage rather than cancerous lesions.

These fragments were observed to have small holes similar to lytic lesions and this was especially seen on WLCS 2, which has post mortem damage along the entire surface of the subchondral bone. Post-mortem damage was confirmed when these specimens were examined microscopically. Normally, pathological lesions appear melted away with smooth, irregular borders, however these lesions appeared ragged or sharp and displayed a different colour than the surface of the bone, which is characteristic of post-mortem damage (Fig. 86). Though they are not cancerous, these specimens show that a neoplastic disease and pathology can be distinguished with the aid of microscopic observations.

The University of Waterloo

Of the specimens from the University of Waterloo, three individuals were identified as having primary cancer and one was diagnosed as metastatic lung cancer.

CA 1

CA 1, an adult male aged 30 to 45 years old, exhibited a small osteoma on the left frontal close to the midline, which measured 0.39 x 0.29mm (Fig. 87). Like the osteoma observed in specimen 62-31, this neoplasm most likely was asymptomatic and unnoticed by the individual.

M 1

Another osteoma was observed in M 1 on the right mandibular ramus (Fig. 88). It was oval in shape and measured 10.55 x 10.03 x 6.43mm. A radiograph of the neoplasm showed that it consisted of solid cortical bone and had clear demarcated borders. This osteoma could have been symptomatic in life if it was in a position that pressed against the

masseter muscle and the trigeminal nerve, in which case the individual would have experienced pain when chewing (Jarmey 2004: 179).

UW 23

UW 23, a juvenile female aged 7-12 years old, exhibited a concentration of fine lytic pitting superior to the frontal crest (Fig. 89). Porosity was also observed at the posterior alveolar processes of the maxilla (Fig. 90) and superior to the external auditory meatus of both temporals (Fig. 91); the internal occipital protuberance also had porosity that is not expected from a juvenile. A differential diagnosis for UW 23 is given in the next chapter.

UW 8

UW8, a male aged 25 to 35 years old, had lesions I classified as metastatic on the axial skeleton and both femora. In the skull, the frontal had small groups of lytic lesions endocranially around the frontal crest, similar to UW 23. An osteoblastic lesion was found on the endocranial surface of the occipital, directly inferior to the lambdoidal suture (Fig. 92). It was 7.4 x 3.5mm, irregular in shape and had a rough texture. This lesion had clear edges that distinguished it from the rest of the endocranial surface, indicating that it was laid down over the normal bone; unfortunately on the radiograph this lesion was unobservable due to the angle of the image. The sella turcica and clinoid process of the sphenoid had undergone lytic destruction and the mandible had a small lytic lesion on the left, posterior aspect of the body that was 0.56 x 0.21mm.

The sternum had three lesions that were only distinguishable with a radiograph. One was located on the inferior manubrium and the others were located on the medial and inferior body. They were all lytic and ranged in size from approximately 2.7 to 10.74mm in length and 1.8 to 10.17mm in width. They had clear borders with no sign of sclerotic activity. All of the left ribs had a mix of osteoblastic and lytic lesions on the pleural side of the shafts; of the right ribs two displayed lytic activity causing marked porosity (Fig. 93). In the spine, porosity was seen on the fifth and sixth thoracic vertebrae at the spinous processes (Fig. 94). The first, fourth and fifth lumbar had depressions in the vertebral bodies but these are most likely Schmorl's nodes.

In the left innominate, a lytic lesion was present inferior to the iliac crest, both anteriorly and posteriorly and had diffused borders (Fig. 95). The right innominate had two lesions that were visible only with a radiograph. One was located at the iliac crest and was approximately 32.9 x 9.3mm; the other lesion was near the auricular surface and was approximately 10.62 x 6.3mm. Both were ovular in shape and had diffused borders. The lesions on the left innominate could have been symptomatic during life as the anterior lesion was located near the iliacus muscle, which flexes the thigh at the hip joint and the posterior lesion was on the border of the gluteus maximus (Jarmey 2004: 251, 313). Finally, on the posterior left femur at the intertrochanteric crest there was a lytic lesion (Fig. 96). It was 40.23 x 23.60mm and had diffused borders along the cortical bone. It does not penetrate the bone, as this lesion does not appear in the radiographic image. This area of the femur serves as an attachment for the iliopsoas muscles, which flex the hip and lumbar area, and pain or discomfort might have been experienced due to the presence of this lesion.

UW 8 was classified as having metastatic lesions that were probably derived from lung cancer. The existing medical literature does not offer any correlation between the risk of lung cancer and age or sex; instead risk of developing this disease is dependent on the chronic exposure to carcinogens such as smoking (Hecht 2006; Carbone 1992). In comparison to the lung cancer cases in the Athens Collection, both UW 8 and WLH 13 displayed similar lytic rib lesions, characterized by large holes penetrating the cortex (Fig. 97). Prostate cancer was also considered but discounted due to the lack of osteoblastic lesions as seen in WLH 29 and the individual's young age.

CHAPTER 6: DIFFERENTIAL DIAGNOSIS AND CANCER

Differential diagnosis allows for greater possibilities in analysis and highlights the similarities and differences in skeletal reactions to disease. A differential diagnosis is accomplished by comparing the observed lesions, in regard to their location, size, character, clinical knowledge and prior bioarchaeological evidence of diseases. Through this method, diseases such as cancer can be brought to the forefront and considered likely options, further adding their presence in the archaeological record. Differential diagnosis is a valuable tool in distinguishing neoplastic diseases that may otherwise be unnoticed or misdiagnosed. Here I present four cases for differential diagnoses that consider a neoplastic option. The first case will demonstrate how a differential diagnosis can be expanded on, by considering lesser-known neoplastic disorders according to their radiographic appearance. The second and third cases will display how a neoplastic disease can be similar to a metabolic disease. Finally, the fourth case will show how different neoplasms can be considered for a differential diagnosis but at times there is no definitive answer.

Specimen 61-10 from Corinth: Giant Cell Tumour versus Langerhans Cell Histocytosis

From Corinth, specimen 61-10 was a tibia from a juvenile, measuring 193mm in length and was aged eight to nine years old (Fox Leonard 1997: 306). Its noticeable diaphyseal swelling was originally diagnosed as a giant cell tumour due to its radiographic appearance (Fox Leonard 1997: 306).

A giant cell tumour is a benign fibroblastic cancer and most commonly manifests between the ages of 20 and 40 years; any earlier than puberty is rare (Netherlands Committee on Bone Tumours 1973: 269). This tumour is commonly found in the long bones, almost always localized to the epiphysis and destroys the pre-existing trabecular bone and original cortex (Campanacci 1990: 118). This allows for the formation of a thin new periosteal cortical shell with rounded perforations and reinforcing ridges on the inner surface (Ortner and Putschar 1985: 375 - 376). In contrast, 61-10 is a juvenile, aged eight to nine years old (Fox Leonard 1997: 306) and it is the diaphysis that is affected.

In radiographs, the cortex shows distinct expanding with a smooth, periosteal bone shell, with small interruptions and irregularities (Netherlands Committee on Bone Tumours 1973: 270, and figure 13:33, page 297. However, these criteria are not reflected in the radiograph of specimen 61-10 (Fig. 73). Here the radiograph does not show small interruptions and irregularities, nor does there appear to be signs of reinforcing ridges or a smooth, periosteal bone shell. Instead the radiograph shows an increase in periosteal bone formation, causing a thickening of the cortical bone, as well as an ovular space within the medullar cavity, with clear sclerotic borders, that extends outward, causing the swelled appearance. Due to these radiographic distinctions, as well as the difference in age and anatomic location predilections, a diagnosis of giant cell tumour does not fit with specimen 61-10.

Langerhans cell histiocytosis, formally known as histiocytosis X, comprises three syndromes (eosinophilic granuloma, Hand-Schüller-Christian disease and Letterer-Siwe disease) that are histologically identical, but different in their clinical presentation,

disability and survival (Mankin 2006: 67). This is a benign reticuloendothelial disease, which can originate in the bone marrow, as well as the lymph nodes and skin (Ortner 2003: 359; Netherlands Committee on Bone Tumours 1973: 501). This type of disease develops through abnormalities and proliferation of histiocytes, which are responsible for the removal of dead and abnormal cells (Ortner 2003: 359, 360). Infant and adolescent skeletons are one of the main organ systems affected by Langerhans cell histiocytosis (Marks and Hamilton 2007: 225). There has been previous paleopathological documentation of histiocytosis in Greece (Liston 1991; Barnes and Ortner 1997) and a suspected case of eosiniphilic granuloma was reported in a prehistoric Illinois child (Morse 1978).

For the purpose of this differential diagnosis I will focus on eosinophilic granuloma. It is most frequent in youth under the age of 15 years with a peak between 5 and 10 years and is usually found in the diaphysis of long bones (Campanacci 1990: 770; Mankin 2006: 68). Radiographically on the long bones, a sclerotic border may surround the radiographic image of eosinophilic granuloma and the lesion can vary in diameter. It can occur anywhere on a long bone and periosteal formation occurs frequently, leading to a local, pronounced thickening of the cortex (Netherlands Committee on Bone Tumours 1973: 502). Comparing the radiograph of 61-10 to examples from the Netherlands Committee on Bone Tumours (1973: 516, figures 27:22a – 27:22b), both show a clear border within the medullar cavity and a pronounced thickening of the cortex due to periosteal formation.

The radiographic appearance, age and anatomic location predilections of a giant cell tumour does not fit with what was observed in specimen 61-10. Instead I propose that

Langerhans cell histiocytosis is a more suitable diagnosis. The radiographic image is similar due to the clear sclerotic borders and the periosteal formation resulting in a thickened cortex. Furthermore, eosinophilic granuloma occurs in the diaphysis of the long bones and is most frequent between the ages of 5 and 10 years (Campanacci 1990:770), which is the same age range that 61-10 is in (Fig. 98).

WL 1 from the Wiener Laboratory and UW 23 from the University of Waterloo: Acute Leukemia versus Juvenile Scurvy

WL 1, a one-year-old infant, from the Wiener Laboratory and UW 23, a female aged seven to twelve years, from the University of Waterloo were two specimens that showed similarities between both leukemia and scurvy. These specimens provide a case study of the phenomenon where neoplastic lesions may be recognized as more common diseases due to their similarity in lesion distribution and appearance; this lead to an increase in the risk of over-diagnosis in some diseases and under-diagnosis in others. Both juvenile scurvy and acute leukemia are different in their causation, as the former is metabolic and the latter is neoplastic, but they are similar in their skeletal reaction due to the amount of porosity caused by excessive and chronic bleeding, as well as the general pattern of where these lesions occur.

Leukemia is a neoplastic disease that arises in the bone marrow and suppresses the formation of normal blood cells. This includes the production of platelets, which are a main factor in producing blood coagulants; as a result haemorrhages may occur in various organs such as the intestine and brain (Aufderheide and Rodrígues-Martin 1998: 355). Acute leukemia can occur at any age with a small peak of incidence in children under the

age of five (Waldron 2009: 183) and proves fatal after a course of six months (Aufderheide and Rodrígues-Martin 1998: 355). Skeletal changes due to this disease appear more so in acute leukemia than in the chronic variant and are therefore more seen in children than in adults; however these changes only occur in 50-70% of cases (Ortner 2003: 376). These skeletal changes include osteopenia and lytic lesions (Waldron 2009: 183; Rubens and Mundy 2000: 128). Aside from these, the most frequent lesion associated with leukemia is a non-specific radiolucent line on the metaphyseal growth plate (Ortner 2003: 376; Rothschild et al. 1997: 489). In regards to leukemic porosity, this is resultant of osteoclastic resorption of the cortical bone, as well as widening of the vascular foramina to accommodate tumour cell colonization of the periosteum (Ortner 2003: 376). Normally, paleopathology guides offer little assistance in identifying leukemic lesions and no archaeological cases have yet been identified (Roberts and Manchester 2005: 260). However, knowledge of leukemia has been further expanded by Rothschild et al. who offer a review of leukemic lesions by examining a 3 year old, black, female from the Hamann-Todd collection (1997: 482). The three observed leukemia cases from the Athens Collection offered additional evidence.

Scurvy is a metabolic disease that is characterized by a deficiency in vitamin C. Humans, other primates, guinea pigs and fruit bats cannot synthesize vitamin C and must obtain it from consuming foods that are high in the nutrient, which include a wide range of fruits and vegetables (Brickley and Ives 2008: 41). The main role of vitamin C is to create and maintain collagen, as well as intercellular cement material, such as the endothelium of blood vessels (Stark 2009: 8-9). When deficient in vitamin C, these processes are neglected and tissues become improperly maintained, leading to weakness and the risk of

hemorrhages (Stark 2009: 9). In children, scurvy symptoms develop more rapidly and

clinical manifestations are likely to occur after a child has been lacking in Vitamin C for six

to ten months (Brickley and Ives 2006: 164). Common symptoms in children are changes

in the gums as haemorrhages can easily arise from newly erupted teeth and during

mastication (Brickley and Ives 2008: 49). The most characteristic skeletal indicator of

scurvy is porosity of the cranial and facial bones, especially on the greater wings of the

sphenoid, the eye orbits, and the maxilla; this is sometimes accompanied with periosteal

new bone formation (Ortner and Ericksen 1997; Brickley and Ives 2008). Porosities are a

result of the associated anatomical position of the muscles, arteries and veins, along with

the mechanical stress and resulting trauma that is placed upon them Lesions on the

maxilla, mandible and sphenoid are due to trauma that occurs in the blood vessels of the

gums during mastication (Brickley and Ives 2006: 165). As an individual chews food, stress

is placed on blood vessels such as the maxillary artery, which supplies blood to the

temporalis muscle, causing chronic haemorrhages. This excessive bleeding triggers an

inflammatory response to create additional blood vessels, as well as more vascular

pathways through the bone, resulting in fine porosity (Ortner et al. 2001: 344),

Porosity of the greater wings of the sphenoid has been previously identified as the most

common skeletal indicator of scurvy (Ortner and Ericksen 1997: 214; Ortner et al. 1999:

322; Ortner et al. 2001: 344; Brickley and Ives 2008: 56). The greater wings of the

sphenoid serve as an attachment site for the temporalis muscles and their use during

mastication causes damage to the weakened maxillary artery, resulting in haemorrhaging

(Ortner et al. 2001: 344). Rothschild et al. (1997) do not note any involvement of the

sphenoid in their study of leukemia and the individuals from the Athens Collection also did

81

not display any porosity. In WL 1 microporosity was seen on the greater wings of the sphenoid (Fig. 99), though it did not penetrate the cortex and in UW 23, the greater wings did not exhibit any porosity. Brickley and Ives (2006: 168) note that, though the greater wings are of great importance in scorbutic changes, they should not be overly relied on as a sole skeletal indicator. In their study sample there were no well-preserved greater wings, however they did observe spicules of disorganized new bone on the lesser wings and sphenoid body (Brickley and Ives 2006: 168). In WL 1 fine porosity was observed on the inferior aspect of the sphenoid body and lesser wings (Fig. 78) and in UW 23, a very faint porosity was seen near the spheno-occipital synchondrosis (Fig. 100).

Scorbutic porosity from the greater wings of the sphenoid can extend to the temporals (Ortner 2001: 349, Fig. 12), though other than this, there is little documented evidence of scorbutic lesions associated with this bone (Stark 2009: 43). In leukemia, porosity due to bone resorption has been noted but only in limited involvement (Rothschild et al. 1997: 484). All three juvenile specimens from the Athens Collection did exhibit similar, lytic, porosity around the external auditory meatus; this was also seen in WL 1 and UW 23 (Fig. 101). UW 23 also exhibited fine, lytic porosity at the tempero-mandibular joint and the bases of the zygomatic processes (Fig. 102), as well as small irregular, lytic lesions on the endocranial surface of the left temporal, measuring approximately 9mm.

On the maxilla, scurvy produces abnormal porosity in the alveolar processes (Ortner et al. 2001: 344) and in leukemia, Rothschild et al. did not report and observable changes aside from discolouration (1997: 484). However, caution must be taken due to the high reactiveness of the alveolus during tooth eruption and to be considered pathological,

alveolar porosity must extend well beyond the alveolar process surrounding an erupting

molar (Brickley and Ives 2006: 164). In the specimens from the Athens Collection, the

Wiener Laboratory and the University of Waterloo, the alveolar processes exhibited

porosity but not to the extent as is seen in the example given by Brickley and Ives (2006:

165, figure 1). In WL 1, the porosity encompasses the entire posterior of the maxilla and

consists of fine speckling along the entire surface. UW 23 has larger porosities than WL 1

that bilaterally extend along the entire length of the posterior maxilla and penetrate the

cortex (Fig. 103).

In the mandible, scorbutic porosity has been observed typically around the coronoid

processes of the mandibular ramii (Ortner et al. 2001: 344) due to chronic bleeding from

the temporalis muscle during mastication (Ortner et al. 1999: 327). This porosity can

continue considerably past the mandibular foramen, but does not reach the inferior line of

the alveolar process at the beginning of the dental arc (Brickley and Ives 2006: 166). In

leukemia, there was no mandibular porosity noted by Rothschild et al. (1997), however in

the Athens Collection ABH 101 had lesions, similar to what was observed on the maxilla of

WL 1, along both mandibular ramii and it extended upwards toward the coronoid

processes (Fig. 104). The other two juveniles, did not exhibit lesions in this area, but

instead porosity was noted around the mental eminence of both. WL 1 also had porosity at

the mental eminence that was characterized by large holes penetrating the cortex (Fig. 79);

UW 23 did not have a mandible for examination.

Porotic lesions of the frontal are not prominently noted in the literature regarding

scurvy except when referring to the orbital plates. In this case, bleeding occurs due to

defective blood vessels brought on by a deficiency in vitamin C and eye movement causing hemorrhaging (Brickley and Ives 2006: 168; Ortner and Eriksen 1997: 213). In leukemia, Rothschild et al (1997: 482) noted that pitting was observed on the orbital roofs. This was observed in WL 1 and UW 23, but the lesions were not extensive (Fig. 105). In these specimens, frontal lesions were also seen on the squama on both the inner and outer tables; this was not seen in the Athens Collection nor by Rothschild et al. (1997). In both individuals, the frontal lesions were centered around the frontal crest, but in WL 1 they were characterised as a cluster of osteoblastic lesions consisting of new periosteal bone, while in UW 23 the lesion consisted of lytic porosity (Fig. 106). A case of archaeological scurvy in a two year old individual from Serbia also exhibited porosity in this area, though it cannot be said if this is feature is diagnostic of scurvy or leukemia (Brown and Ortner 2011: 199).

On the occipital of WL1 and ABH 101, a similar porosity was seen on the internal protuberance, with macroscopic holes penetrating the inner table as a result of osteoclastic resorption; in both specimens the lesions are of similar size and dimension. UW 23 also has some porosity in this area but not to the extent of those previously mentioned (Fig. 107). Rothschild et al. (1997: 482) note endocranial occipital lesions but do not specify where this was seen or to what extent. Brickley and Ives observed endocranial bone changes to the occipital in scorbutic cases, which included an increased vascularization of the cortex, characterized by large holes, as well as irregular plaques of new bone formation; however they note that this might be due to another pathology, rather than scurvy (2006: 168).

Postcranially, Ortner noted scorbutic porosity on the supraspinous and infraspinous areas of the scapulae due to trauma in the blood vessels that supply the supraspinous and infraspinous muscles (2001: 347); Rothschild et al. (1997: 484) also noted similar scapular lesions in the leukemia case from the Hamann-Todd Collection. In the scapulae of both WL 1 and ABH 101 porosity was observed on the scapular spine, the inferior angle and margins of the body (Fig. 108). On the spinal column, Rothschild et al (1997: 488) observed variable distribution and periosteal reaction on all of the vertebrae. This consisted of porosity along the vertebral arches of the cervical vertebrae and the bodies of the thoracic and lumbar vertebrae; the vertebral bodies of ABH 187 and WLH 15 also exhibited some porosity. In scurvy, spinal changes are very rare in children under 12 months (Edeiken and Hodes 1973: 425) but aside from this, the vertebrae are not mentioned in the paleopathological literature. In WL 1, the vertebral bodies showed some minor porosity but these were not deemed pathological and are probably a result of normal vascularization.

In juvenile long bones, porosity is normally due to growth, however this typically does not extend more than 5–10 mm beyond the metaphysis (Ortner et al. 2001: 348). In juvenile scurvy, abnormal porosity is often seen along the metaphyses (Ortner 2003: 15) due to haemorrhages and weakening of the growth plate attachment (Stark 2009: 51). Furthermore, scorbutic long bones exhibit periosteal new bone formation, reaching a thickness of up to 1cm (Ortner 2003: 386). In their study of leukemia, Rothschild et al (1997) noted porosity in all of the long bones with focuses also at the metaphyses. Interestingly, the lower limb had the most extensive porosity, avoiding only the lateral aspects of the tibia, however there is no explanation as to why this is (Rothschild et al.

1997: 486). In specimens WL 1 and ABH 101 from the Athens Collection, the ulnae both showed coarse porosity on the proximal metaphysis (Fig. 109). On WL 1 it is inferior to the coronoid process and in ABH 101 it is inferior to the radial notch. Furthermore the lesions observed on WL 1's long bones seemed to be asymmetrically focused to the left side, similar to Rothschild et al. noting that only the right radius exhibited porosity (1997: 484).

The differential diagnosis of WL 1 includes both leukemia and scurvy. The distribution of lesions between the two diseases is similar to what is seen in the individual from the Wiener Laboratory including porosity of the facial bones and the scapulae, as well as some periosteal new bone growth (Figs. 110, 111). In contrast, UW 23 is differentially diagnosed tentatively as a case of leukemia, rather than scurvy. Since there are no postcranial bones to aid in this diagnosis, leukemia seems to be the better option because there is no porosity on the greater wings of the sphenoid, which has been noted as the most diagnostic lesion attributed to scurvy (Ortner and Ericksen 1997: 214; Ortner et al. 1999: 322; Ortner et al. 2001: 344; Brickley and Ives 2008: 56); there is also no periosteal new bone formation and instead the lesions exhibit porosity in the cortical bone. With these two examples in mind, future differential diagnosis of porous lesions in juveniles should strongly consider leukemia along with scurvy.

AA 83b from the Athenian Agora: Metastatic Prostate Cancer versus Osteosarcoma and Chondrosarcoma

In the Athenian Agora, specimen AA 83b was initially diagnosed as a metastasis of prostate cancer due to the presence of proliferative osteoblastic lesions (Little 1997)[6]. With this case, I will review the individual's lesions focusing on the most severe that were found on the left femur, innominate, tibia and the right scapula. This will be followed by a discussion regarding how I considered this to be a possible case of osteosarcoma or chondrosarcoma as an alternative option to Little's (1997) original diagnosis. The goal of this case study will be to show how different neoplasms can be considered in a differential diagnosis, but at times there is no definitive answer.

AA 83b was a male aged, 35-39 years old. I determined age by examining the morphology of the auricular surface, using the criteria that were developed by Lovejoy et al. (1985). The auricular surface was course with a decrease in billowing and striae, as well as microporosity; there was also some activity at the retro-auricular surface and none at the apex (Fig. 112).

Lesions were distributed throughout the skeleton with the most severe lesions concentrated on the left proximal femur and innominate (Fig. 21). These were characterized as a mix between lytic destruction and blastic formation. The blastic lesions on the left proximal femur consisted of sclerotic growths around the greater and lesser trochanters, with spicules of bony growth projecting outward (Fig. 63). On the innominate, similar lesions were observed on the ischium and lateral aspect of the body; the

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[6] As cited in Bourbou (2003: 183).

acetabulum also exhibited destruction and subsequent development of the lunate surface

(Fig. 61). The left tibia and right scapula both displayed round, lytic lesions with chewed

edges that were similar to metastatic lesions found in WLH 14 from the Athens Collection

(Figs. 66 and 113).

Carcinoma of the prostate has a 2.52% chance of developing in men aged 40 to 50 years

(Siegel et al. 2011: 217). This probability increases to 6.62% in men aged 60-69 years and

then nearly doubles to 12.60% in men aged 70 years and older; men aged younger than 40,

such as AA 83b, have a 0.01% chance of developing prostate cancer (Siegel et al. 2011:

217). The distribution of metastatic prostate cancer to the skeleton includes a high

concentration on the pelvis, sacrum, lumbar and lower thoracic vertebrae (Cumming et al.

1990: 412, Fig 1), all of which was seen on AA 83b. However, though prostate cancer

metastases are characteristically osteoblastic in nature, this should not be the only

criterion considered for a diagnosis. In his study of metastatic prostate cancer, Waldron

noted that the skeletal lesions consisted of widespread periosteal new bone (1997: 241).

While specimen AA 83b had periosteal new bone on the innominate and femur, it was not

widespread throughout the skeleton. In a Swiss case of metastatic prostate cancer, lesions

were limited to the periosteal surface of the ilium and consisted of fine porous bony build-

up with a similar reaction seen on the anterior, proximal femur (Ortner and Putschar 1985:

395). AA 83b had extensive blastic activity at the proximal left femur and innominate with

extreme destruction of the acetabulum. Though the lesions appear to be a result of

metastasis, this individual is younger than would be expected for prostate cancer and at his

age the risk of developing this disease is 0.01%. Moreover, the extent of the sclerotic

lesions on the left femur was not observed in the case from the Athens Collection or in the paleopathological literature.

Another option I considered was osteosarcoma. This primary malignancy has a predilection for males (Campanacci 1990: 455) and its second highest occurrence is in the proximal femur (Campanacci 1990: 459). Osteosarcomas tend to originate in the metaphysis and can extend into the epiphysis in adults (Campanacci 1990: 459), which was seen in AA 83b. The disease's course is usually rapid but there have been cases where it progresses slowly and more often has a sclerotic characteristic (Campanacci 1990: 476). However, this malignancy usually occurs between the ages of ten and thirty, which is slightly younger than AA 83b. Like other malignancies, an osteosarcoma can metastasize to other regions of the body, however 90% of metastases occur first in the lungs and then to the skeleton, at which the disease is in its terminal stage (Aufderheide and Rodrígues-Martin 1998: 379; Ortner and Putschar 1985: 384). Furthermore, osteosarcoma does not normally progress into the joints, leaving the subchondral bone intact, but AA 83b the acetabulum was almost completely destroyed. Despite the predilection for sex and anatomic location, osteosarcoma was discounted as an option for differential diagnosis due to the lack of age agreement, the low rate of metastasis to the skeleton and the characteristic of sparing the joint surfaces.

Chondrosarcoma was the second option I considered for this differential diagnosis as it also has a predilection for males and the proximal and distal metaphyses of the femur (Aufderheide and Rodrígues-Martin 1998: 382; Ortner 2003: 526). Furthermore, the age range for this neoplasm is wider than in osteosarcoma and prostate cancer, being inclusive

of late adolescence through adult age (Ortner 2003: 526). This is a malignant primary cancer of the cartilage, in which advanced cases the endochondral bone can undergo ossification (Ortner 2003: 526), however in AA 83b, the acetabulum showed some form of bony development. Despite the similar predilection for sex, age and anatomic location, chondrosarcoma was also discounted because of the bony development in the acetabulum and this type of cancer has no distinctive features and is difficult to diagnose in dry bone without the use of histology (Waldron 2009: 181) (Fig. 114).

AA 83b from the Athenian Agora provides an example of how a differential diagnosis is not always possible or clear for neoplastic diseases. Although AA 83b's lesions were identified as neoplastic, it is difficult to specify exactly which neoplasm was the cause. As cancer is an abnormality of the tissues, this disease ranges in its affects on the skeleton and in turn conflates a number of possibilities, each of which can be struck down based on the presence or absence of a characteristic such as age, anatomic region or it's effect on different types of bone such as the subchondral bone of joint surfaces.

CHAPTER 7: CONCLUSIONS

At the beginning of this thesis, I suggested four aims for this project. The first was to review previously identified neoplastic lesions in modern and archaeological skeletal remains from Greece; the second was to develop diagnostic criteria to aid in identifying cancer in skeletal remains; the third was to create differential diagnoses that consider neoplasms as an option; and the fourth was to determine if ancient cancers can be identified and diagnosed effectively. Of these four aims, three were met successfully.

My first aim was accomplished through the examination of the cancer cases in the Athens Collection, the Athenian Agora and the Corinth excavations. My second aim was accomplished in two ways. The first was through my development of two neoplastic recording forms. These were made out of necessity, as there is no standardized form for the recording of neoplastic lesions. These forms enabled me to gather appropriate data for neoplastic diseases including measurements, anatomic locations and detailed descriptions. The second way in which I was able to develop diagnostic criteria was through the examination of the cancer cases in the Athens Collection. This collection had over fifty cases of diverse primary and secondary cancers, along with biographic data including age and sex. With this collection, I reviewed ten different types of soft tissue cancer, including leukemia, a disease that does not have a high amount of paleopathological scholarship.

However, amid the benefits of the Athens Collection there were drawbacks, the first of which was at least twelve of the specimens are not exact in their cause of death, with only "cancer" or a variation of, being listed in the catalogue. These specimens display skeletal lesions that may help in distinguishing cancer from other pathologies in bone, but I

91

could not go further into differentiating these lesions, as it was unknown what kind of cancer was present. Another drawback of the Athens Collection was the absence of primary bone cancers. Having representation of primary bone malignancies would have been useful in offering further data regarding what these cancers looked like and in constructing a differential diagnosis. Paleopathological guides, though useful in their knowledge on various cancers, often do not have a substantial photographic representation of primary bone malignancies, except for various extreme examples, and usually these consist of only a few types. The medical literature also does not offer many visual representations of cancer, especially examples consisting of dry bone. As such, not having any examples of primary bone neoplasms in the Athens Collection made it more difficult to confidently identify such diseases in the archaeological remains. Another problem is that the term, "cancer" is too general and encompasses a wide variety of diseases that have different etiologies and epidemiologies. As such, there may be value in focusing future research on a specific type of neoplasm to better develop its diagnosis in skeletal remains and answer questions regarding its prevalence in antiquity.

Furthermore, paleo-oncological research should consider the effect of various treatments, such as radiation and chemotherapy, when studying remains in modern skeletal collections. This was an issue that I could not address in this thesis due the absence of medical histories. For this reason, other skeletal collections may be useful in future research. This includes the Universitat Autònoma de Barcelona Collection of Identified Human Skeletons in Spain, where biographical data is available for each specimen including: age, sex, city of origin, cause of death, pathological diagnosis and a wax plaster bust to demonstrate the appearance of the pathology in life (Rissech and Steadman 2011:

319). The Galler Collection in Switzerland could also be beneficial as this is a pathological

collection and houses 47 specimens of cancer diagnosed at autopsy, including primary

bone malignancies. Most of these specimens are complete with the original autopsy report,

which includes information on age, sex, origin, and profession of the individual, detailed

macroscopic and microscopic description of the cadaver, clinical history, autopsy findings,

and medical treatment history (Rühli et al 2003: 16).

My third aim was accomplished through the four differential diagnoses I created for

cases from Corinth, the Wiener Laboratory, the University of Waterloo and the Athenian

Agora. Each of these cases considered a neoplasm in their diagnosis and two considered a

metabolic disease as well. The differential diagnoses I created expanded on existing

diagnoses and showcased that at times a definitive answer cannot be reached.

When neoplasms are recognized archaeologically they can easily be misdiagnosed

or confused with each other. This stems from unfamiliarity with the disease beyond what

can be found in paleopathological guides. However, by considering the anatomic location

of the lesions observed and the age and sex of the individual, a differential diagnosis can be

narrowed significantly (Miller 2008: 663-664). The main risk in identifying neoplasms and

constructing effective differential diagnoses is when the paleopathologist is presented with

skeletal lesions that are normally associated with another more common disease. In the

example of leukemia and scurvy, both are similar in their lesion distribution pattern, the

anatomical regions affected and the chronic bleeding which results in marked porosity.

Neoplasms are not the first options to be considered in differential diagnoses because of

their supposed rarity in the bioarchaeological record and the lack of scholarship regarding

93

its appearance in skeletal remains, this in turn enforced the notion that cancers are not prevalent in the archaeological record. With this concept of rarity, scholars do not actively look for cancer and thus they do not find it, creating a version of the osteological paradox (Woods et al. 1992). As paleopathologists do not look for cancer, they will not find it and instead neoplasms will continue to be misdiagnosed or overlooked. To combat this, differential diagnoses must be made to consider neoplastic diseases. This is not to say that every skeletal lesion discovered is a good candidate for cancer, but instead is meant to further the possibility that neoplasms were present in the past and a viable option for differential diagnosis.

The last of my thesis aims, determining if ancient cancers can be identified and diagnosed effectively, was not accomplished in its entirety. Neoplasms can be identified effectively using clinical data and a modern reference collection, such as the one in Athens. But there is difficulty in the possible confusion between neoplasms due to their similar appearances to each other and other diseases. Cancers are not always clear in their diagnosis, as was seen in the example from the Agora. The difficulty in differentiation between neoplasms should not discourage paleopathologists from considering neoplasms for future research or as an option in differential diagnosis. When this disease category is not considered because of the belief that cancer was infrequent, then this results in not only less cases being identified but it also enforces the notion of cancer as uncommon.

FIGURES

	Incidence of Bone Metastasis	Osteolytic	
Myeloma	70-95%		
Renal	20-25%		
Melanoma	14-45%		
Bladder	40%		
Thyroid	60%		
Lung	30-40%		
Breast	65-75%		
Prostate	65-75%		
			Osteoblastic

Fig. 1: The incidence of bone metastasis among soft tissue cancers and the spectrum of lytic and blastic activity (after Coleman 2001: 166).
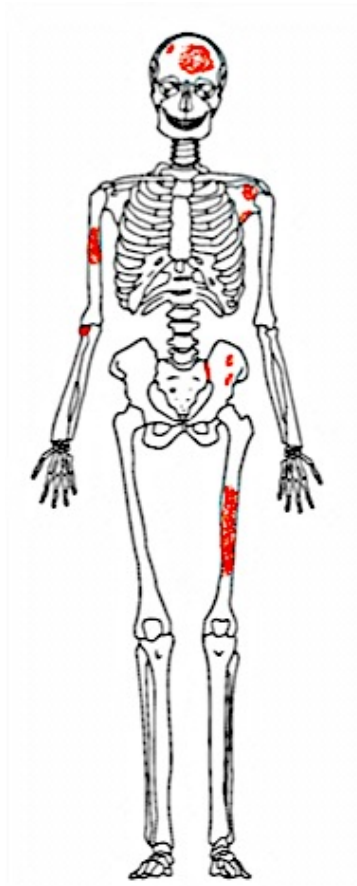
Fig. 2: Distribution of lesions in WLH 4, cancer with widespread metastasis and wasting.
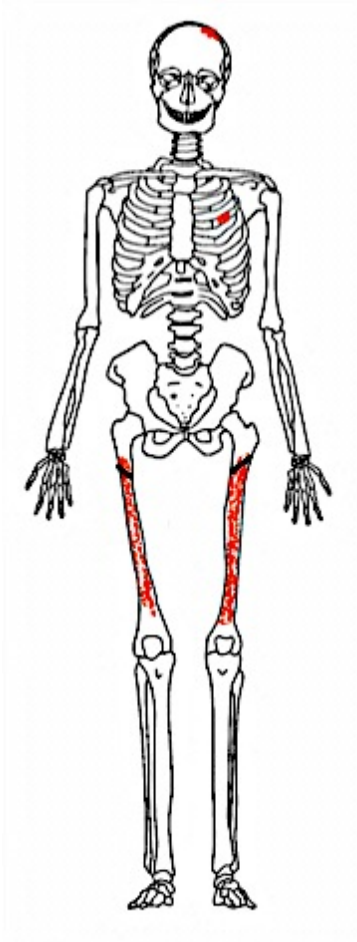
Fig. 3: Distribution of lesions in WLH 13, lung cancer with multiple metastases.

Fig. 4: A mixed lesion on the frontal of WLH 13.

Fig. 5: The right femur of WLH 13. A pathological fracture has separated the proximal end and a periosteal reaction is seen along the diaphysis; notice that it does not reach the metaphysis.
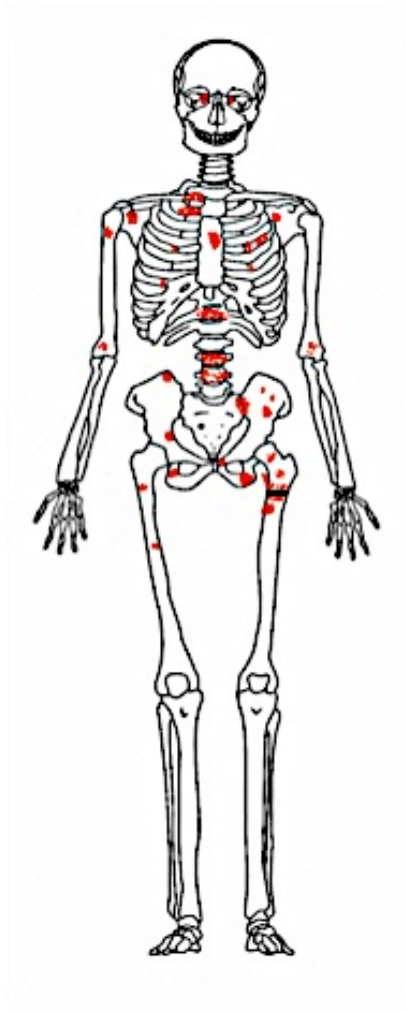
Fig. 6: Distribution of lesions in WLH 14, cancer with metastasis to the brain.
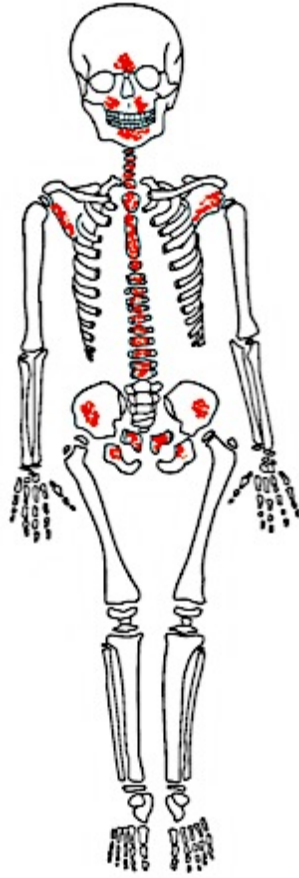
Fig. 7: Distribution of lesions in WLH 15, leukemia.
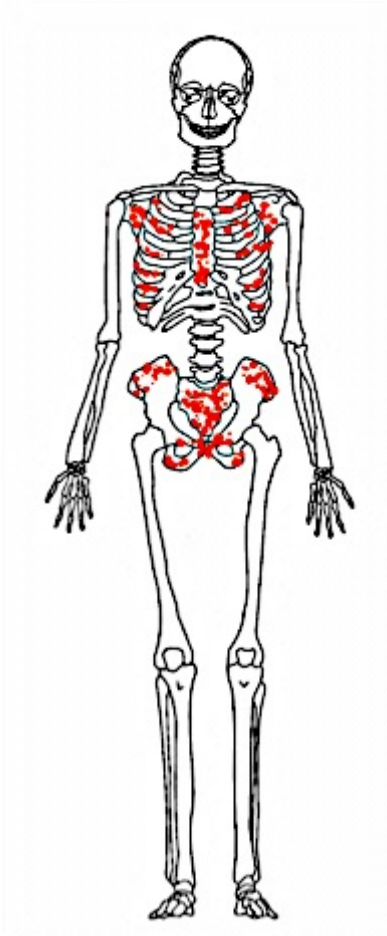
Fig. 8: Distribution of lesions in WLH 29, prostate cancer.
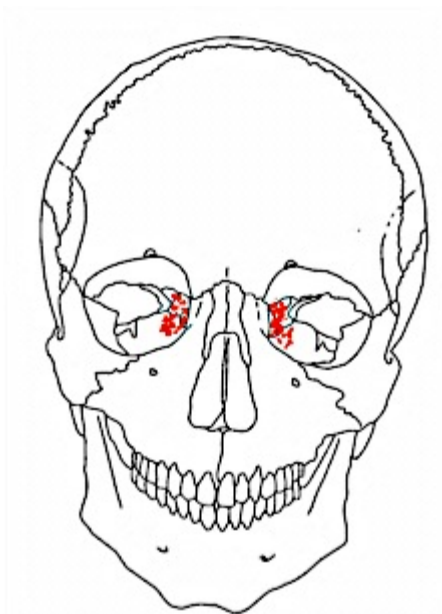
Fig. 9: Distribution of lesions in WLH 32, brain cancer.

Fig. 10: Evidence of a trephination in WLH 62.
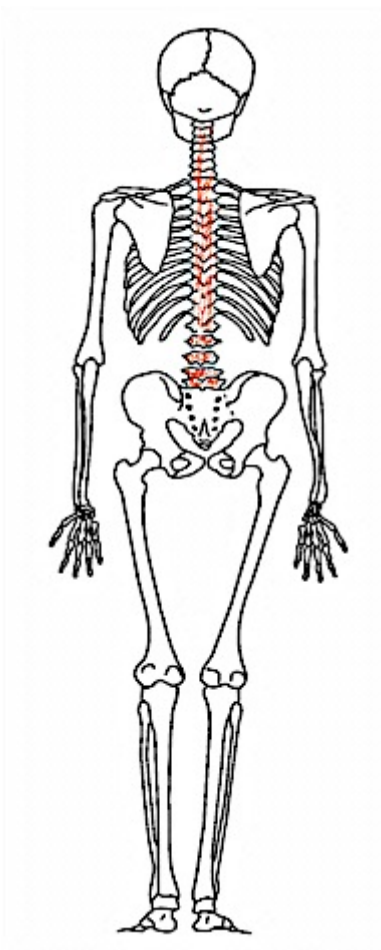
Fig. 11: Distribution of lesions in ABH 84, generalized carcinomatosis and heart and respiratory failure.
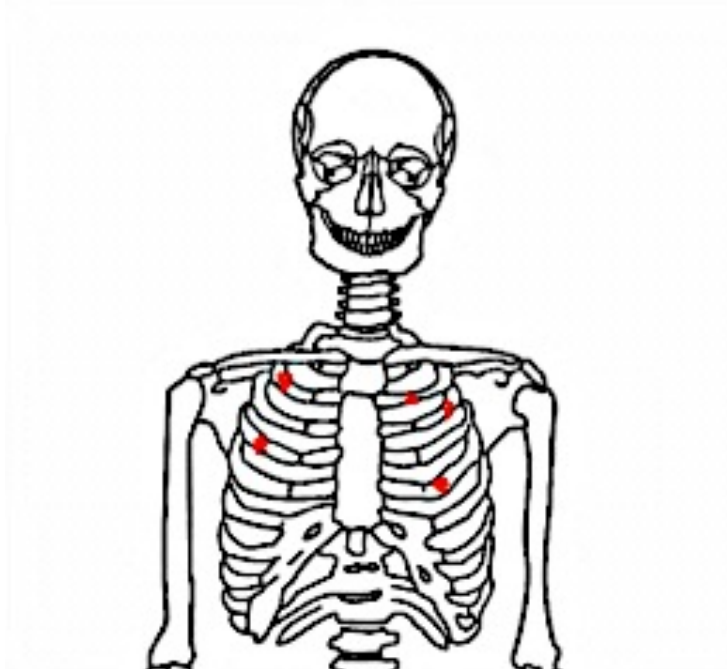
Fig. 12: Distribution of lesions in ABH 88, breast cancer.
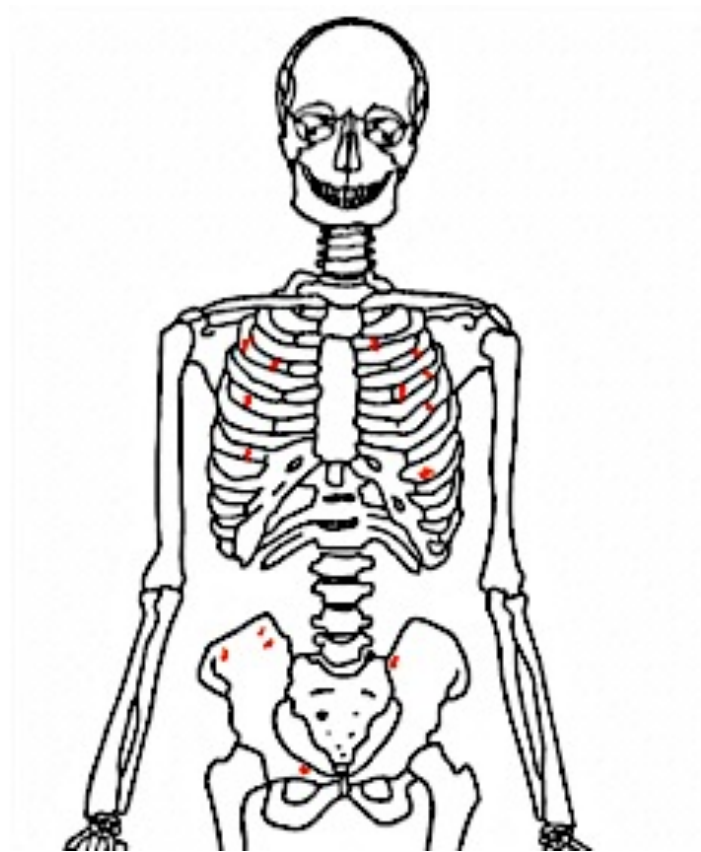
Fig. 13: Distribution of lesions in ABH 91, breast cancer.
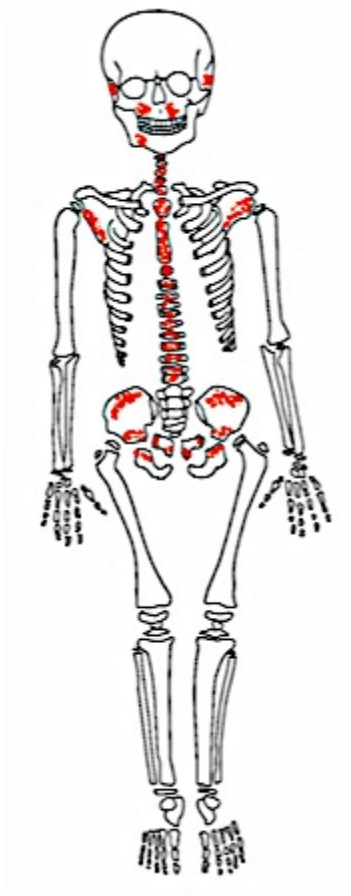
Fig. 14: Distribution of lesions in ABH 101, leukemia.
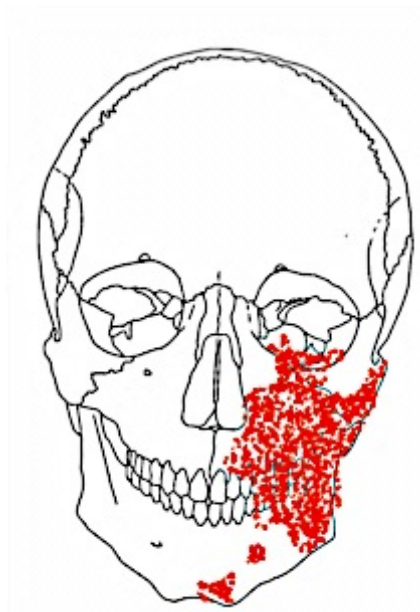
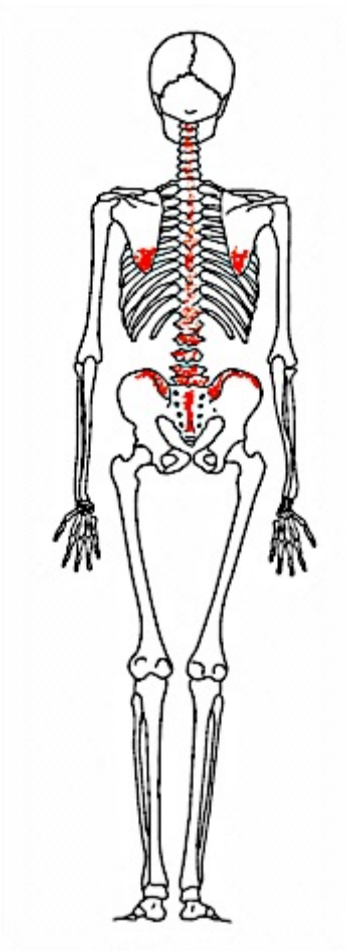**Fig. 15:** Distribution of lesions in ABH 112, buccal cancer.

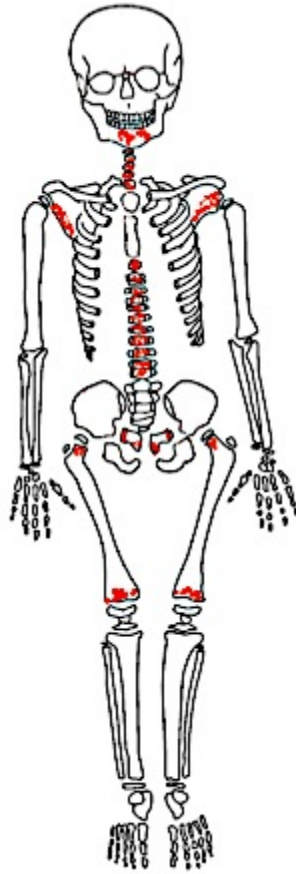**Fig. 16:** Distribution of lesions in ABH 147, lung cancer.

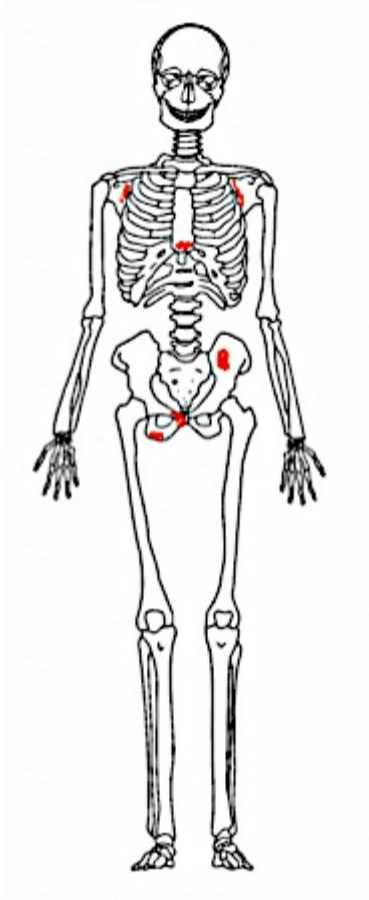**Fig. 17:** Distribution of lesions in ABH 187, leukemia.
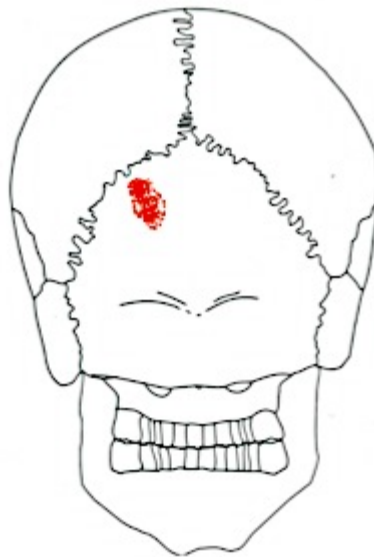
Fig. 18: Distribution of lesions in ABH 202, leukemia.
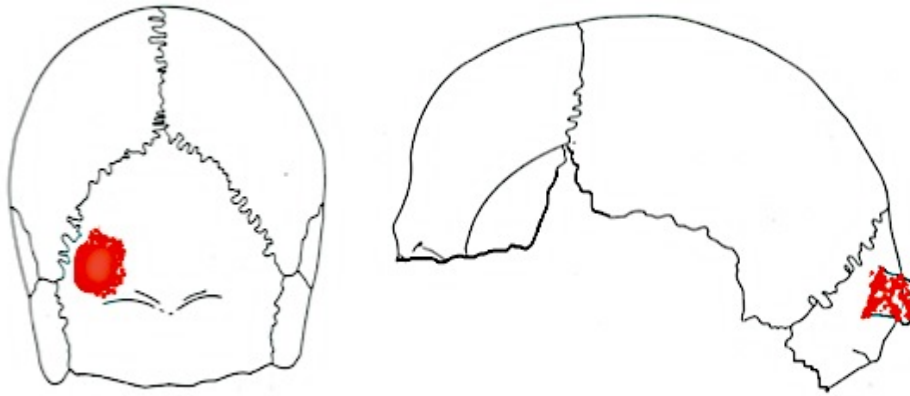

Fig. 19: Distribution of lesions in AA 13.

Fig. 20: Distribution of lesions in AA 32.
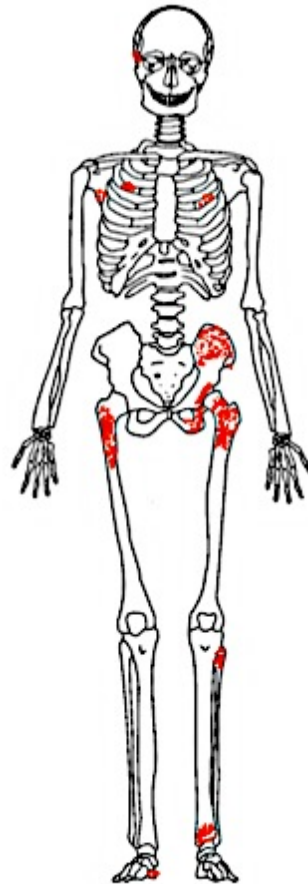

Fig. 21: Distribution of lesions in AA 83b.

Fig. 22: Distribution of lesions in 61-10.
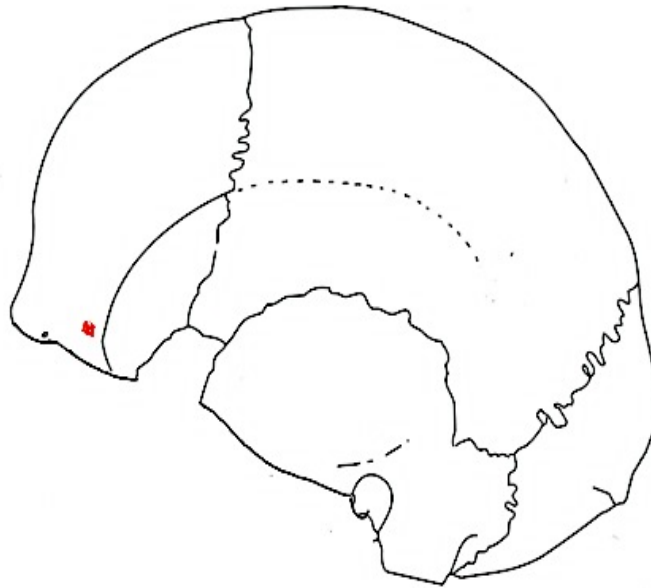

Fig. 23: Distribution of lesions in 62-31.
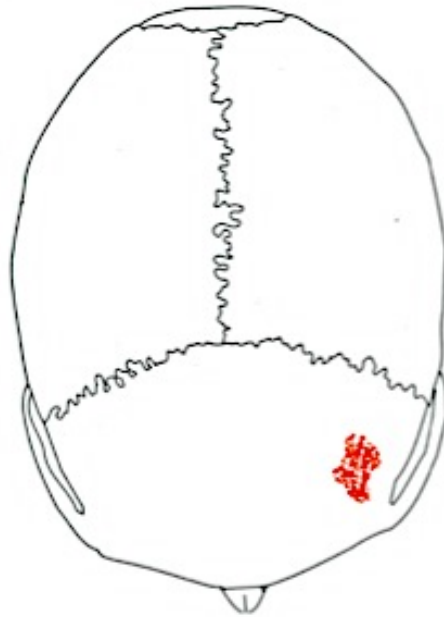
Fig. 24: Distribution of lesions in 2000-09.

Fig. 25: Pelvis lesions in 2002-1b.
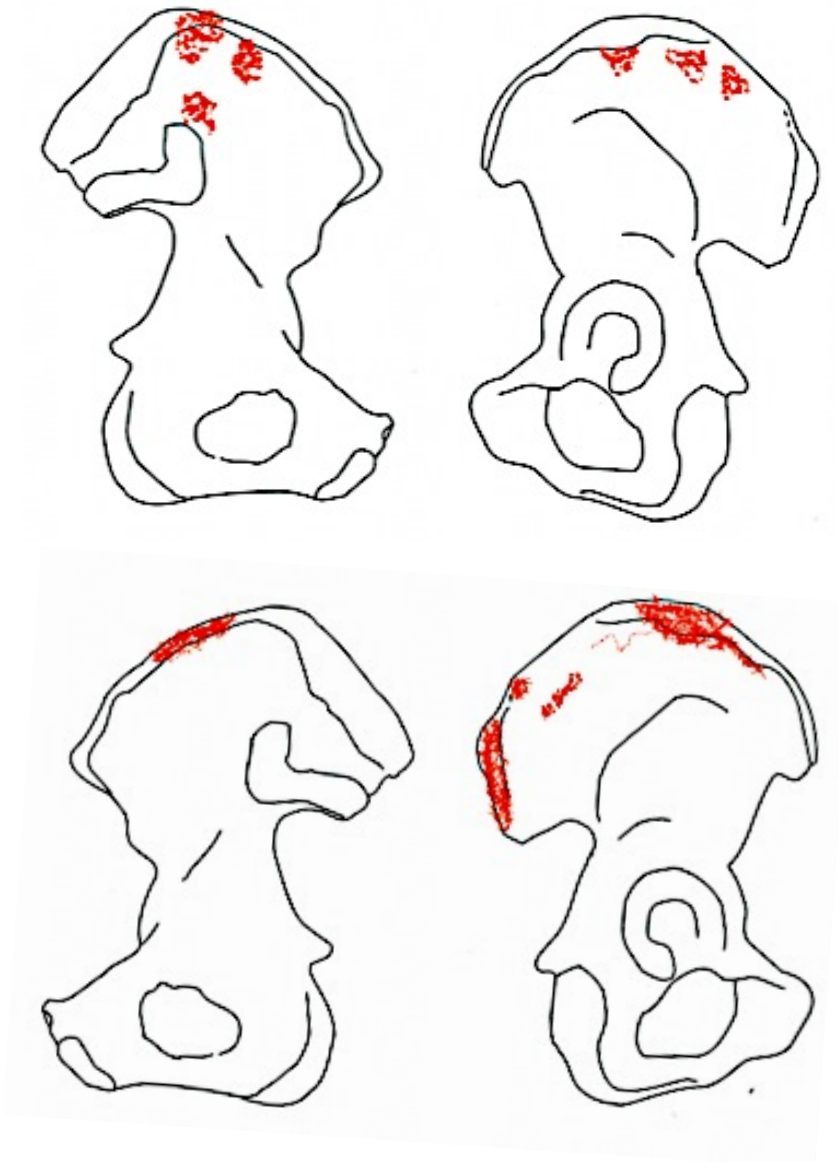
Fig. 26: Distribution of lesions in L1.
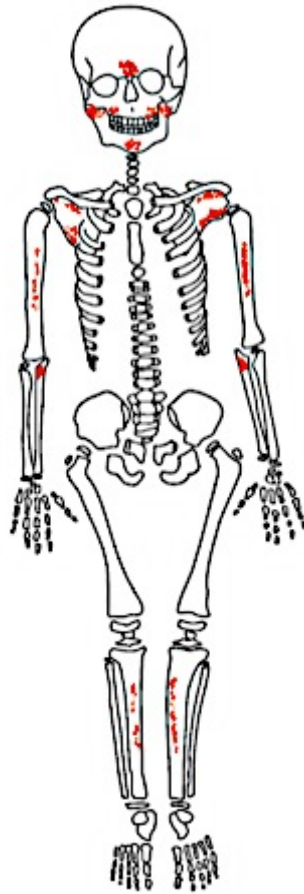
Fig. 27: Distribution of lesions in WL 1.
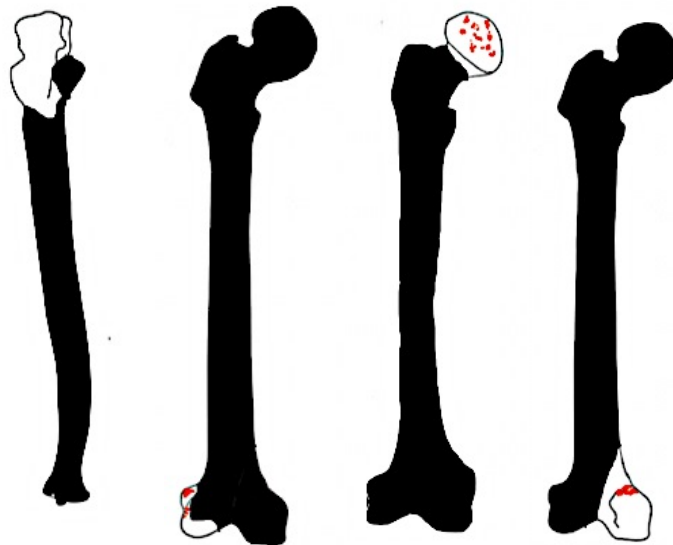
Fig. 28: WLCS 1, 2, 3 and 4 (from left to right).
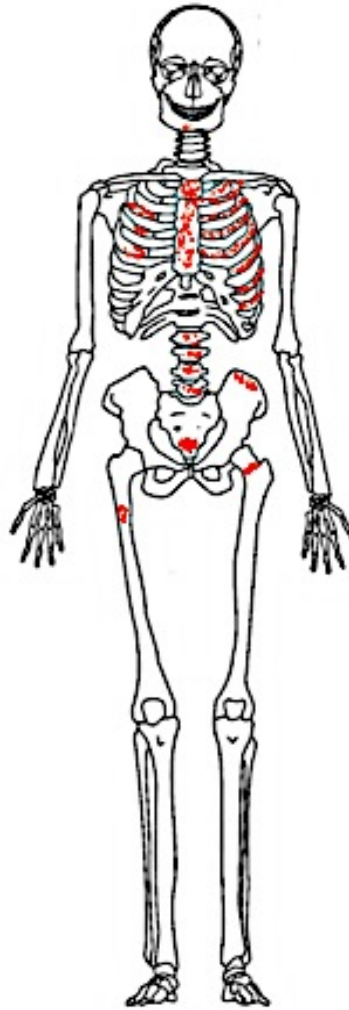
Fig. 29: Distribution of lesions in UW 8.
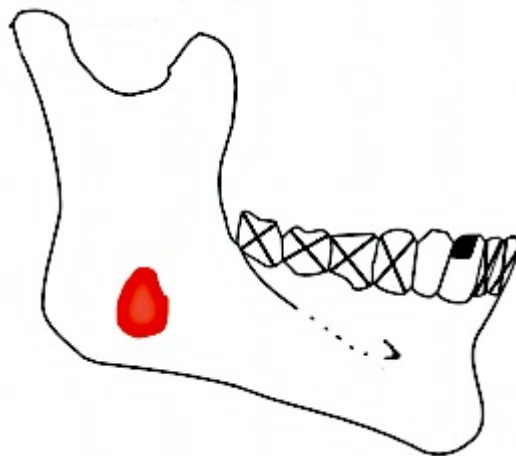
Fig. 30: Distribution of lesions in M 1.
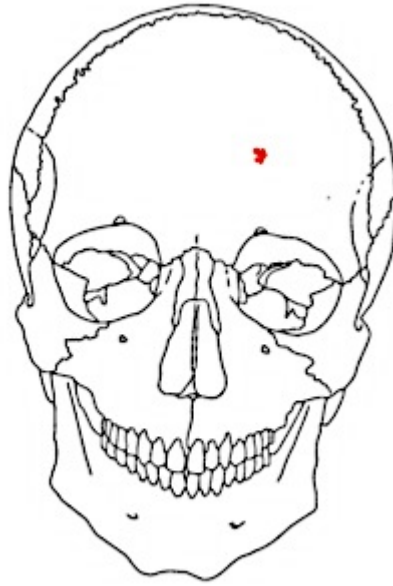
Fig. 31: Distribution of lesions in CA 1.
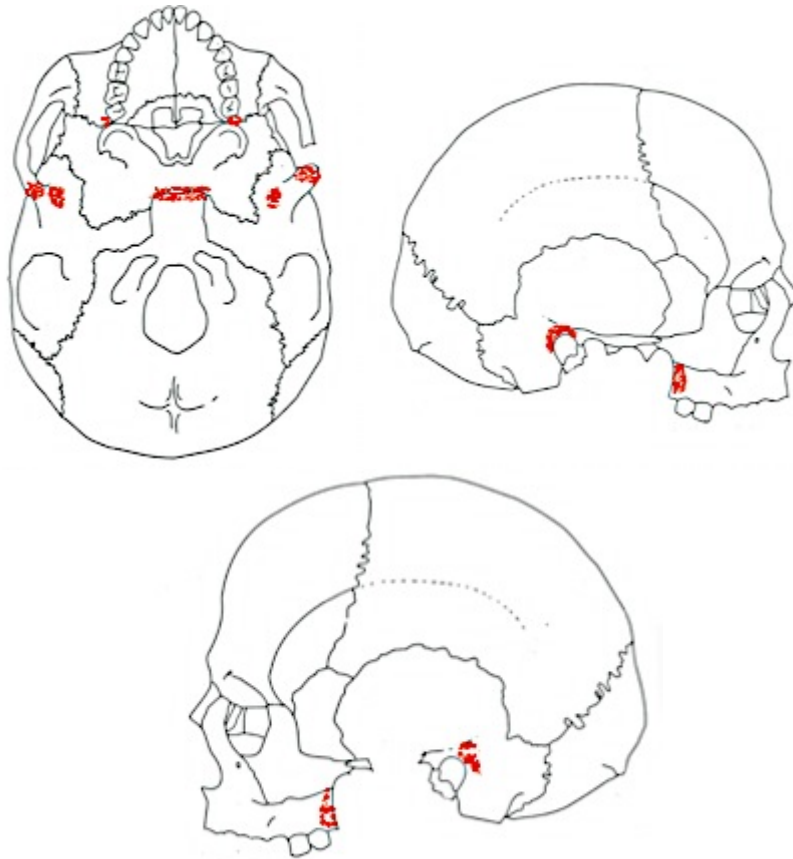
Fig. 32: Distribution of lesions in UW 23.

Fig. 33: Blastic lesion on the frontal of WLH 4.
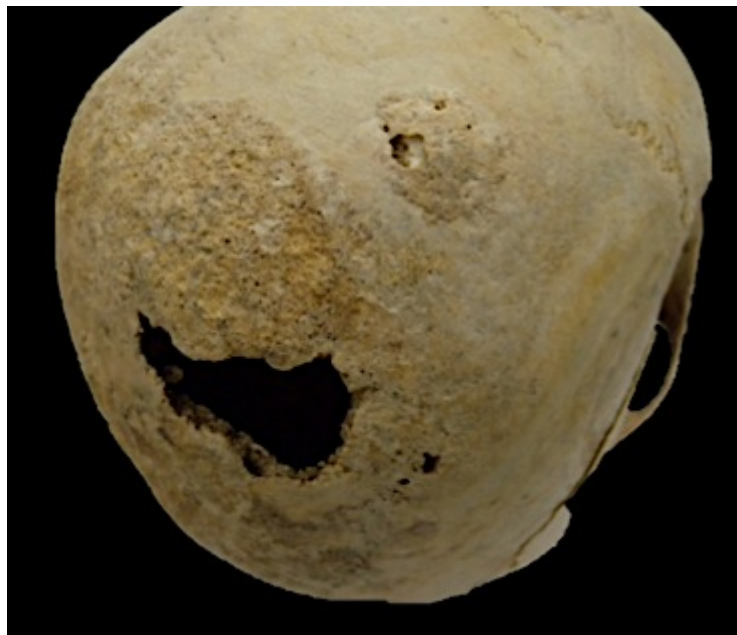
Fig. 34: Blastic and lytic lesions on the right parietal of WLH 4.
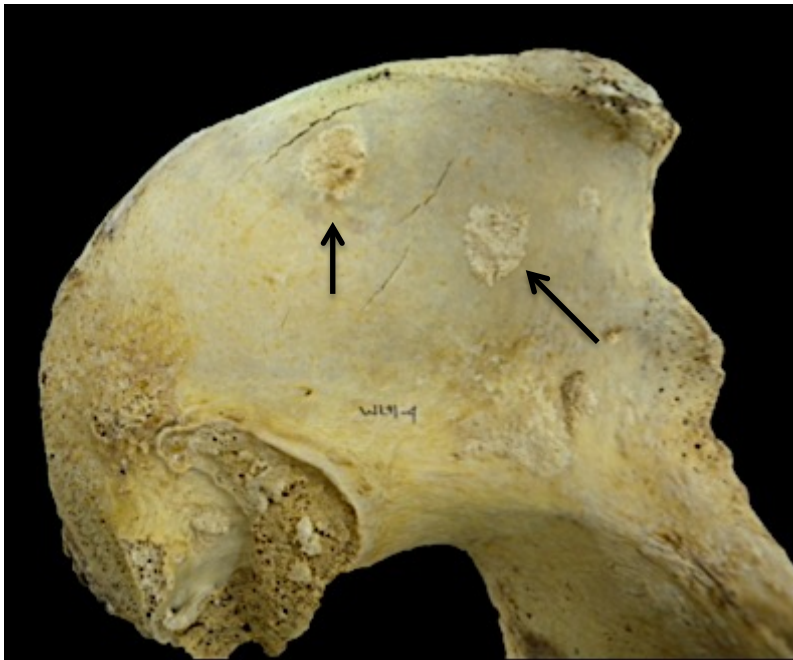
Fig. 35: Blastic lesions on the ilium of WLH 4.

Fig. 36: Blastic lesions on the auricular surface of WLH 4.

Fig. 37: Blastic lesions on the left, anterior scapula of WLH 4.
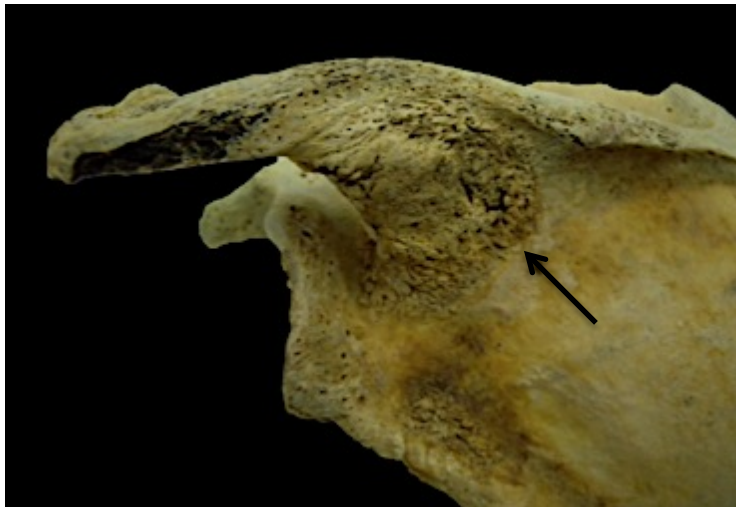
Fig. 38: Blastic lesion on the left, posterior scapula of WLH 4.

Fig. 39: Lytic lesion on the cranial base of WLH 14

Fig. 40: Lytic lesions on the pelvis of WLH 14

Fig. 41: A space-occupying lesion in the ilium of WLH 14.
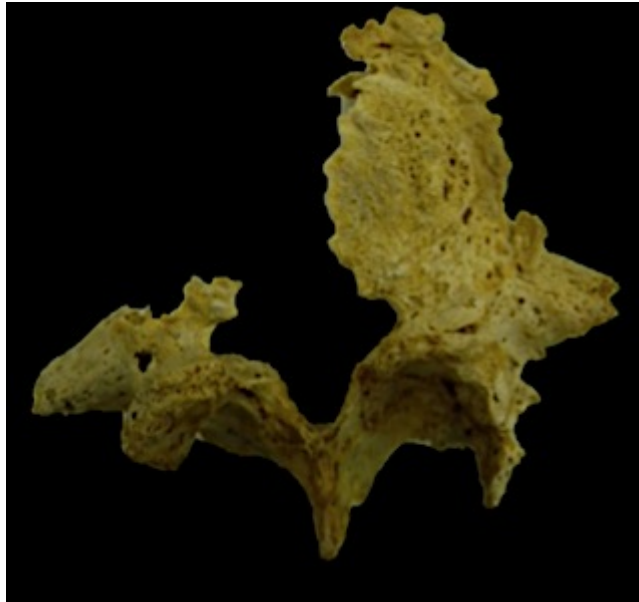
Fig. 42: A Lytic lesion resulting in the destruction of the centrum in a lumbar vertebra from WLH 14.

Fig. 43: A Lytic lesion on the sternum of WLH 14

Fig. 44: Lytic lesions on the femoral diaphysis of WLH 14 that appear punched out.
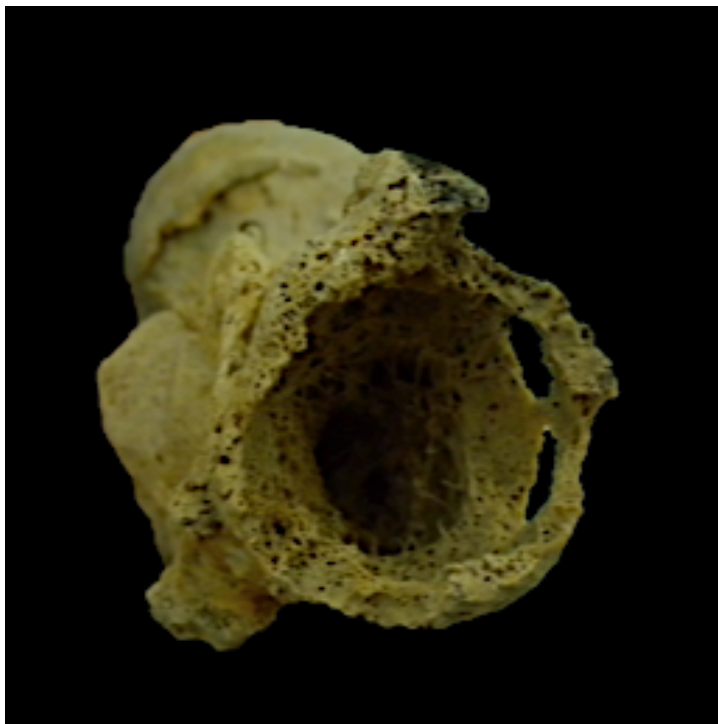
Fig. 45: Lytic destruction on the interior of the femoral epiphysis in WLH 14.

Fig. 46: Rib lesion in ABH 88.

Fig. 47: Lytic lesions on the ilum of ABH 91.

Fig. 48: A blastic lesion on the occipital of ABH 91.

Fig. 49: A lytic lesion, resulting in a pathological fracture in a rib WLH 13.
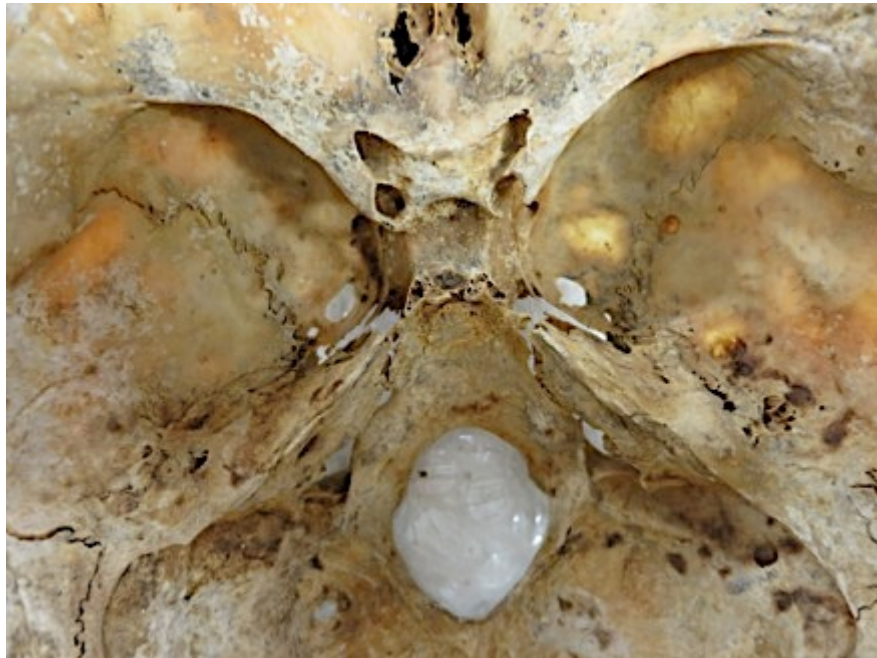
Fig. 50: The sphenoid of WLH 32, with destruction of the clinoid process.
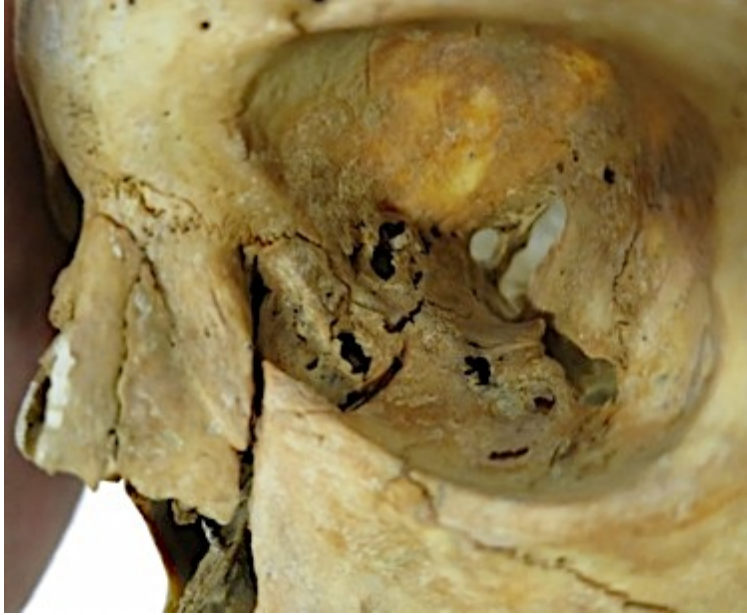
Fig. 51: Lytic lesions in the left eye orbit of WLH 32.

Fig. 52: Lytic lesions on the sphenoid of WLH 50 at the sella turcica and left greater wing.
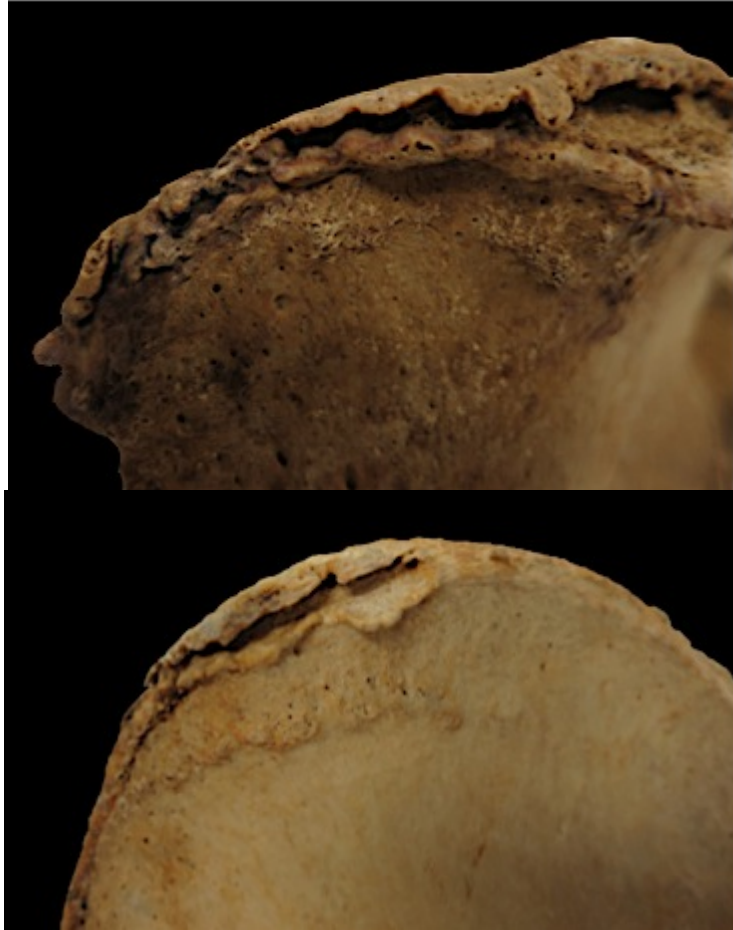
Fig. 53: Sclerotic pelvic lesions on the iliac crests from WLH 33 (above) and WLH 50 (below), similar to what was observed in WLH 29.
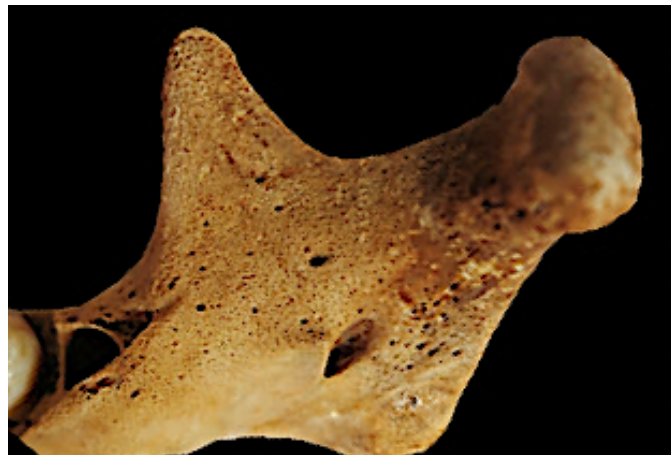
Fig. 54: Lytic porosity on the coronoid process of the mandible from ABH 101.

Fig. 55: Lytic porosity on the right scapula of ABH 101.

Fig. 56: A large osteoma on the occipital of AA 32.

Fig. 57: A lytic lesion on the occipital of AA 13.

Fig. 58: A lytic lesion superior to the petrous portion of the left temporal of AA 83b.
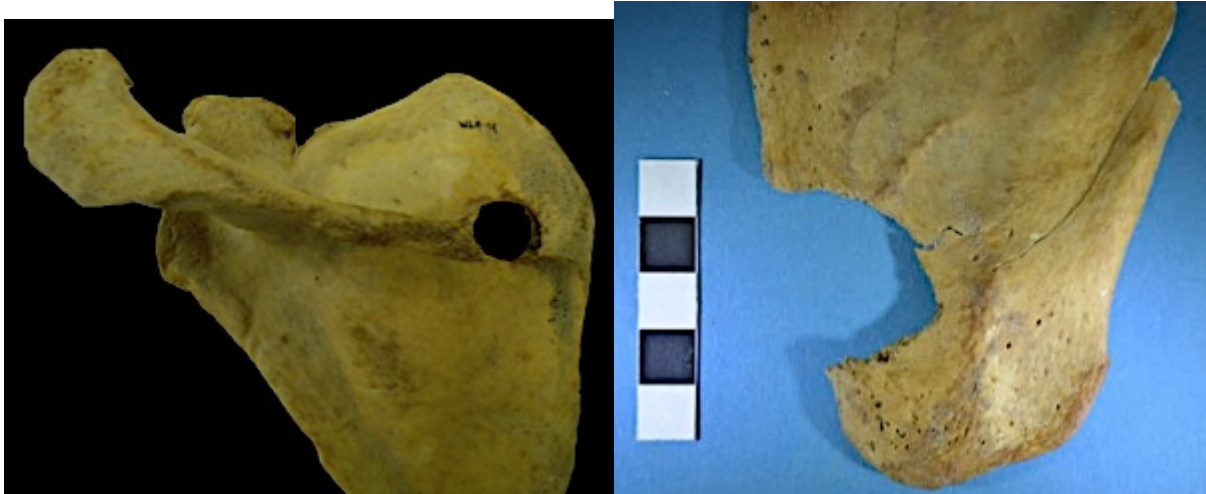
Fig. 59: A lytic lesion on the scapula of AA 83b (below) compared to a similar lytic lesion from WLH 14 (above).

Fig. 60: A space-occupying lesion in the centrum of a thoracic vertebra in AA 83b. A single column of trabecular bone bifurcates the lesion.

Fig. 61: Lytic destruction of the acetabulum in the left innominate of AA 83b.
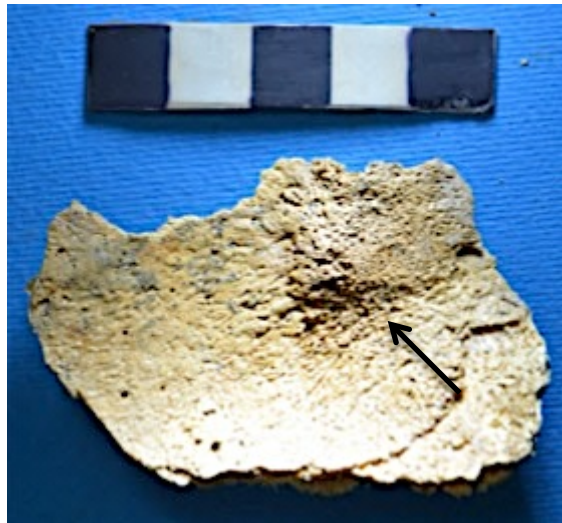
Fig. 62: A blastic lesion on a fragment of the iliac blade from AA83b.

Fig. 63: Sclerotic lesions at the proximal end of the left femur of AA 83b.

Figure 64: A comparison between the blastic lesions of AA 83b (above) and WLH 4 (below). Notice that the metaphysis of WLH 4 is unaffected.

Fig. 65: The right femur of AA 83b.

Fig. 66: A lytic lesion at the medial malleolus of the left tibia from AA 83b.

Fig. 67: A lytic lesion on the lateral aspect of the right calcaneus of AA 83b.

Fig. 68: A small osteoma superior to the left orbital margin of 62-31

Fig. 69: Specimen 61-10, a juvenile tibia with pronounced swelling of the diaphysis.
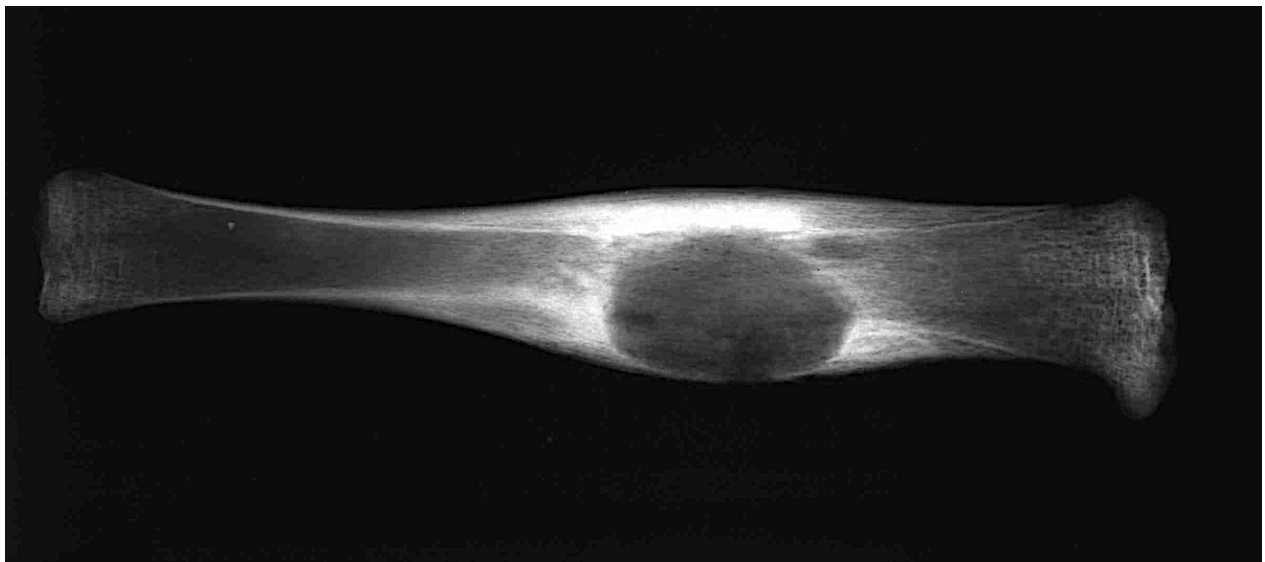
Fig. 70: A radiograph of specimen 61-10.

Fig. 71: An endocranial imprint on the left parietal and occipital from specimen 2002-1b.

Fig. 72: Small lytic lesions on the left innominate of specimen 2002-1b.

Fig. 73: A lytic lesion on the left frontal of specimen 2009-09.

Fig. 74: Lytic lesions on the superior aspect of the centrum in a thoracic vertebra from specimen 2009-09.

Fig. 75: A periosteal reaction at glabella and remnants of the metopic suture in WL 1.

Fig. 76: A cluster of osteoblastic lesions around the frontal crest of WL 1.

Fig. 77: Faint porosity on the basilar and lateral occipital portions from WL 1.

Fig. 78: Lytic activity on the inferior aspect of the body and lesser wings of the sphenoid from WL 1.

Fig. 79: Porosity of the mental eminence of WL 1.

Fig. 80: Periosteal activity on the posterior diaphysis of the left humerus from WL 1.

Fig. 81: Lytic (black arrow) and post-mortem damage (yellow arrows) on the iliac crest of the left innominate of L 1.
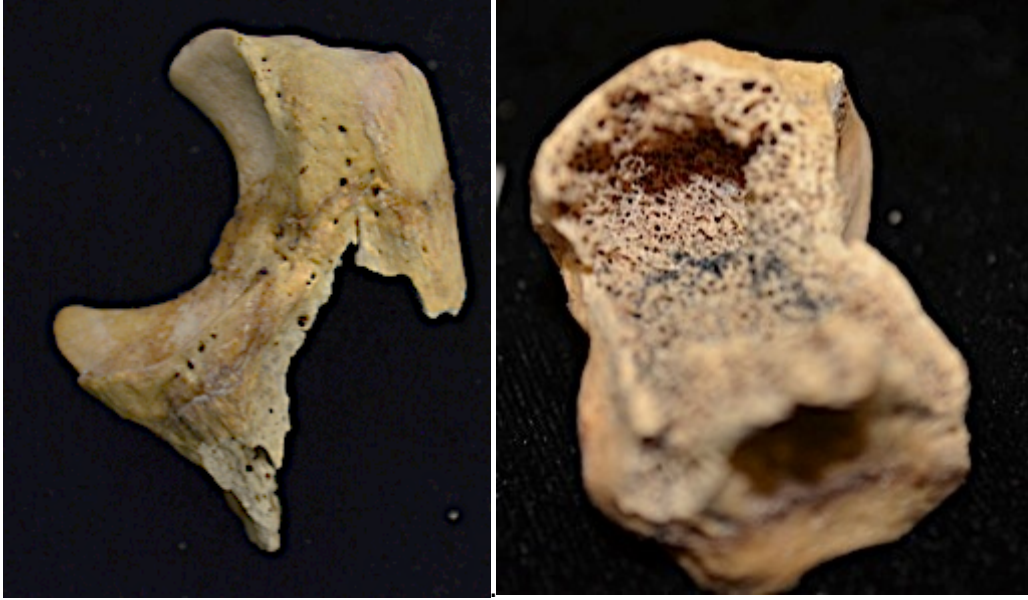
Fig. 82: WLCS 1, an ulnar fragment (left). Inside is a space-occupying lesion (right, inferior view).

Fig. 83: WLCS 3, a fragment of the distal femur, with a lytic lesion above the condyle.

Fig. 84: WLCS 2, a femoral head with post-mortem damage that was mistaken as pathological lesions.

Fig. 85: WLCS 4, a fragment of the distal femur with a mistaken post-mortem lesion.
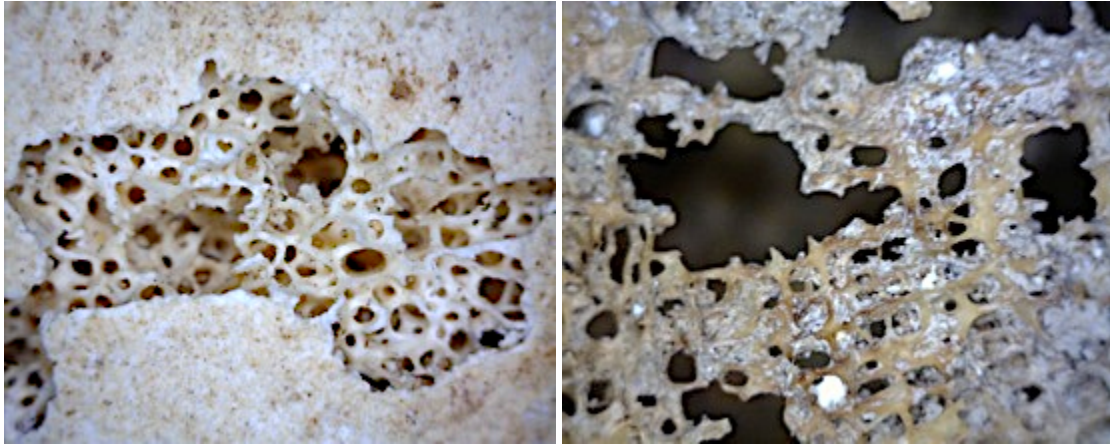
Fig. 86: Microscopic images of post-mortem damage to WLCS 2 (49x magnification) (left) and lytic destruction on the calcaneus of AA 83b (25x magnification) (right). On the left, the trabecular bone is intact and the edges of the cortical bone are a brighter colour than that of the surface. On the right the trabecular bone has been almost completely destroyed and the edges appear smooth.
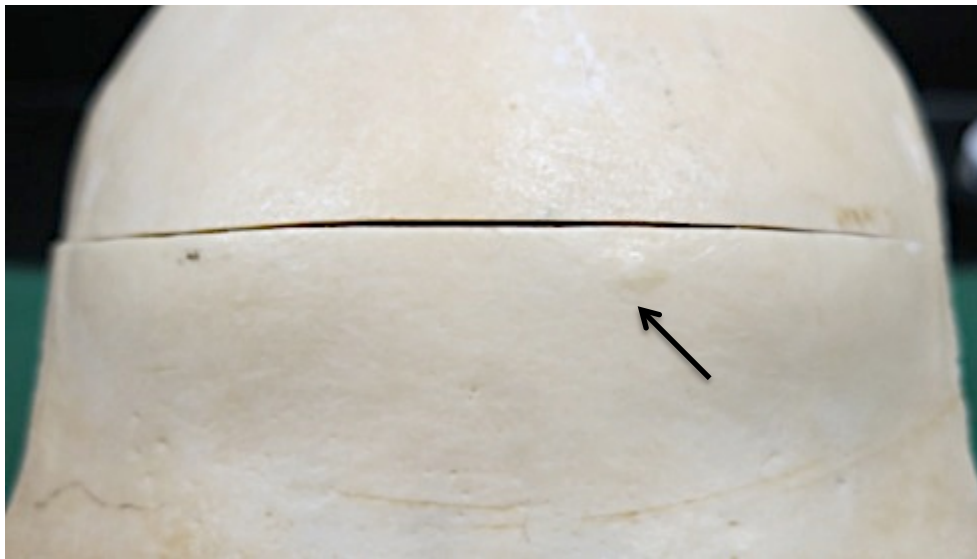
Fig. 87: A small osteoma on the frontal squama of CA 1.
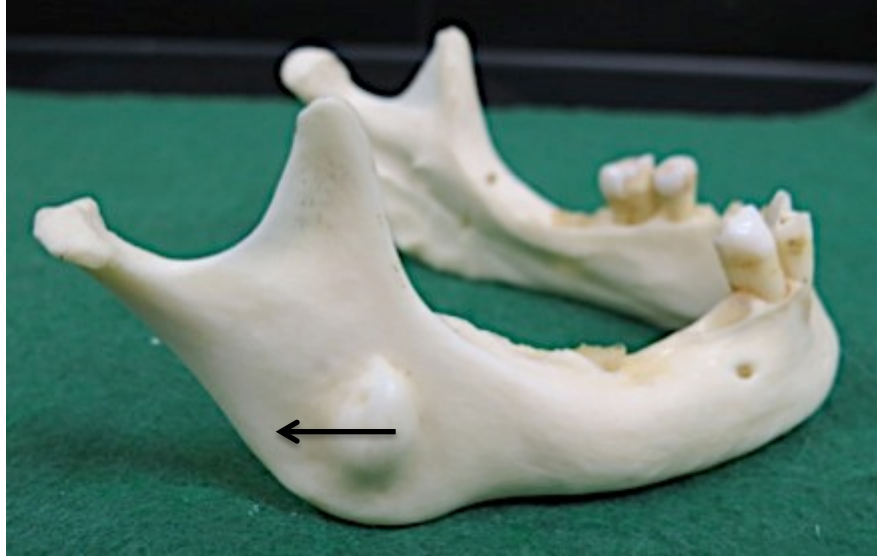
Fig. 88: A large osteoma on the mandibular ramus of M 1.
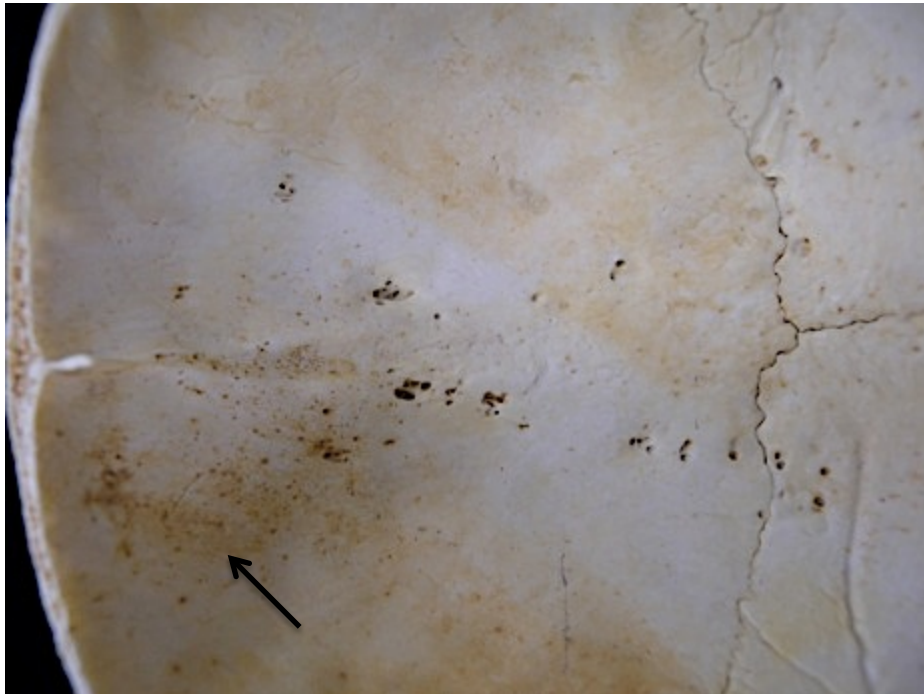
Fig. 89: Porosity along the frontal crest of UW 23.

Fig. 90: Porosity on the posterior alveolar process of the right maxilla of UW 23.

Fig. 91: Porosity superior to the auditory meatus of the right temporal of UW 23.

Fig. 92: A blastic lesion on the endocranial surface of the occipital squama from UW 8.

Fig. 93: Blastic lesions along the pleural surface of one of the left ribs of UW 8.
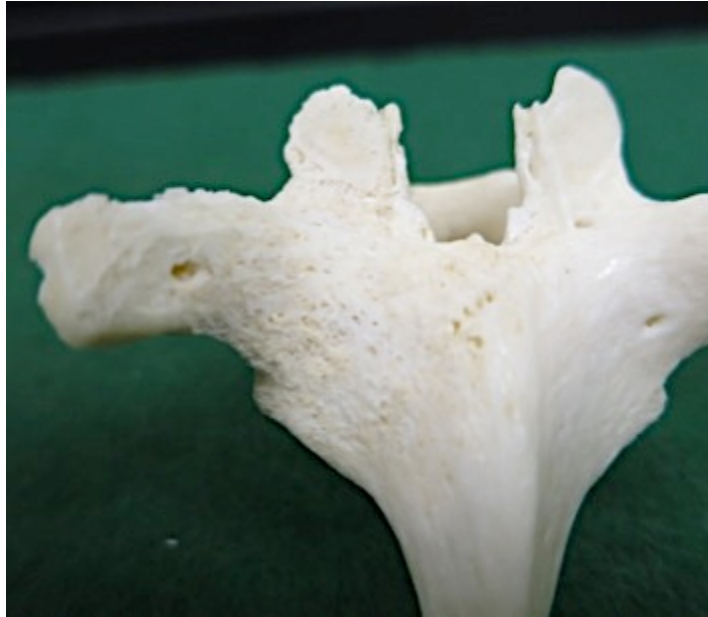
Fig. 94: Lytic activity on the right transverse process of the sixth thoracic vertebra from UW 8.

Fig. 95: A lytic lesion at the iliac crest of the left innominate of UW 8.

Fig. 96: A lytic lesion on the intertrochanteric crest of the left femur of UW 8.

Fig. 97: A comparison between a lytic lesion caused by lung cancer in an individual, WLH 13 from the Athens Collection, (above) and a suspected case neoplastic lesion from the a rib in UW 8 (below).

	Giant Cell Tumour	Langerhans Cell Histiocytosis	61-10
Age	20-40 years	5-10 years	6-9 years
Anatomic Region	Long bones, localized to epiphysis	Long bone diaphysis	Tibial diaphysis
Radiographic Appearance	Periosteal cortical shell with reinforcing ridges	Erosion of cortex and stimulation of overlying reactive periosteum	Diaphyseal swelling at proximal end
Macroscopic Appearance	Cortical expansion; smooth periosteal bone shell with small interruptions and irregularities	Thickening of the cortex	Thick cortical bone; clear demarcated borders

Fig. 98: A differential diagnosis for the Corinthian specimen 61-10.

Fig. 99: Porosity along the greater wing of WL 1.

Fig. 100: Porosity around the spheno-occipital synchondrosis of UW 23.
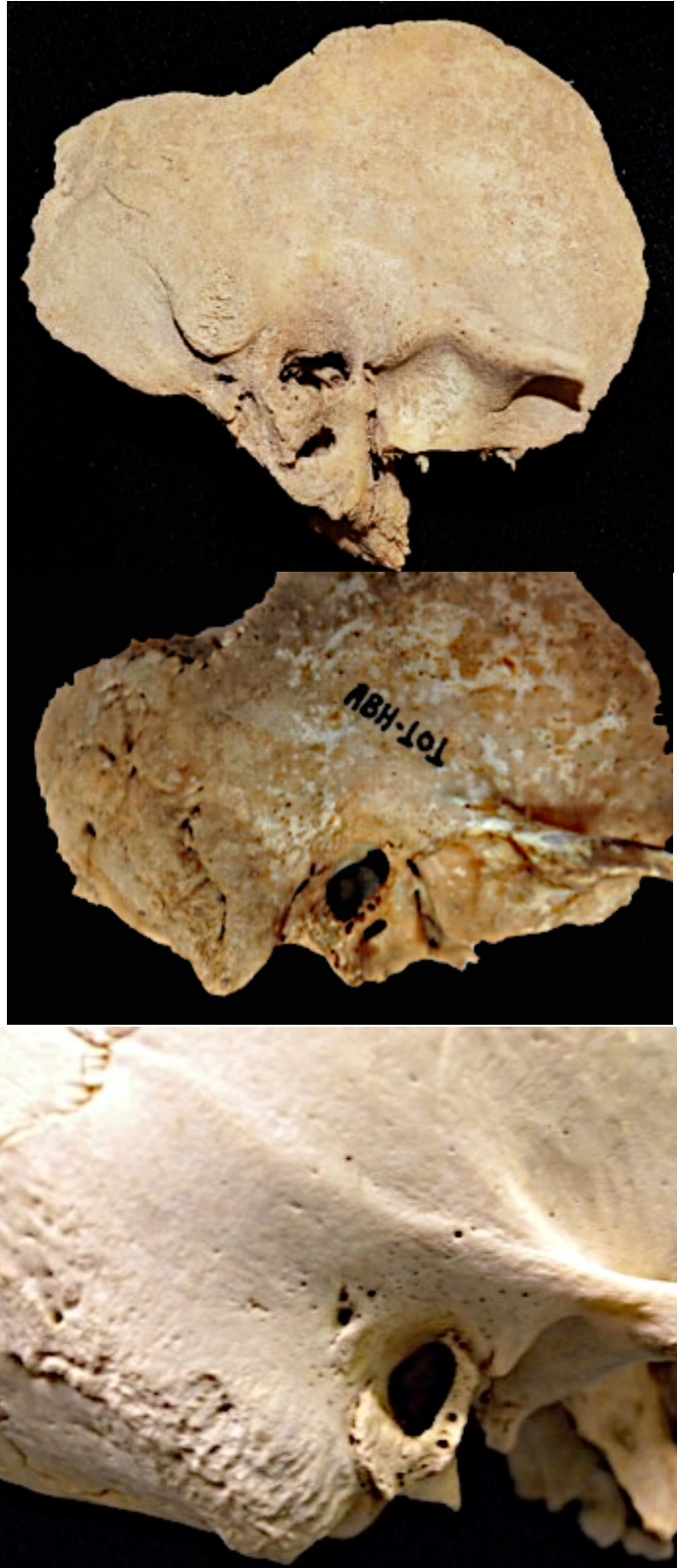
Fig. 101: The right temporals of WL 1 (above), ABH 101 (centre) and UW 23 (below) exhibiting porosity superior to the external auditory meatus.

Fig. 102: Porosity near the temporomandibular joint and the base of the zygomatics process of UW 23.

Fig. 103: The left maxilla of UW 23 (above) and WL 1 (below) with porosity at the posterior alveolar process.
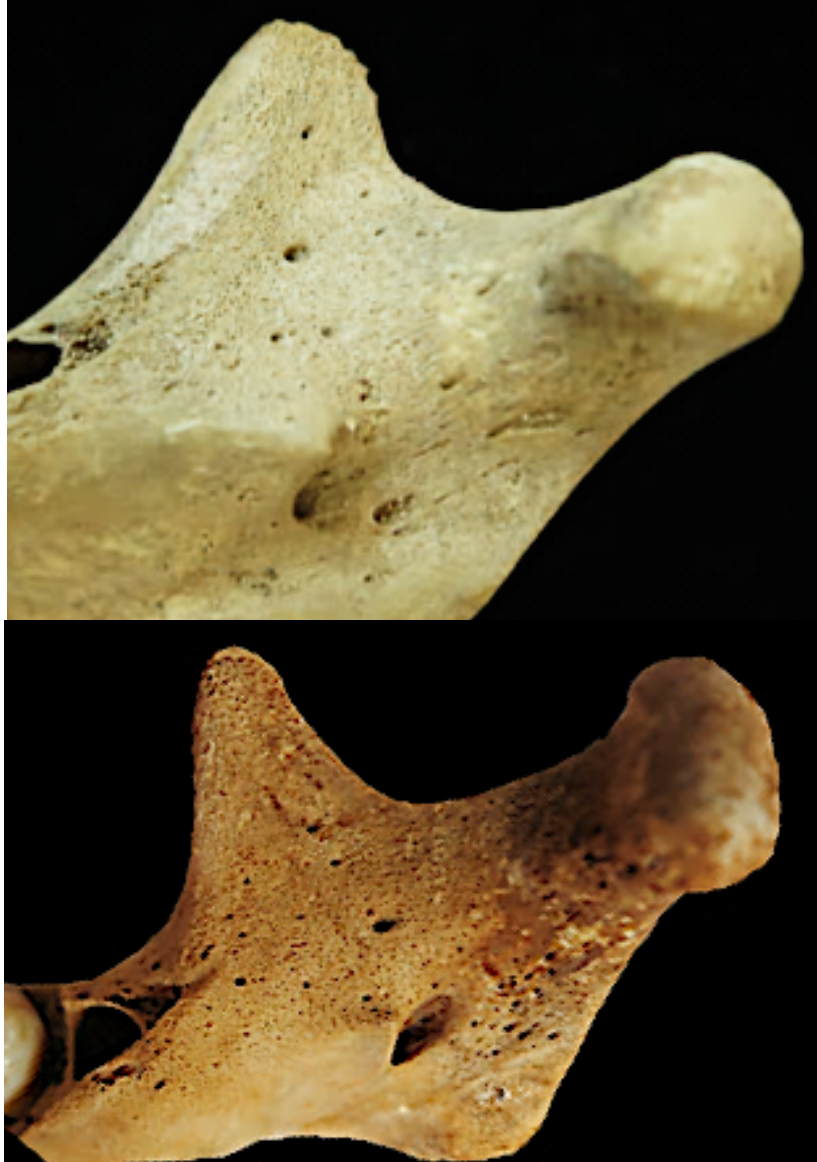
Fig. 104: Porosity along the coronoid processes of WL 1 (above) and ABH 101 (below).

Fig. 105: Some porosity in the upper eye orbits of UW 23.

Fig. 106: Porotic lesions along the frontal crest of UW 23 (above) and blastic lesions around the frontal crest of WL 1 (below).
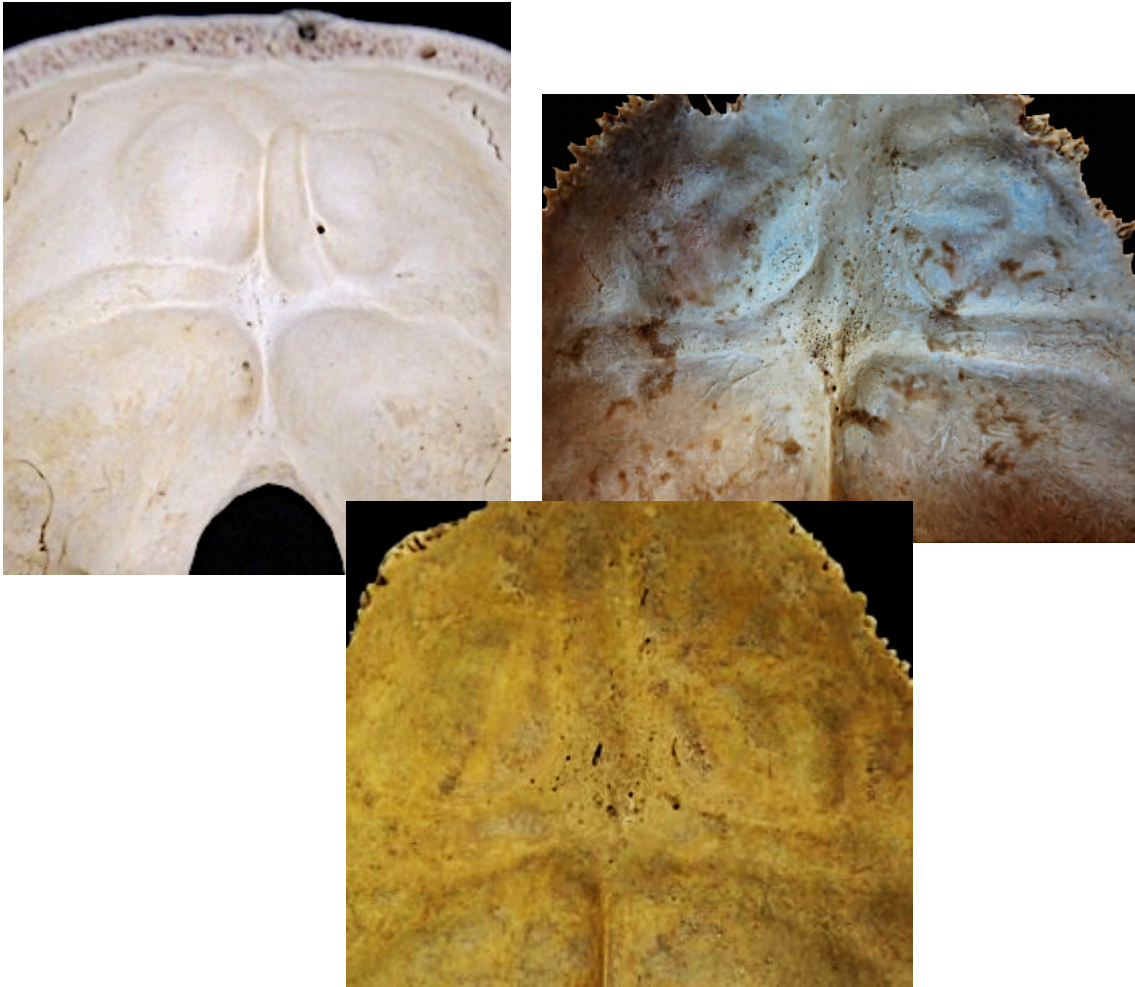
Fig. 107: The internal occipital protuberances of UW 23 (top left), ABH 101 (top right) and WL 1 (below).
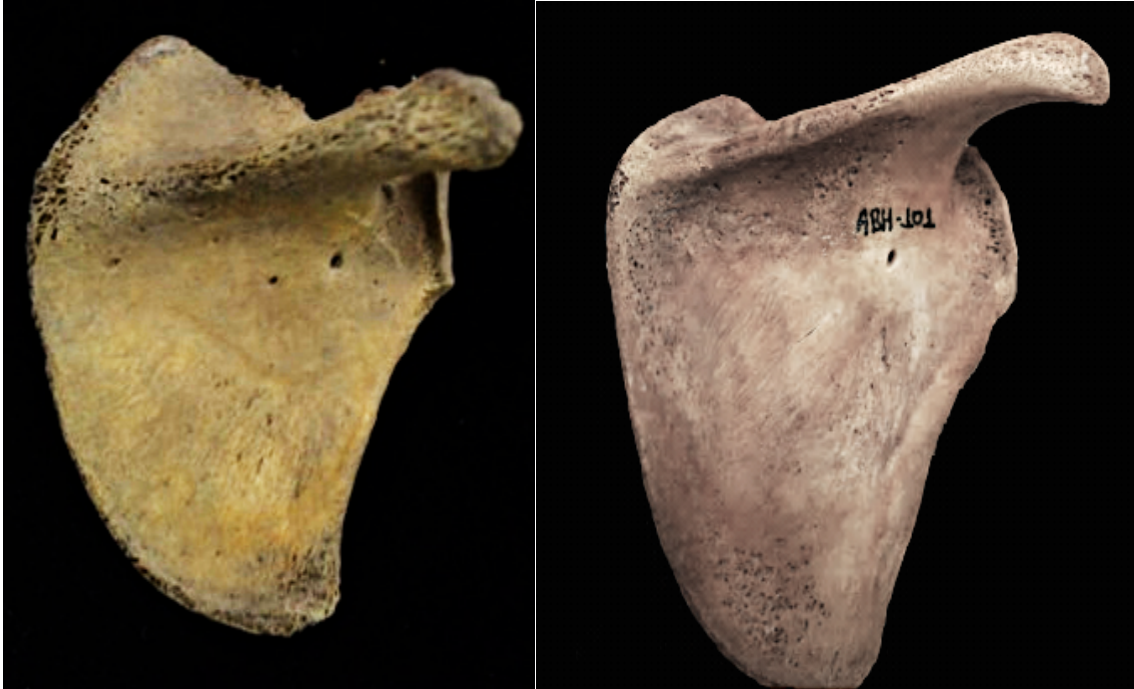
Fig. 108: The right scapulae of WL 1 (left) and ABH 101 (right) with porosity at the inferior aspect of the blade and at the scapular spine.

Fig. 109: Porosity of the ulnae from both ABH 101 (above) and WL 1 (below).

	Leukemia	Scurvy	WL 1	UW 23
Periosteal lesions		X	X	
Cortical resorption	X	Less Common	X	X
Temporal	X	Less Common	X	X
Sphenoid, greater wing	Less common	X	X	
Maxilla, alveolus	X	X	X	X
Mandible, ramus	X	X	X	N/A
Scapula	X	X	X	N/A

Fig. 110: A differential diagnosis for the Wiener Laboratory and University of Waterloo specimens, WL 1 and UW 23.
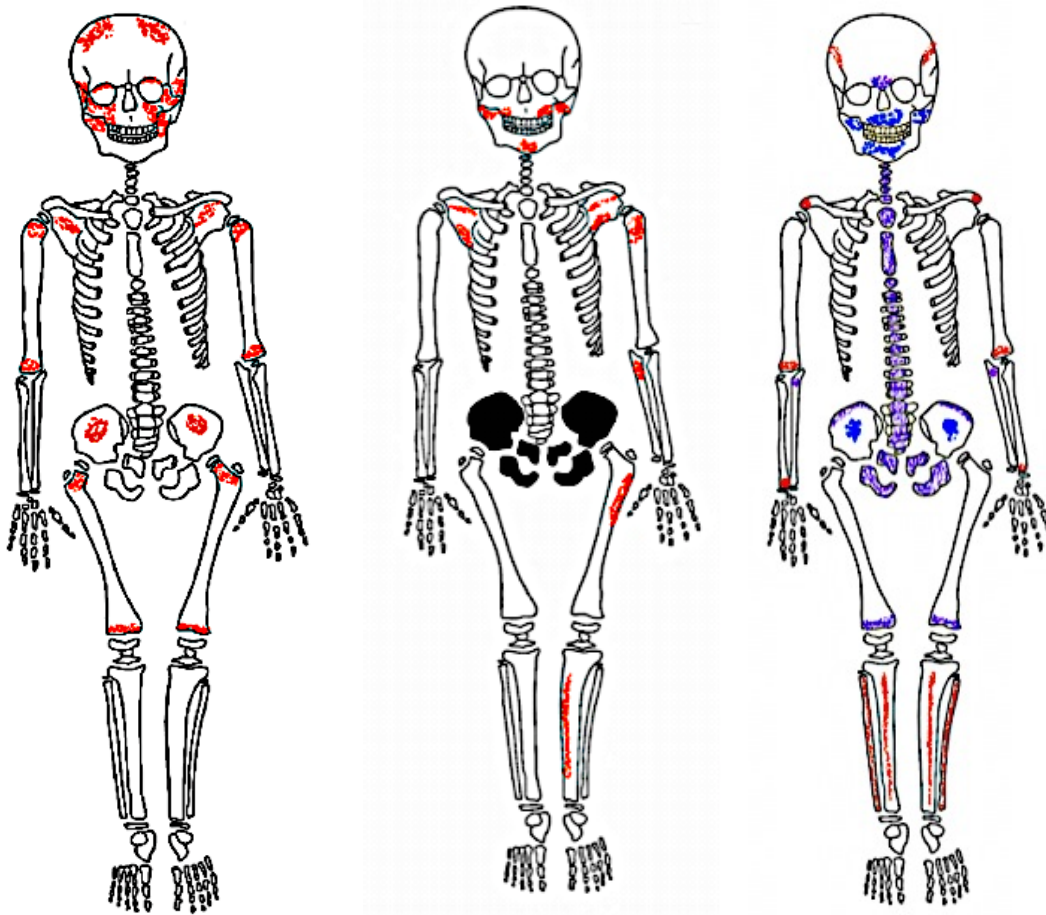
Fig. 111: A comparison between WL 1 (centre) and composite diagrams of scurvy (left) (compiled from: Ortner and Ericken 1997; Ornter et al. 1999; Ortner et al. 2001; Ortner 2003; Brickley and Ives 2006) and leukemia (right) (complied from Rothschild et al. 1997 in red; the Athens Collection cases in blue; purple denotes being found in both Rothschild et al. (1997) and the Athens Collection).

Fig. 112: The left innominate of AA 83b.
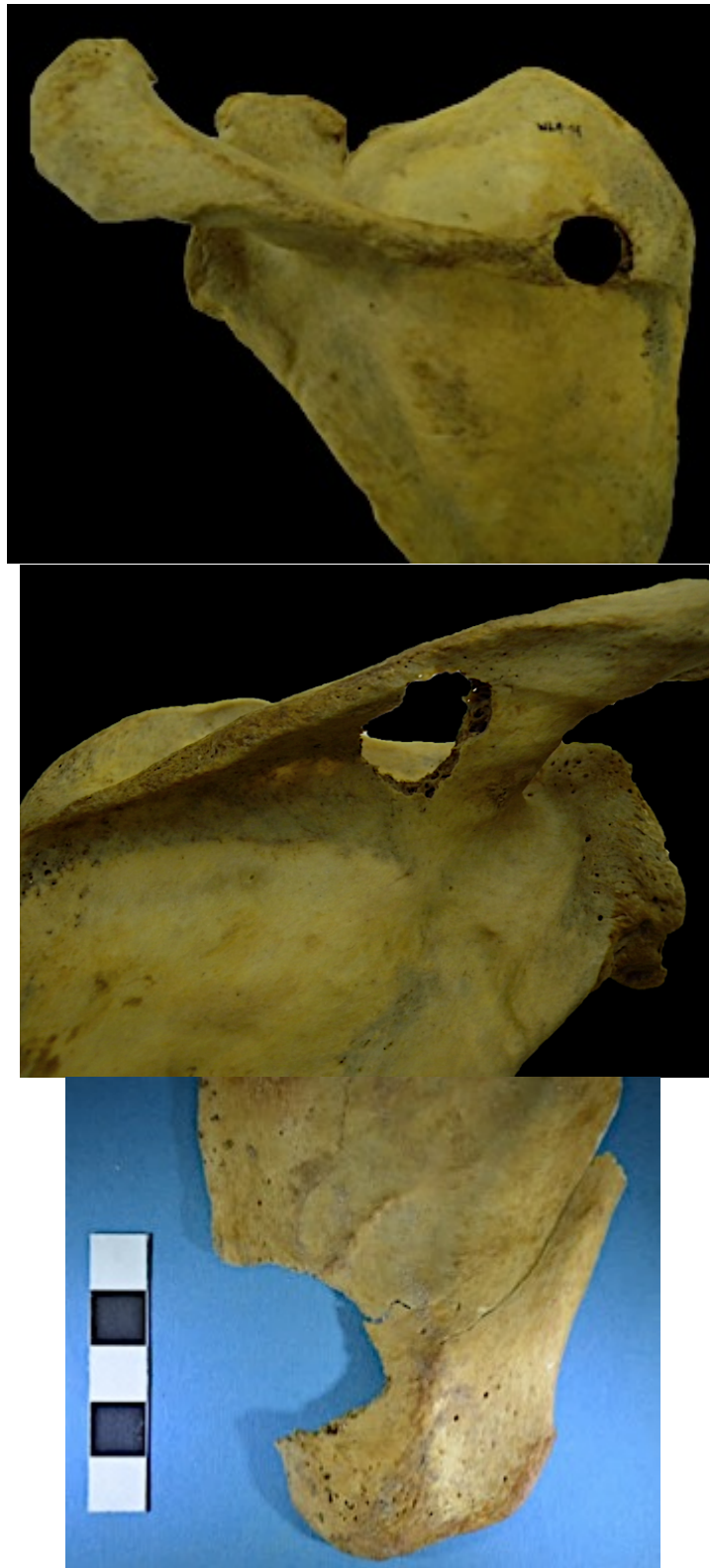
Fig. 113: Lytic lesions on the scapulae of WLH 14 (above and center) compared to a scapular lesion in AA 83b.

	Metastatic Prostate Cancer	Osteosarcoma	Chondrosarcoma	AA 83b
Age	Increase in risk over age of 40-50 years	10-30 years	30-60 years	35-39 years
Sex	Male	Male	Male	Male
Anatomic Region Predilection	Pelvis, sacrum, lumbar and thoracic vertebrae	Proximal femur, metaphysis	Pelvis, long bones	Pelvis, long bones, skull, scapula
Lesion Type	Osteoblastic	Sclerotic	Sclerotic	Mixed lytic and sclerotic
Periosteal new bone	Widespread throughout skeleton	None	None	Some on ilium

Fig. 114: A differential diagnosis for the Athenian Agora individual, AA 83b.

References

Abbot KH, Courville CB. 1939. Historical Notes on the Meningiomas. I. A Study of the Hyperostoses in Prehistoric Skulls. Bull. Los Angeles Neurol. Soc. 4: 101-113.

Abnet CC. 2007. Carcinogenic Food Contaminants. Cancer Investigation 25: 189-196.

Agelarakis A. 2002. Investigations of Physical Anthropology and Paleopathology Of The Ancient Necropolis of Thassos. Excavating Classical Culture: Recent Archaeological Discoveries in Greece 1031, 12-19.

Alleyne R. 2010. Cancer Caused By Modern Man As It Was Virtually Non-Existent Ancient World. The Telegraph, 14 October.

Allison MJ, Gerszten E, Munizaga J, Santoro C. 1980. Metastatic Tumor of Bone in a Tiahuanaco Female. Bull. N.Y. Acad. Med 56: 581-587.

Ames BN. 1978. Environmental Chemicals Causing Cancer and Genetic Birth Defects: Developing a Strategy to Minimize Human Exposure. California: Institute of Governmental Studies.

Anderson T, Wakley J, Carter A. 1992. Medieval Example of Metastatic Carcinoma: A Dry Bone, Radiological, and SEM Study. Am J Phys Anthropol 89: 309-323.

Angel JL. 1945. Skeletal Material from Attica. Hesperia 14: 279-363.

Angle JL. 1947. The Length of Life in Ancient Greece. Journal of Gerontology 2: 18-24.

Angel JL. 1984. Health as a Crucial Factor in the Changes from Hunting to Developed Farming in the Eastern Mediterranean. *In* Paleopathology at the Origins of Agriculture. Mark Nathan Cohn and George J. Armelagos, eds. Pp. 51-73. Orlando: Academic Press, Inc.

Anton SC. 1988. Bony Criteria for the Differentiation of Metastatic Carcinoma, Multiple Myeloma, Major Infectious Diseases, and Hyperparathyroidism: A Case Study Approach. Human Skeletal Biology: Contributions to the Understanding of California's Prehistoric Populations 24: 43-68.

Armstrong RW, Imrey PB, Lye MS, Armstrong MJ, Yu MC, Sani S. 1998. Nasopharyngeal Carcinoma in Malaysian Chinese: Salted Fish and Other Dietary Exposures. Int. J. Cancer 77: 228-235.

Arney K. 2010. Claims That Cancer Is Only a 'Modern, Man-Made Disease' Are False and Misleading. Cancer Research UK, 14 October. http://scienceblog.cancerresearchuk.org/2010/10/14/claims-that-cancer-is-only-a-%E2%80%98modern-man-made-disease%E2%80%99-are-false-and-misleading/, Accessed 22 December 2013.

Ascenzi A, Bianco P, Nicoletti R, Ceccarini G, Fornaseri M, Graziani G, Giuliano MR, Rosicarello R, Ciuffarella L, Granger-Taylor H. 1996. The Roman Mummy of Grottarossa. *In*: Spindler K, Wilfing H, Rastbichler-Zissernig E, zur Nedden D, Nothdurfter H, editors. Human Mummies: A Global Survey of Their Status and the Techniques of Conservation. New York: Springer. 205-217.

Assis S, Codhina S. 2010. Metastatic Carcinoma in a 14th-19th Century Skeleton from Constância (Portugal). International Journal of Osteoarchaeology 20: 603-620.

Aufderheide AC, Rodrígues – Martín, C. 1998. The Cambridge Encyclopedia of Human Paleopathology. Cambridge: Cambridge University Press.

Baan R, Straif K, Grosse Y, Secretan B, El Ghissassi F, Cogliano V. 2006. Carcinogenicity of Carbon Black, Titanium Dioxide and Talc. The Lancet Oncology 7: 295-296.

Baraybar JP, Shimada I. 1993. A Possible Case Of Metastatic Carcinoma In A Middle Sican Burial From Batan Grande, Peru. International Journal of Osteoarchaeology, 3: 129-135.

Barnes E, Ortner DJ. 1997. Multifocal Eosinophilic Granuloma with a Possible Trepanation in a Fourteenth Century Greek Young Skeleton. International Journal of Osteoarchaeology 7:542-547.

Batson OV. 1940. The Function of the Vertebral Veins and There Role in the Spread of Metastases. Annals of Surgery 112: 138-149.

Bilimoria MM, Morrow M. 1995. The Woman at Increased Risk for Breast Cancer: Evaluation and Management Strategies. Ca Cancer J Clin 45: 263-278.

Bourbou C. 2003. A Survey of Neoplastic Disease in Ancient and Medieval Greek Populations. Eulimene 4: 181-188.

Brickley M, Ives R. 2006. Skeletal Manifestations of Infantile Scurvy. American Journal of Physical Anthropology 129: 163-172.

Brickley M, Ives R. 2008. The Bioarchaoelogy og Metabolic Bone Disease. New York: Elsevier

Brooks ST, Melbye J. 1967. Skeletal Lesions Suggestive of Pre-Columbian Multiple Myeloma in a Burial from the Kane Mounds, Near St. Louis, Missouri. Miscellaneous Papers in Paleopathology 1: 23-29.

Brooks ST, Suchey JM. 1990. Skeletal Age Determination Based on the Os Pubis: A Comparison of the Acsádi-Nemeskéri and Suchey-Brooks Methods. Human Evolution 5: 227-238.

Brothwell D. 1961. The Palaeopathology of Early British Man: An Essay on the Problems of Diagnosis and Analysis. Journal of the Royal Anthropological Institute of Great Britain and Ireland 91: 318-344.

Brothwell D. 1967. The Evidence for Neoplasms *In* Diseases in Antiquity: A Survey of the Diseases, Injuries and Surgery of Early Populations. Brothwell D and Sandison AT, eds. Pp.320-345. Springfield, Illinois: Charles C Thomas.

Brothwell D. 2012. Tumours: Problems of Differential Diagnosis in Paleopathology *In* A Companion to Paleopathology. Grauer, A, ed. Pp. 420-433. Chichester, West Sussex: Wiley-Blackwell.

Brown M, Ortner DJ. 2011. Childhood Scurvy in a Medieval Burial From Mačvanska Mitrovica, Serbia. International Journal of Osteoarchaeology 21: 197-207.

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

Camp JM. 2003. The Athenian Agora: A Short Guide to the Excavations. Athens: American School of Classical Studies at Athens.

Campanacci M. 1990. Bone and Soft Tissue Tumors. New York: Springer-Verlag Wien.

Campillo D. 1998. Primary Benign Skull Tumors in Paleopathology. Journal of Paleopathology 10: 73-89.

Campillo D. 2005. Paleoradiology III: Neoplastic Conditions. Journal of Paleopathology 17: 93-135.

Capasso L, Di Tota G. 1996. The Antiquity of Osteosarcoma. International Journal of Osteoarchaeology 6: 512-514.

Capasso L. 2000. Indoor Pollution and Respiratory Diseases in Ancient Rome. The Lancet 356: 1774.

Capasso L. 2005. Antiquity of Cancer. International Journal of Cancer 113: 2-13.

Carbone D. 1992. Smoking and Cancer. The American Journal of Medicine 93: 1A-13S – 1A-17s.

Carrascal S, Chimenos-Küstner E, Isidro A, Malgosa A. 2013. Cystic Mandibular Lesion in the Antiquity: A Rare Finding. International Journal of Osteoarchaeology 23: 319-323.

Centers for Disease Control and Prevention. 2013. Genital HPV Infection – Fact Sheet. http://www.cdc.gov/std/HPV/STDFact-HPV.htm Accessed 17 September 2013.

Cheng SJ, Sala M, Wang MY, Pot-Deprun J, Chouroulinkov I. 1980. Mutagenic, Transforming and Promoting Effect of Pickled Vegetables from Linxian County, China. Carcinogenesis 1: 685-692.

Choi CQ. 2010. Cancer Is A Man-Made Disease, Controversial Study Claims. Livescience, 15 October. http://www.livescience.com/10822-cancer-man-disease-controversial-study-claims.html, Accessed 22 December 2013.

Cole P. 1971. Coffee-Drinking and Cancer of the Lower Urinary Tract. Lancet 297: 1335-1337.

Coleman RE. 2001. Metastatic Bone Disease: Clinical Features, Pathophysiology and Treatment Strategies. Cancer Treatment Reviews 27: 165-176.

Coleman RE. 2006. Clinical Features of Metastatic Bone Disease and Risk of Skeletal Morbidity. Clinical Cancer Research 12: 6243s-6249s.

Corrales S. 1987. Skeleton Shortage is Giving Medical Schools a Headache. Los Angeles Times, 21 April.

Cumming J, Hacking N, Fairhurst J, Ackery D, Jenkins JD. 1990. Distribution of Bony Metastases in Prostatic Carcinoma. British Journal of Urology 66: 411-414.

David R, Zimmerman M. 2010. Cancer: An Old Disease, a New Disease or Something in Between? Nature Reviews Cancer 10: 728-733.

De la Chapelle A. 2004. Genetic Predisposition to Colorectal Cancer. Nature Reviews Cancer 4: 769-780.

De Gruijl FR. 2000. Skin Cancer and Solar Radiation. European Journal of Cancer 35: 2003-2009.

Dorfman HD, Czerniak B. 1995. Bone Cancers. Cancer 74: 203-210.

Edeiken J, Hodes PJ. 1973. Roentgen Diagnosis of Diseases of Bone. Baltimore: The Williams & Wilkins Company.

Eliopoulos C, Lagia A, Manolis S. 2007. A Modern Documented Human Skeletal Collection From Greece. Homo 58: 221-228.

Fornaciari G, Giuffra V. 2012. Soft Tissue Tumors in Palaeopathology: A Review. Pathobiology 79:257-267.

Fox Leonard SC.1997. Comparative Health from Paleopathological Analysis of the Human Skeletal Remains Dating to the Hellenistic and Roman periods, from Paphos, Cyprus and Corinth, Greece. Ph.D. dissertation, Department of Anthropology, University of Arizona.

Frank SA. 2004. Genetic Predisposition to Cancer – Insights from Population Genetics. Nature Reviews: Genetics 5: 764-772.

Galasko CSB. 1981. The Anatomy and Pathways of Skeletal Metastases. *In* Bone Metastases. Boston: GK Hall 49-63.

Gall RJ, Sim FH, Pritchard DJ. 1976. Metastatic Tumours to the Bones of the Foot. Cancer 37: 1492-1495.

Głydykowska-Rzeczycka J. 1978. Mandibular Tumor in a Male Skeleton From a Medieval Burial Ground in Czersk. Folia Morphologica 37: 191-196.

Głydykowska-Rzeczycka J, Myśliwski A. 1986. Osteoid-Osteoma from Middle-Ages Cemetary in Poland. Ossa 12: 33-39.

Głydykowska-Rzeczycka J. 1997. Osteosarcoma and Osteochondroma From Polish Medieval Cemeteries. Journal of Paleopathology 9: 47-53.

Greenspan A, Jundt G, Remagen W. 2007. Differential Diagnosis in Orthopaedic Oncology. Philadelphia : Lippincott Williams & Wilkins.

Grupe G. 1988. Metastasizing Carcinoma in a Medieval Skeleton: Differential Diagnosis and Etiology. Am J Phys Anthropol 75: 369-374.

Halperin E. 2004. Paleo-Oncology: The Role of Ancient Remains in the Study Of Cancer. Perspectives in Biology and Medicine 47: 1-14.

Hecht SS. 2006. Cigarette Smoking: Cancer Risks, Carcinogens and Mechanisms. Langenbecks Arch Surg 391: 603-613.

Heighway J, Thatcher N, Cerny T, Hasleton PS. 1986. Genetic Predisposition to Human Lung Cancer 53: 453-457.

Henneberg M, Henneberg RJ. 2006. Human Skeletal Material from Pompeii: A Unique Source of Information about Ancient Life. Rivista di Natura 1: 23-37.

Hrdlička A. 1927. Anthropology and Medicine. American Journal of Physical Anthropology 10: 1-9.

Ito Y, Yanase S, Kishishta M, Harayama T, Hirota M, Oohigashi H, Koshinizu K. 1983. The Roles of Epstein-Barr Virus, Normal Bacterial Flora and Promotor Plant Diterpene Esters in Causation of Nasopharygneal Carcinoma. *In* Prasad U, Ablashi DV, Levine PH, Pearson GR, eds. Nasopharyngeal carcinoma: current concept. Kuala Lumpur: University of Malaysia Press: 321–327.

Jarmey C. 2004. The Atlas of Musculo-Skeletal Anatomy. Berkley, California: North Atlantic Books.

Jónsdóttir B, Ortner D, Frohlich B. 2003. Probable Destructive Meningioma in an Archaeological Adult Make Skull from Alaska. Am J Phys Anthropol 122: 232-239.

Kirkpatrick-Smith S. 2010. Differential Diagnosis and Discussion of a Large Nasal Neoplasm from a Late Bronze Age Athenian Male. International Journal of Osteoarchaeology 20: 731-736.

Klaus HD, Ericksen CM. 2013. Paleopathology of an Ovarian Teratoma: Description and Diagnosis of an Exotic Abdominal Bone and Tooth Mass in a Historic Peruvian Burial. International Journal of Paleopathology.

Kornafel D, Kwiatkowska B, Pospieszny N, Trnka J, Garcarek J. 2000. A Medieval Skull with a Neoplastic Lesion Found in Wrocław, Poland. Journal of Paleopathology 12: 29-35.

Krishnamurthy GT, Tubis M, Hiss J, Blahd WH. 1977. Distribution Pattern of Metastatic Bone Disease. JAMA 237: 2504-2506.

Lagier R, Baud CA, Arnaud G, Arnaud S, Menk R. 1982. Lesions Characteristic Of Infection Or Malignant Tumor in Paleo-Eskimo Skulls. Virchows Archiv, 395: 237-243.

Leekley D, Noyes R. 1976. Archaeological Excavations in Southern Greece. New Jersey: Noyes Press.

Levesque J, Marx R, Bell RS, Wunder JS, Kandel R, White L. 1998. A Clinical Guide to Primary Bone Tumors. Baltimore: Williams & Wilkins.

Libson E, Bloom RA, Husband JE, Stoker DJ. 1987. Metastatic Tumours of Bones of the Hand and Foot. Skeletal Radiol 16: 387-392.

Liston MA. 1991. Histiocytosis in Crete? A Possible Case from the Early Iron Age Site of Kavousi.

Little ML. 1997. A Possible Example of Malignant Neoplasm from a Medieval Period Grave in Athens, Greece. Poster at the 24th Annual Meeting of Paleopathology Association, St. Loius. As cited in Bourbou C. 2003. A Survey of Neoplastic Disease in Ancient and Medieval Greek Populations. Eulimene 4: 181-188.

Liu J, Waalkes MP. 2008. Liver is a Target of Aresnic Carcinogenesis. Toxicological Sciences 105: 24-32.

Logothetis CJ, Lin SH. 2005. Osteoblasts in Prostate Cancer Metastasis to Bone. Nature Reviews Cancer 5: 21-28.

Lovejoy CO, Meindel RS, Przybeck TR, Mensforth RP. 1985. Chronological Metamorphosis of the Auricular Surface of the Ilium: A New Method for the Determination of Age at Death. American Journal of Physical Anthropology 68: 15-28.

Lu SH, Camus AM, Tomatis L, Bartsch H. 1981. Mutagenicty of Extracts of Pickled Vegetables Collected in Linhsien County, a High-Incidence Area for Esophageal Cancer in Northern China. JNCI 66: 33-36.

Luna LH, Aranda CM, Bosio LA, Beron MA. 2008. A Case Of Multiple Metastases in Late Holocene Hunter-Gatherers From the Argentine Pampean Region. International Journal of Osteoarchaeology, 18: 492-506.

Macrae F. 2010. Cancer 'Is Purely Man-Made' Say Scientists After Finding Almost no Trace of Disease in Egyptian Mummies. Daily Mail, 15 October. http://www.dailymail.co.uk/sciencetech/article-1320507/Cancer-purely-man-say-scientists-finding-trace-disease-Egyptian-mummies.html, Accessed 22 December 2013.

MacCurdy GG. 1923. Human Skeletal Remains from the Highlands of Peru. American Journal of Anthropology 6: 218-329.

Manchester K. 1983. Secondary Cancer in an Anglo-Saxon Female. Journal of Archaeological Science 10: 475-482.

Mankin HJ. 2006. Pathophysiology of Orthopaedic Diseases. USA: American Academy of Orthopaedic Surgeons.

Marks M, Hamilton M. 2007. Metastatic Carcinoma: Paleopathology and Differential Diagnosis. International Journal of Osteoarchaeology 17: 217-234.

Marques C, Santos A, Cunha E. 2011. Better a Broader Diagnosis than a Misdiagnosis: The Study of a Neoplastic Condition in a Male Individual Who Died in Early 20th century (Coimbra, Portugal). International Journal of Osteoarchaeology.

Mays S, Strouhal E, Vyhnanek L, Nemeckova A. 1996. A Case of Metastatic Carcinoma of Medieval Date from Wharram Percy, England. Journal of Paleopathology 8: 33-42.

McGeorge PJP. 1988. Health and Diet in Minoan Times. *In* New Aspects of Archaeological Sciences in Greece. Proceedings of a Meeting Held at the British School at Athens 1987. R.E. Jones and H.W. Catling, eds. Athens: 47-54.

Mellon CD, Carter JE, Owen DB. 1988. Ollier's Disease and Maffucci's Syndrome: Distinct Entities or a Continuum. J Neurol 235: 376-378.

Micozzi M. 1991. Disease in Antiquity: the Case of Cancer. Arch Pathol Lab Med 115: 838-844.

Miller TT. 2008. Bone Tumours and Tumour like Conditions: Analysis with Conventional Radiography. Radiology 246: 662-673.

Møller P, Møller-Christensen V. 1952. A Mediaeval Female Skull Showing Evidence Of Metastases From A Malignant Growth. Acta Pathologica Microbiologica Scandinavica, 30: 336-342.

Moodie RL. 1923. Paleopathology: An Introduction to the Study of Ancient Evidences of Disease. Urbana Illinois: University of Illinois Press.

Morgan JWM, Adcock KA, Donohue RE. 1990. Distribution of Skeletal Metastases in Prostatic and Lung Cancer. Urology 36: 31-34.

Morse D, Dailey RC, Bunn J. 1974. Prehistoric Multiple Myeloma. Bull. N.Y. Acad. Med. 50: 447-458.

Morse D. Ancient Disease in the Midwest. Springfield, III, Illinois State Museum: 13-14.

Mossman KL. 2007. Radiation Risks in Perspective. New York: Taylor and Francis Group.

Nerlich A, Rohrbach H, Bachmeier B, Zink A. 2006. Malignant Tumors in Two Ancient Populations: An Approach to Historical Tumor Epidemiology. Oncology Reports 16: 197-202.

Netherlands Committee on Bone Tumours. 1973. Radiological Atlas of Bone Tumours. The Hague: Mouton & Co.

Ning JP, Yu MC, Wang QS. 1990. Consumption of Salted Fish and Other Risk Factors for Nasopharyngeal Carcinoma (NPC) in Tainjin, a Low-Risk Region for NPC in the People's Republic of China. Journal of National Cancer Institute 82: 291-296.

Nordqvist C. 2010. Cancer Is Probably Man Made Caused By Pollution and Diet. Medical News Today, 15 October. http://www.medicalnewstoday.com/articles/204809.php, Accessed 22 December 2013.

Nriagu J. 1996. A History of Global Metal Pollution. Science 272: 223-224.

Ortner DJ. 1981. Bone Tumors in Archaeological Human Skeletons (Paleopathology of Human Bone Tumors). *In* Neoplasms – Comparative Pathology of Growth in Animals, Plants and Man. H.E. Kaiser, ed. Lippincott Williams & Wilkins. 733-738.

Ortner DJ, Putschar WGJ. 1985. Identification of Pathological Conditions in Human Skeletal Remains. Washington: Smithsonian Institution Press.

Ortner DJ, Manchester K, Lee F. 1991. Metastatic Carcinoma in a Leper Skeleton From a Medieval Cemetery in Chichester England. International Journal of Osteoarchaeology, 1: 91-98.

Ortner DJ, Ericksen MF. 1997. Bone Changes in the Human Skull Probably Resulting from Scurvy in Infancy and Childhood. International Journal of Osteoarchaeology 7: 212-220.

Ortner DJ, Kimmerle EH, Diez M. 1999. Probably Evidence of Scurvy in Subadults From Archaeological Sites in Peru. American Journal of Physical Anthropology 108: 321-331.

Ortner DJ, Butler W, Cafarella J, Milligan L. 2001. Evidence of Probably Scurvy in Subadults From Archaeological Sites in North America. American Journal of Physical Anthropology 114: 343-351.

Ortner DJ. 2003. Identification of Pathological Conditions in Human Skeletal Remains. New York: Academic Press.

Prates C, Sousa S, Oliveira C, Ikram, S. 2011. Prostate Metastatic Bone Cancer in an Egyptian Ptolemaic Mummy, a Proposed Radiological Diagnosis. International Journal of Paleopathology, 1: 98-103.

Putschar WG. 1966. Problems in the Pathology and Paleopathology of Bone. New Haven: Yale University Press.

Reeves AL. 1976. The Carcinogenic Effect of Inhaled Asbestos Fibers. Ann Clin Lab Sci 6: 459-466.

Ricci R, Lama R, Di Tota G, Capelli A, Capasso L. 1995. Some Considerations about the Incidence of Neoplasms in the Human History. Journal of Paleopathology 7: 5-11.

Rissech C, Steadman DW. 2011. The Demographic, Socio-economic and Temporal Contextualisation of the Universitat Auto`noma de Barcelona Collection of Identified Human Skeletons (UAB Collection). Int. J. Osteoarchaeol 21: 313-322.

Ritchie WA, Warren SL. 1932. The Occurrence of Multiple Bony Lesions Suggesting Myeloma in the Skeleton of a Pre-Columbian Indian. American Journal of Roentgenology, Radium Therapy and Nuclear Medicine 28: 622-628.

Roberts C, Manchester K. 2005. The Archaeology of Disease. Ithaca, New York: Cornell University Press.

Rogers, L. 1949. Meningiomas in Pharaoh's People: Hyperostosis in Ancient Egyptian Skulls. British Journal of Surgery 36: 423-424.

Roodman GD. 2004. Mechanisms of Bone Metastasis. New England Journal of Medicine 350: 1655-1664.

Roth ES, Fetzer DT, Barron BJ, Joseph UA, Gayed IW, Wan DQ. 2009. Does colon cancer ever metastasize to bone first? A temporal analysis of colorectal cancer progression. BMC Cancer 9: 1-6.

Rothschild BM, Rothschild C. 1995. Comparison of Radiologic and Gross Examination for Detection of Cancer in Defleshed Skeletons. Am J Phys Anthropol 96: 357-363.

Rothschild BM, Hershkovitz I, Dutour O, Latimer B, Rothschild C, Jellema LM. 1997. Recognition of Leukemia in Skeletal Remains: Report and Comparison of Two Cases. Am J Phys Anthropol. 102: 481-496.

Rubens RD, Mundy GR. 2000. Cancer and the Skeleton. London: Martin Dunitz Ltd.

Ruffer MA, Willmore JG. 1913. Studies in Palaeopathology. Note on a Tumour of the Pelvis Dating From Roman Times (250 A.D.), and Found in Egypt. Journal of Pathology 18: 480-484.

Rühli FJ, Hotz G, Böni T. 2003. Brief Communication: The Galler Collection: A Little-Known Historic Swiss Bone Pathology Reference Series. Am J Phys Anthropol 121: 15-18

Russell JC. 1958. Late Ancient and Medieval Population. Transactions of the American Philosophical Society 48: 1-152.

Sant M, Aareleid T, Berrino F, Bielska Lasota M, Carli PM, Faivre J, Grosclaude P, Hédelin G, Matsuda T, Møller H, Möller T, Verdecchia A, Capocaccia R, Gatta G, Micheli A, Santaquilani M, Roazzi P, Lisi D, EUROCARE Working Group. 2003. EUROCARE-3:

Survival of Cancer Patients Diagnosed 1990–94—Results and Commentary. Annals of Oncology 14: v61-v118.

Šefčáková A, Strouhal E, Němečková A, Thurzo M, Staššíková-Štukovská D. 2001. Case of Metastatic Carcinoma From End of the 8th–early 9th Century Slovakia. Am J Phys Anthropol 116: 216-229.

Shear TL. 1940. The Campaign of 1939. Hesperia 9: 261-308.

Siegel R, Ward E, Brawley O, Jemal A. 2011. Cancer Statistics, 2011. CA: A Cancer Journal For Clinicians, 61: 212-236.

Sigerist HE. 1951. A History of Medicine. New York: Oxford University Press.

Smith MO. 2002. A Probable Case Of Metastatic Carcinoma From The Late Prehistoric Eastern Tennessee River Valley. International Journal of Osteoarchaeology, 12: 235-247.

Stark AM, Eichmann T, Mehdorn HM. 2003. Skull metastases: clinical features, differential diagnosis, and review of the literature.

Stark RJ. 2009. A Radiographic Investigation of Juvenile Scurvy Among the Sub-Adult Remains from Stymphalos and Zaraka, Greece. M.A. thesis, Department of Anthropology, University of Alberta.

Strouhal E, Vhynánek L, Horáčková L, Benešova L, Němečkova A. 1996. Two Unusual Benign Tumours in Skulls from the Ossuary at Křtiny (Czech Republic). International Journal of Osteoarchaeology 6: 289-299.

Strouhal E. 1998. Survey and analysis of malignant tumours of past populations in England and Scotland. Journal of Paleopathology 10: 10-109.

Suchey J, Katz D. 1986. Skeletal Age Standards Derived from an Extensive Multiracial Sample of Modern Americans. Abstract. American Journal of Physical Anthropology 69: 269.

Suzuki T. 1987. Paleopathological Study on a Case of Osteosarcoma. American Journal of Physical Anthropology 74: 309-318.

Suzuki T. 1989. Paleopathological Study on a Malignant Bone Tumor in Japan: Differential Diagnosis on Osteolytic Lesions in the Skull. Zeitschrift für Morphologie und Anthropologie 78: 73-88.

Taphoorn MJB, Klein M. 2004. Cognitive Deficits in Adult Patients with Brain Tumours. Lancet Neurol 3: 159-168.

Tashiro K. 1982. Paleopathological Study Of Human Bones Excavated in Kyushu, Japan. Nagasaki Medical Journal 57: 77-102.

Tkocz I, Bierring F. 1984. A Medieval Case of Metastasizing Carcinoma with Multiple Osteosclerotic Bone Lesions. Am J Phys Anthropol 65: 373-380.

Ubelaker DH. 1989. Human Skeletal Remains: Excavation, Analysis, Interpretation. Chicago: Aldine Publishing Company.

University of Manchester. 2010. Scientists Suggest Cancer is Man-Made. http://www.manchester.ac.uk/aboutus/news/display/?id=6243 Accessed 19 November 2013.

Viscolli CM, Lachs MS, Horwitz RI. 1993. Bladder Cancer and Coffee Drinking: a Summary of Case-Control Research. The Lancet 341: 1432-1437.

Vinholes J, Coleman R, Eastell R. 1996. Effects of bone metastases on bone metabolism: implications for diagnosis, imaging and assessment of response to cancer treatment. Cancer Treatment Reviews 22: 289-331.

Wakely J, Strouhal E, Vyhnánek L, Němečková A. 1998. Case of a Malignant tumour from Abindon, Oxfordshire, England. Journal of Archaeological Science 25: 949-955.

Waldron T. 1996. What Was the Prevalence of Malignant Disease in the Past? International Journal of Osteoarchaeology 6: 463-470.

Waldron T. 1997. A Nineteenth-century case of carcinoma of the Prostate, with a note on the early history of the disease. International Journal of Osteoarchaeology 7: 241-247.

Waldron T. 2009. Paleopathology. Cambridge: Cambridge University Press.

Weiss L. 2000. Observations on the antiquity of cancer and metastasis. Cancer and Metastasis Reviews 19: 193-204.

Wells LH. 1960. Notes on the Human Remains from West Kennet Barrow. Unpublished manuscript. Cited in Brothwell D. 1961. The Palaeopathology of Early British Man: An Essay on the Problems of Diagnosis and Analysis. Journal of the Royal Anthropological Institute of Great Britain and Ireland 91: 318-344.

Wells C. 1963. Ancient Egyptian Pathology. J Laryngol Otol 77: 261-265.

Wells C. 1965. A Pathological Anglo-Saxon Femur. Brit. J. Radiol. 38: 393-394.

Wood JW, Milner GR, Harpending HC, Weiss KM. 1992. The Osteological Paradox: Problems of Inferring Prehistoric Health from Skeletal Samples. Current Anthropology 33: 343-358.

World Health Organization. 2013. Health Topics: Cancer. http://www.who.int/topics/cancer/en/ Accessed June 25, 2013.

Zervos OH, Rohn AH, Barnes E, Sanders GDR. 2009. An early Ottoman Cemetery at Ancient Corinth. Hesperia 78: 501-615.

Zimmerman MR. 1977. An Experimental Study of Mummification Pertinent to the Antiquity of Cancer. Cancer 40: 1358-1362.

Zindrick MR, Young MP, Daley RJ, Light TR. 1982. Metastatic Tumors of the Foot: Case Report and Literature Review. Clinical orthopaedics and related research 170: 219-225.

zur Hausen H. 2000. Papillomaviruses in Human Cancers. *In* Infectious Causes of Cancer. Goedert, James, ed. Pp. 245-261. Totowa, New Jersey: Humana Press.

Neoplastic Lesion Summary Form

Date: _____   Observer: _____

Site/Collection: _____   Specimen number: _____

Age at death: _____ (additional forms Y N)   Sex: _____ (additional forms Y N)

Skull

Frontal	L __	R__		Zygomatic	L __	R__
Parietal	L __	R__		Maxilla	L __	R__
Occipital	L __	R__		Palatine	L __	R__
Temporal	L __	R__		Mandible	L __	R__
Sphenoid	L __	R__				

Ribs and Sternum

Rib 1   L __   R__

Rib 2   L __   R__

Rib 11 L __   R__

Rib 12 L __   R__

Ribs 3-10

    #L __   #R__

Sternum

    Manubrium

    Sternal Body

Spine

C1	L3
C2	L4
C7	L5
T10	T1 – 9:
T11	
T12	_____
L1	C3 – 6:
L2	
	_____

Pelvis

Ilium   L __   R__

Ischium L __   R__

Pubis   L __   R__

Acetabulum L __   R__

Auricular Surface L __   R__

Sacrum L __   R__

Other

_____

_____

_____

_____

_____

_____

APPENDIX B

<u>Neoplastic Lesion Recording Form</u>

Date: _____   Specimen number: _____

Observer: _____   Bone: _____

Site/Collection: _____

Condition of bone: complete OR fragmentary

Other pathologies: _____

Documentation:

Photos: Y   N   Micro-photos: Y   N

X-rays: Y   N   Drawings Y   N

Total number of lesions observed: _____

Position of lesion(s) on bone:

1. _____   4. _____

2. _____   5. _____

3. _____   6. _____

    Primary: Metastatic: Unknown:

_____   _____   _____

    Benign: Malignant: Unknown:

_____   _____   _____

    Lytic: Blastic: Mixed:

_____   _____   _____

Max. Length/Min. Length

1. _____   4. _____

2. _____   5. _____

3. _____   6. _____

Max Width/Min. Width

1. _____   4. _____

2. _____   5. _____

3. _____   6. _____

Max. Depth/Min. Depth

1. _____   4. _____

2. _____   5. _____

3. _____   6. _____

Margins:

        Abrupt   Diffuse

    _____

                                                  _____

Comments:

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APPENDIX C Neoplastic Specimens In the Athens Collection

Specimen Number	Sex	Age	Cause of Death
WLH 004	Female	68	Cancer, widespread metastasis, wasting
WLH 013	Female	49	Lung cancer, multiple metastasis
WLH 014	Male	65	Cancer, brain metastasis
WLH 015	Female	5	Leukemia
WLH 017	Male	76	Stomach cancer
WLH 026	Male	46	Generalized cancer
WLH 029	Male	96	Prostate cancer
WLH 030	Female	66	Colon cancer
WLH 032	Female	44	Brain neoplasm
WLH 033	Female	72	Breast cancer
WLH 037	Female	44	Liver cancer
WLH 040	Female	71	Liver cancer
WLH 042	Female	50	Breast cancer, respiratory failure
WLH 043	Male	55	Lymphoma
WLH 045	Male	57	Liver cancer
WLJ 046	Male	60	Pancreatic cancer
WLH 049	Male	56	Lymphoma
WLH 050	Male	51	Brain neoplasm
WLH 055	Male	58	Lung cancer, brain

			metastasis
WLH 060	Female	45	Stomach cancer
WLH 062	Male	41	Brain neoplasm
WLH 064	Male	65	Bladder cancer
WLH 072	Male	27	Pancreatic cancer
ABH 026	Male	46	Generalized cancer
ABH 081	Male	87	Cyst cancer, stroke
ABH 085	Female	58	Pancreatic cancer
ABH 088	Female	35	Breast cancer, lung metastases
ABH 091	Female	51	Breast cancer, generalized carcinomatosis
ABH 092	Female	54	Ovarian cancer
ABH 093	Female	47	Ovarian cancer
ABH 101	Female	2	Acute myeloblastic leukemia
ABH 131	Female	46	Ovarian cancer, generalized carcinomatosis, heart failure
ABH 188	Female	38	Cancer
ABH 199	Male	26	Cancer

APPENIDX D Archaeological Specimens Included In This Study

Specimen	Sex	Age	Skeletal Involvement
Athenian Agora			
AA 13	Female	30-39	Left occipital
AA 32	Male	Young adult	Left occipital
AA 83b	Male	35-39	Left acetabulum
			Left femur
			Left fibula
			Left ilium
			Left ischium
			Left radius
			Left tibia
			Right calcaneus
			Right femur
			Right rib fragments
			Right scapula
			Right temporal
			Thoracic vertebrae
Corinth Excavations			
61-10	Unknown	6-9	Right tibia
62-31	Female	Unknown	Left frontal
2000-09	Female	25-27	Right frontal
2002-1b	Male	39-44	Left occipital
			Left ilium

APPENDIX E: UNKNOWN CASES

Wiener Laboratory at American School of Classical Studies in Athens			
WL 1	Unknown	1	Frontal
			Occipital
			Left temporal
			Right temporal
			Maxilla
			Mandible
			Right scapula
			Left scapula
			Left humerus
			Left ulna
			Left tibia
			Left femur
L1	Male	21-35	Left ilium
			Right ilium
WLCS	Unknown		Right ulna (fragment)
			Left femur (fragment)
			Right femur (fragment)
Anthropology Department at University of Waterloo			
CA 1	Male	30-45	Frontal
M 1	Female	Adult	Mandible
UW 8	Male	25-35	Frontal
			Occipital

			Sphenoid
			Mandible
			Left ribs
			Right ribs
			Sternum
			Thoracic vertebrae
			Lumbar vertebrae
			Left femur
			Right femur
			Left ilium
			Sacrum
UW 23	Female	7-12	Frontal
			Temporal
			Occipital
			Maxilla