



## Review

# The diagnostic value of microscopy in dry bone palaeopathology: A review



H.H. De Boer<sup>a,\*</sup>, A.E. Van der Merwe<sup>b</sup>, G.J.R. Maat<sup>a</sup>

<sup>a</sup> Barge's Anthropologica – Leiden, Department of Anatomy and Embryology, Leiden University Medical Center, Postzone S-01-P, P.O. Box 9600, 2300 RC Leiden, The Netherlands

<sup>b</sup> Barge's Anthropologica – Amsterdam, Department of Anatomy, Embryology and Physiology, Amsterdam Medical Center, P.O. Box 22660, 1100 DD Amsterdam, The Netherlands

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## ABSTRACT

Over recent decades histology has increasingly been used as a diagnostic tool in human dry bone palaeopathology. Still, the use of histology in human dry bone is associated with various problems, including a lack of pathognomonic histomorphology and a need for more experimental data. Consequently, the value of histology as diagnostic tool in human dry bone remains a subject for debate.

Here we review all published palaeohistopathological research in human dry bone. A systematic search identified 3363 articles, with the 64 most relevant citations studied in depth. We specifically focused on the interpretation of histomorphological parameters and the use of comparative fresh bone tissue and/or experimental data.

Our literature review shows that only a few disorders demonstrate a 'specific' histomorphology: Paget's disease, osteoporosis, hyperparathyroidism and possibly osteomalacia. In all other cases, histology may aid during the differential diagnostic process, but it is unable to confirm a definitive diagnosis. The histological diagnostic process and consequential recommendations for the use of histology are discussed per following disease categories: metabolic disease, neoplasm, infectious disease and trauma.

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## Contents

1. Introduction .....	113
1.1. Limitations of palaeohistopathology .....	114
1.2. Palaeohistopathological research in the past decades .....	114
2. Methods .....	114
3. Results and discussion .....	115
3.1. Possible and potential diagnostic features .....	116
3.1.1. Metabolic disorders .....	116
3.1.2. Neoplasms .....	117
3.1.3. Infectious diseases .....	118
3.1.4. Mechanical trauma .....	119
4. Conclusion .....	119
Acknowledgements .....	119
References .....	119

## 1. Introduction

Numerous papers have been published in which the palaeopathological diagnosis of disease was supported by histological investigation. However, no recent reviews regarding the impact of these efforts have been published. Here we discuss the limitations of palaeohistopathological investigation in general and systematically review palaeohistopathological diagnostic efforts

\* Corresponding author. Tel.: +31 6 51700931.

E-mail addresses: [hanshdeboer@gmail.com](mailto:hanshdeboer@gmail.com), [h.h.deboer@amc.nl](mailto:h.h.deboer@amc.nl) (H.H. De Boer), [a.e.vandermerwe@amc.uva.nl](mailto:a.e.vandermerwe@amc.uva.nl) (A.E. Van der Merwe), [g.j.r.maat@lumc.nl](mailto:g.j.r.maat@lumc.nl) (G.J.R. Maat).

and/or potential per disease category. Special emphasis will be placed on the difficulties associated with the interpretation of palaeohistopathological images. This paper will also focus on the interplay between palaeopathological findings, fresh tissue pathology and experimental research. Our aim is to add depth to ongoing debates about the diagnostic value of microscopy in dry bone tissue.

### 1.1. Limitations of palaeohistopathology

In palaeopathology, the identification of gross anatomical processes in human skeletal remains and their interpretation are considered challenging (Aufderheide and Rodríguez-Martín, 1998; Ortner, 2003; Wood et al., 1992). The same challenges are relevant in palaeohistopathology. Dry bone remains are void of soft tissue and bone tissue cells, and it is just these components that provide fresh tissue pathologists with the pathognomonic features leading to a reliable diagnosis (e.g. Rosai and Ackermans, 2011; Ross et al., 1995; Vigorita, 1999). This problem is further complicated by the nature of bone tissue, which only reacts to a stimulus (disease) in three ways visible on a microscopic level: resorption of bone tissue (an osteoclastic bone response), deposition of new bone tissue (an osteoblastic bone response) or a combination of the two (Frost, 1985). Only a small subset of diseases can be associated with such characteristic histological alterations that they can be regarded as pathognomonic. For all other diseases, microscopic changes appear to be similar, and as a result various authors have downplayed the value of palaeohistopathology as a diagnostic tool (Putschar, 1966; Stout and Simmons, 1979; Waldron, 2009).

Bianco and Ascenzi (1993) stated that the lack of pathognomonic histological information derived from skeletal remains, in combination with a lack of independent extra source information, such as medical data, posed a fundamental problem to the advance of palaeohistopathology. According to these authors, palaeohistopathologists risk 'making non-scientific statements', i.e. statements that cannot be proven false; a problem that could be minimized by new knowledge on the visibility of changes that specific diseases show in dry bone. They stressed the need for research in which palaeohistopathological diagnoses are supported by experimental research or comparative research with the use of current documented dry bone reference specimens.

### 1.2. Palaeohistopathological research in the past decades

The popularity of histology as a diagnostic tool for archaeological remains has increased over recent decades. In 2001, pronouncements on the value of microscopy as a diagnostic tool were

generally optimistic (Schultz, 2001). Palaeohistopathology was said to be a dependable tool in the differentiation between tumors, metabolic disorders and infectious diseases since specific histo-architectural characteristics could be linked to specific diseases. This latter statement contrasted sharply with earlier consensus, which was generally more skeptical (Bianco and Ascenzi, 1993; Putschar, 1966; Stout and Simmons, 1979). Several examples were presented to prove the specificity of morphological features, such as those for the diagnosis of syphilis in dry bone tissue (Schultz, 2001, 2003; Von Hunnius et al., 2006).

However, the diagnostic power of these features has been challenged. For instance, Weston (2009) and Van der Merwe et al. (2010) showed that microarchitectural features alone were by no means diagnostic for specific diseases such as treponematosi, and Schutkowski and Fernandez-Gil (2010) came to the same conclusions for tuberculosis and leprosy. All in all, more recent publications challenged the diagnostic value of microscopy, a debate that is pressing due to the questioned acceptance of destructive sampling.

## 2. Methods

To avoid bias from expert-based reviewing, we used a systematic and sequential inclusion-exclusion strategy to select relevant articles. Ten keynote articles were selected prior to key word article retrieval to test the adequacy of the search (Table 1). Since palaeohistopathological papers are distributed widely throughout the medical, anthropological and archaeological literatures, a general search was executed for both Pubmed and Web of Science references. The search strategy consisted of the key word combination of 'physical anthropology AND histology'. The search details can be found in Table 2. In order to ensure that no relevant articles were missed, publications from the American Journal of Physical Anthropology, Journal of Archaeological Science, International Journal of Osteoarchaeology and International Journal of Paleopathology with the terms 'histolog\*' or 'microscop\*' in the title were also included.

A total of 4155 articles were automatically retrieved of which 792 duplicates could be excluded. To continue in the study sample, the remaining articles had to comply with the following: (1) the article was written in English, (2) histological investigation was performed on human dry bone, (3) microscopic investigation (light microscopy, microradiography or scanning electron microscopy) was used as a palaeopathological diagnostic tool, (4) the article was an original research paper. An exception for the latter criterion was made for the review article by Schultz (2001), since it added a substantial amount of key data from outside the English literature. Other relevant citations were also included, for instance

**Table 1**  
Keynote articles used for testing the sensitivity of the inclusion criteria.

Authors	Year	Title	Journal
Aaron et al.	1992	Paleohistology of Pagets-disease in two medieval skeletons	International Journal of Osteoarchaeology
Blondiaux et al.	1994	Microradiographs of leprosy from an osteoarchaeological context	International Journal of Osteoarchaeology
Cuijpers	2009	Distinguishing between the bone fragments of medium-sized mammals and children. A histological identification method for archaeology	Anthropologischer Anzeiger
Guarino et al.	2006	Bone preservation in human remains from the Terme del Sarno at Pompeii using light microscopy and scanning electron microscopy	Journal of Archaeological Science
Von Hunnius et al.	2006	Histological identification of syphilis in pre-Columbian England	American Journal of Physical Anthropology
Hackett	1981	Development of caries sicca in a dry calvaria	Virchows Archiv
Hanson and Chester	2007	Examining histology to identify burned bone	Journal of Archaeological Science
Maat et al.	2001	Manual preparation of ground sections for the microscopy of natural bone tissue: update and modification of Frost's 'rapid manual method'	International Journal of Osteoarchaeology
Schultz	2001	Paleohistopathology of bone: a new approach to the study of ancient diseases	Yearbook of Physical Anthropology
Stout and Teitelbaum	1976	Histomorphometric determination of formation rates of archaeological bone	Calcified Tissue Research

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