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Three-dimensional imaging of past skeletal TB: From lesion to process

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S U M M A R Y

3D imaging has become an essential tool in the field of biological anthropology, notably for human evolution purposes. High resolution virtual 3D reconstructions of original specimens contribute to their preservation and broaden the ability for research, teaching and exchanges. Paleopathology can get substantial benefit from these methods, among others for reconstructing infectious pathological processes on ancient bones.

Tuberculosis is frequently diagnosed on ancient human remains; however, some osseous expressions are difficult to interpret using classical methods.

We illustrate here the interest of 3D methods for reconstructing processes involved in pathological bone changes due to *Mycobacterium tuberculosis* infection.

Four paleopathological specimens attributed to this infection, dating from different time periods and concerning diverse parts of the skeleton have been analyzed using a specific 3D digital chain we have previously developed. These 3D analyses allow to virtually reconstruct the initial location and aspect of the infectious process, its extension as well as its possible diffusion to the surrounding soft tissues. This possible virtual follow-up of the disease leads to the concept of *processual paleopathology* that we would like to introduce in the field.

The 3D methodology can help to improve our knowledge of natural history and evolution of ancient human infections such as tuberculosis.

1. Introduction

Tuberculosis is frequently identified on ancient human remains [1,2]. X-ray imaging does help for retrospective diagnosis in paleopathology since the very beginning of this discipline and became a subfield of it, known as paleoradiology [3]. Most of the time, diagnosis on paleopathological material is performed on 2D imaging (by using plain X-ray or CT scan, analyzed slice by slice). Indeed radiologists do not need 3D reconstructions for performing their diagnosis, as their experience allowed them to visualize a volume from surfaces. However, in paleopathology, the intrinsic nature of the material, ancient remains, which can only exhibit

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'static' lesions (frozen at the time of death) that are moreover exposed to taphonomic changes, makes the retrospective diagnosis more complex than the clinical one [4]. Taphonomic conditions could indeed mimic real pathological changes, both macroscopically and radiologically, known as pseudopathologies [5] or "paleopathomimesis" (false paleopathological lesions taphonomically induced) [4]. Therefore the osseous expressions of diseases on ancient material are sometimes difficult to interpret.

3D imaging has become since the early '80 an essential tool for bio-anthropologists, notably for human evolution purposes: high resolution virtual 3D reconstructions of original fossils contribute to their preservation and broaden the ability for research, teaching and exchanges. This approach lead to a new scientific field which is virtual paleoanthropology [6]. In contrast, virtual 3D approach is not yet extensively used in paleopathology although it presents a set of specific interests [7]. Even if 2D approach in paleoradiology keeps all its semeiological value to perform efficiently the paleopathological diagnosis, 3D methodology, because of its unique possibility to compute a global visualization of a given paleopathological specimen, provides additional information that cannot be directly obtained from 2D imaging. For instance, 3D analyses allow reconstructing virtually the initial location and aspect of infectious process, its extension as well as its possible diffusion to the surrounding soft tissues. This digital "follow-up" of the disease led to the concept of *virtual processual paleopathology* [8]. This approach can help to improve our knowledge of natural history and evolution of ancient human infections such as tuberculosis.

We illustrate here the interest of this approach by reconstructing some processes at the origin of pathological changes observed on ancient bone and attributed to *Mycobacterium tuberculosis*.

2. Material and methods

Four paleopathological specimens (3 skeletons and one mummified body) have been analyzed by 3D imaging. These cases have been previously attributed to tuberculosis on the basis of typical morphological criteria, with a molecular confirmation for two of them. Lesions involved axial skeleton (spine and sacroiliac joint). They are dated from Upper Palaeolithic to medieval periods and are coming from European and Near Eastern geographic areas.

We used a specific 3D digital chain named VIRCOPAL® (standing for VIRtual COllection of PALeo-specimens) which includes acquisition, reconstruction, segmentation and printing, and that has been developed for archaeological purposes [9]. Digital acquisitions were issued from medical CT scan or industrial microCT scan. The high fidelity quality of the 3D reconstructions is due to a specific software program, TIVMI® (Treatment and Increased Vision for Medical Imaging), based on HMH (Half Maximum Height) algorithm [10] and extended to 3D [11]. It allows locating on CT slices, accurately and reliably, the precise interface between tissues having different densities. It has been proved to be less observer-dependant than other software programs based on different algorithms [12].

Lesions, anatomical structures and areas of interest were manually segmented, slice by slice. This procedure requires indeed an experienced-based decision for each slice (in this case, corresponding to both anthropological and pathological expertise) and cannot be automatically performed.

3. Results

3.1. Evaluate functional consequences of spinal involvement (Pott's disease)

A typical Pott's disease coming from a medieval cemetery in Angoulême, central-western France [13] has been studied. Its aspect matches the typical paleopathological criteria for diagnosing vertebral tuberculosis [2]. The well preserved spine, almost complete (only the two first cervical vertebrae are missing), was dislocated before the study in a thoracic block with fused ribs and 14 separated vertebrae. It has been virtually reassembled to better evaluate the spinal deformation in the living state. Spine presents an angular kyphosis at the thoracic level. This deformation involves 8 thoracic vertebrae, from T4 to T11, that have fused in a single block. The angle apex corresponds to T7; its value is about 100°. Most of the ribs are present and still attached to the spine, due to the associated ankylosis of the costo-vertebral joints.

Assessing possible functional consequences of this severe angular deformation is not an easy task. Besides the gibbosity, neurological disorders may have resulted from the vertebral collapse: paraplegia is classically observed in vertebral TB due to compression of the spinal cord by narrowing of spinal canal [14]. Measurements of spinal canal diameters can help in evidencing a spinal stenosis, however in such a case, the spine angulation has strongly changed the orientation of the vertebrae in the three planes of the space, making thus difficult reliable measurements of the spinal canal only on 2D slices. Furthermore, morphological volumetric changes of the spinal canal are only accessible using 3D rendering.

Volumetric reconstruction of the spinal canal surprisingly showed very few consequences on its size and shape, relatively to the severity of vertebral changes (Figure 1). At the level of the angular kyphosis, the osseous diameter of the spinal canal only presents a little narrowing and keeps its regular shape, besides the angular deformation. Measurements taken at the level of T7 (angle apex) and at the two vertebrae immediately above and below the fusion (T3 and T12) shows the following values (antero-posterior and transversal diameters, respectively), from up to do down: T3 = 14.8 mm × 15.8 mm; T7 = 14.6 mm × 11.7 mm; T12 = 18.2 × 18.1 mm. For the antero-posterior diameters, these values are ranging in the normal variation of thoracic spinal canal among human adults [15]. If the transversal diameter appears to be slightly narrowed at the level of the deformation, when compared to the over (T3) and underlying (T12) vertebrae, however the canal doesn't appear to be stenotic.

This 3D evidence confirms that the spinal canal size can be preserved even in case of severe vertebral deformation, due to destructive spondylodiscitis followed by fusion. The latter represents a way of healing [16]. This aspect illustrates the adaptive capacity of the human organism to control infectious spread and to keep some of its vital functions when faced to a slow infectious process, such as tuberculosis.

3.2. Evidence microarchitectural changes due to an early stage of vertebral infection

A vertebral body of a young immature from Dja'de el Mughara site (Syria) dating from Early Pre-Pottery Neolithic B (10,450–10,150 B.P. cal) [17] has been micro-CT scanned (resolution of 3 microns in the 3 planes of space, GE V/tome/x).

Early presence of tuberculosis has been identified on 3 individuals of this site, both morphologically and molecularly [18]. This third lumbar vertebra belongs to one of the two young immature individuals presenting periosteal reactions on long bones as well as minor changes on anterior part of thoracic and lumbar vertebrae [17]. This aspect combines a slight periosteal reaction on the anterior part of the vertebral body with a relative widening of the vascular foramina (anterior external vertebral venous plexus).

In contrast with these minor and subjective changes, the 3D reconstruction evidenced clear focal microarchitectural changes on the antero-lateral inner part of the body, when it is sectioned along