Preliminary paleohistological observations of the StW 573 (‘Little Foot’) skull

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Abstract

Numerous aspects of early hominin biology remain debated or simply unknown. However, recent developments in high-resolution imaging techniques have opened new avenues in the field of paleoanthropology. More specifically, X-ray synchrotron-based analytical imaging techniques have the potential to provide crucial details on the ontogeny, physiology, biomechanics, and biological identity of fossil specimens. Here we present preliminary results of our X-ray synchrotron-based investigation of the skull of the 3.67-million-year-old Australopithecus specimen StW 573 (‘Little Foot’) at the I12 beamline of the Diamond Light Source (United Kingdom). Besides showing fine details of the enamel (i.e., hypoplasias) and cementum (i.e., incremental lines), as well as of the cranial bone microarchitecture (e.g., diploic channels), our synchrotron-based investigation reveals for the first time the 3D spatial organization of the Haversian systems in the mandibular symphysis of an early hominin.

Introduction

Applications of X-ray synchrotron-based analytical techniques in evolutionary studies have opened up new avenues in the field of paleoanthropology. In particular, X-ray synchrotron microtomography has been proved to be particularly useful for imaging anatomical structures in extant and fossil hominins that are traditionally observed through destructive histological methods (e.g., Tafforeau and Smith, 2008; Maggiano et al., 2016; Andronowski et al., 2017; Mani-Caplazi et al., 2017; Gunz et al., 2020). For instance, microscopic analyses of fossil craniodental specimens using synchrotron radiation have revealed previously unknown aspects of the ontogeny of extinct hominin taxa (Tafforeau and Smith, 2008; Gunz et al., 2020).

Besides its geological age of 3.67 million years, StW 573 (‘Little Foot’) is remarkable for its outstanding degree of preservation and completeness (Clarke and Kuman, 2019). The high-resolution virtual exploration of the ‘Little Foot’ skull is thus expected to provide new insights into the Pliocene Australopithecus biology. Here, we present preliminary results of our X-ray synchrotron-based investigation of the dentition and cranial bones of ‘Little Foot’. The main aim of our study is to identify and assess the degree of preservation of craniodental microstructures that could contribute to the
reconstruction of Australopithecus’ biology. To the best of our knowledge, this is the first time that histological features of the compact bone of a Pliocene hominin skull have been non-invasively observed.

Results

Histology of dental tissues

Figure 1 shows two dimensional (2D) sections through the roots of the upper right first molar with a resolution of 3.25 μm. These sections reveal the presence of cementum between the dentine and sediments filling the tooth alveolus (Figure 1A,B). The dentine–cementum junction and the boundary between the cementum and the sediments are clearly visible. Cementum microstructures, such as incremental lines, are discernible (Figure 1B). Additionally, we reconstructed in three dimensions (3D) the enamel cap of the lower left canine using image stacks at 21.23 and 7.91 μm resolution (Figure 2). Lines and pits observable on the distal-buccal aspect of the 21.23-μm reconstruction are
located at about 2.4 and 3.6 mm from the cemento-enamel junction, which represents 36% and 54% of the crown height, respectively. While fine details of the pits are clearly visible in the 3D reconstruction using synchrotron-based data sets at 7.91 μm, the color map reveals that they are slightly less clearly rendered in the 21.23-μm 3D reconstruction, especially on the mesial-buccal aspect (Figure 2C,D). These reductions in the normal thickness of enamel correspond to disruptions to the normal growth of enamel (i.e., hypoplasias) and indicate two disruptive events in StW 573’s life history.

### Histology of bone tissues

*Figure 1C–E* show 2D sections through the cranial vault and the mandibular symphysis with a resolution of 3.25 μm. The voids in the spongious bone have been partially or completely filled by calcite. The opening of the diploic channel through the inner table in the cranial vault could be identified (*Figure 1C*). The Haversian system is discernible in the outer and inner tables of the cranial vault (*Figure 1C,D*) and clearly visible in the compact bone of the mandible (*Figure 1E*). *Figure 1F* shows a 3D reconstruction of the canal network and branching and interconnections between the Haversian systems. Based on the terminology defined by Maggiano et al., 2016, we identify a Type 2 (i.e., dichotomous) branching pattern. Furthermore, a linear transverse connection (i.e., Volkmann’s canal) can be observed. Vascular canals are proportionally more abundant close to the trabecular bone than in the rest of the compact bone (*Figure 1F*). The Haversian canals globally lie parallel to the external surface.

### Discussion

Collectively, our results show that the virtual histological investigation of both dental and bone tissues in complete fossil hominin skulls by using high-resolution synchrotron radiation may be possible. Contrary to traditional histological analyses based on physical sections of the bone (e.g., Bartsiokas, 2002) and imaging-based exploration of volumes of interest physically extracted from bones (e.g., Maggiano et al., 2016; Andronowski et al., 2017), this method, as previously demonstrated in landmark papers for dental microstructures using dentognathic remains (e.g., Tafforeau and Smith, 2008), offers the possibility of non-invasively investigating microscopic structures in complete crania that have deep implications for the ontogeny, physiology, biomechanics, and biological identity of fossil specimens.

More specifically, our observations reveal that ‘Little Foot’ preserves fine cementum microstructures that can be quantitatively explored. Because cementum is rarely remodeled during life, it may preserve valuable information about hominin paleobiology (rev. in Tang et al., 2016). In particular, the incremental lines may be used to determine age-at-death as well as specific stress periods that might be related to life-history events (e.g., pregnancies) or diseases (rev. in Tang et al., 2016). Moreover, our high-resolution synchrotron images of the skull reveal the presence of enamel defects in ‘Little Foot’s’ teeth. Enamel hypoplasias are indicators of physiological stress experienced during childhood and may be related to diseases or dietary deficiency/nutritional stress (rev. in Guatelli-Steinberg and Huffman, 2012). Interestingly, enamel defects in StW 573’s lower left canine are...
found at the same distance of the cemento-enamel junction as in other Australopithecus lower canines from Sterkfontein (Guatelli-Steinberg, 2003). Our study thus further confirms that high-resolution synchrotron radiation may reveal very fine details of enamel defects, with substantial differences in the appreciation of hypoplasia between 21.23 and 7.91 microns of spatial resolution.

Additionally, the opening of the diploic vessels in the cranial vault of ‘Little Foot’ could be imaged. Since this structure may be involved in brain thermoregulation, future synchrotron-based 3D virtual reconstruction of the diploic network in early hominin skulls could be particularly useful for determining when and how the complex human-like thermal regulation system emerged (rev. in Bruner, 2017). In particular, such data would contribute to explore the potential correlations between large proportions of diploic bone in Australopithecus and related expansion of the diploic vessels (Beaudet et al., 2018).

To the best of our knowledge, this is the first time that histological features of the compact bone of a Pliocene hominin skull have been non-destructively observed. Since the microscopic organization of the compact bone may have age-related biological significance, the presence, identification, and characterization of such histological structures are of particular interest for determining the age-at-death of fossil specimens (e.g., Eriksen, 1991), particularly in combination with the dental markers discussed above. For example, the branching patterns identified in this study are also found in extant humans (Maggiano et al., 2016). In the sample analyzed here, we could only identify one transverse connection, which confirms the advanced age of StW 573 since this type of branching is more common in young individuals (Maggiano et al., 2016; Clarke and Kuman, 2019). Similarly, the spatial organization of the vascular canal network has been suggested to reflect functional adaptation throughout the individual’s life and/or growth rate in fossil long bones (Ricqlès et al., 2000). Consequently, this histomorphological parameter represents a relevant proxy for evaluating the properties of the loading environment or developmental pattern in fossil specimens (Ricqlès et al., 2000). In our preliminary results, the vascular canals are more abundant close to the trabecular bone in the mandible of StW 573, which may indicate an area of intense bone remodeling, potentially in response of biomechanical loading. The fact that the vascular canals could be successfully reconstructed in 3D in the mandible of a 3.67-million-year-old fossil specimen such as ‘Little Foot’ reveals the invaluable contribution of synchrotron radiation in refining our knowledge of fossil hominin paleobiology at a histological level. For instance, a more comprehensive analysis of the compact bone microstructures should provide new insights into the evolution of the bone modeling/remodeling process, which is a fundamental aspect of bone functional adaptations in the human lineage. We might expect that, because of changes in the biomechanical environments (in the masticatory system but also in relation with locomotory adaptations), the organization of the Haversian system in the skeleton may have varied throughout the hominin lineage.

Materials and methods

X-ray synchrotron microtomography

We performed propagation phase-contrast synchrotron X-ray micro-computed tomography (PPC SXCT) at the I12 beamline of the Diamond Light Source, United Kingdom (Drakopoulos et al., 2015). We used two setups to (1) image the full skull with an isotropic voxel size of 21.23 μm and (2) image regions of interest with an isotropic voxel size of 7.91 and 3.25 μm. PPC SXCT of the full skull was performed using the External Hutch Two of I12, providing the largest beam allowing for imaging the whole skull at once. The X-ray beam was set to a monochromatic energy of 140 keV (double bent Laue Si 111 monochromator). At the level of the detector, the beam size was 75.84 mm horizontally and 19.28 mm vertically. Projections were recorded using the large field of view indirect detector from I12 comprising a cadmium tungstate scintillator, 0.3× magnification optical lenses and two PCO.edge 5.5 sCMOS cameras (PCO AG, Kelheim, Germany). Complete imaging of the specimen consisted of 21 individual acquisitions, moving the specimen vertically each time by 10 mm, to use the brightest part of the beam providing an overlap of slightly over 50%, which was used later to increase the signal to noise ratio. The centre of rotation was shifted near the edge of the projection, effectively doubling the reconstructed field of view, by reflecting and assembling the complementary image sections as described. Each acquisition consisted of 9000 projections of 0.25 s each over a 360° rotation of the sample. Additionally, 50 flatfield images (sample out of the beam) were
recorded before and after the series of acquisition as well as 10 dark images (X-ray beam off to record the noise of the camera). The regions of interest were scanned in I12 Experimental Hutch One using the beamline’s modular imaging system. This indirect detector consists of a PCO. edge 5.5 sCMOS camera and four user-selectable optical modules, each comprising a scintillator, 90-degree turning mirrors, and a visible light lens. We used modules 2 and 3 with a magnification of 0.820× and 2×, respectively, corresponding to a recorded pixel size of 7.91 μm and 3.25 μm, respectively.

Reconstruction

The full-skull images taken with the large field of view camera were reconstructed using prototype processing scripts implemented in Python and using the ASTRA library for the tomographic reconstruction step. The radiographs were pre-processed using X-ray noise removal, reference image ratio (flatfield correction), ring artifact suppression (Vo et al., 2018), and a low-pass phase-propagation-based filter (after Paganin et al., 2002). Tomographic reconstruction used the Filtered Back-Projection algorithm on a graphical processing unit (GPU) via the ASTRA library (Ramachandran and Lakshminarayan, 1971; van Aarle et al., 2016). The image data for the whole skull consisted of 21 individual, overlapping, vertical segments. Each segment was pre-processed and reconstructed with fine adjustment of the overlap determined by slice-by-slice comparison in the reconstructed images. Due to synchrotron beam loss during the pre-programmed scan, two segments had to be re-scanned subsequently resulting in small additional variations in the contrast for that segment.

The region-of-interest tomographs were reconstructed using the SAVU tomographic processing software (Atwood et al., 2015; Wadeson and Basham, 2016) developed at Diamond Light Source. In the reconstruction process, ringartifact removal (Vo et al., 2018) and autocentering (Vo et al., 2014) were applied, as well as distortion correction as necessary (Vo et al., 2015). The low-pass filter approach (Paganin et al., 2002) was applied, and both filtered and unfiltered reconstructions were evaluated; the filtered output exhibits increased visible contrast between materials and decreased noise, but suffers some blurring of boundaries. Filtered back-projection reconstructions were performed using the Astra library (Ramachandran and Lakshminarayan, 1971; van Aarle et al., 2016), and the whole process was applied on an HPC cluster system using the SAVU tomography pipeline.

2D and 3D observations

We focused our preliminary qualitative observations on the microstructural organization of the teeth and of the compact bone of the cranial vault and the mandible. We thus selected 2D sections from the high-resolution (i.e., 3.25 μm) X-ray volumes documenting structures of interest in (1) the roots of the upper right first molar, (2) the parietal eminence, and (3) the mandibular symphysis (Figure 1). Moreover, we reconstructed in 3D (1) the enamel surface of the lower left canine (at 21.23 and 7.91 μm; Figure 2) and (2) the vascular canals preserved in the mandibular symphysis (at 3 μm, Figure 1F) using the segmentation tools available in Avizo v9.0 (Visualization Sciences Group Inc).

3D reconstructions of the enamel cap of the lower left canine using the 21.23 and 7.91 μm scans were automatically aligned, and the distances between the two were mapped onto the enamel surface using the Avizo modules ‘Align surfaces’ and ‘Surface distance’ (Beaudet et al., 2018).

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**Additional files**

**Data availability**

All data generated or analysed during this study are included in the manuscript and supporting files.
References

Andronowski JM, Pratt IV, Cooper DML. 2017. Occurrence of osteon banding in adult human cortical bone.
American Journal of Physical Anthropology 164:635–642. DOI: https://doi.org/10.1002/ajpa.23297, PMID: 28832945

Atwood RC, Bodey AJ, Price SWT, Basham M, Drakopoulos M. 2015. A high-throughput system for high-quality
tomographic reconstruction of large datasets at diamond light source. Philosophical Transactions of the Royal
Society A: Mathematical, Physical and Engineering Sciences 373:20140398. DOI: https://doi.org/10.1098/rsta.2014.0398

Bartosikas A. 2002. Hominid cranial bone structure: a histological study of omo 1 specimens from Ethiopia using
different microscopic techniques. The Anatomical Record 267:52–59. DOI: https://doi.org/10.1002/ar.10083,
PMID: 11984792

Beaudet A, Carlson KJ, Clarke RJ, de Beer F, Dhaene J, Heaton JL, Pickering TR, Stratford D. 2018. Cranial vault
thickness variation and inner structural organization in the Sw 578 hominin cranium from Jacovec Cavern,
south africa. Journal of Human Evolution 121:204–220. DOI: https://doi.org/10.1016/j.jhevol.2018.04.004,
PMID: 29793791

Bruner E. 2017. The fossil evidence of human brain evolution. In: Kaas J (Ed). Evolution of Nervous Systems.
Elsevier. p. 63–92. DOI: https://doi.org/10.1016/978-0-12-80584-6.00032-5

Clarke RJ, Kuman K. 2019. The skull of Sw 573, a 3.67 ma Australopithecus prometheus skeleton from
Sterkfontein Caves, South Africa. Journal of Human Evolution 134:102634. DOI: https://doi.org/10.1016/j.
Jhevol.2019.06.005, PMID: 31446970

Drakopoulos M, Connolley T, Reinhard A, Atwood R, Magdysyuk O, Vo N, Hart M, Connor L, Humphreys B,
Howell G, Davies S, Hill T, Wilkin G, Pedersen U, Foster A, De Maio N, Basham M, Yuan F, Wanelik K. 2015.
I12: the joint engineering, environment and processing (JEEP) beamline at diamond light source. Journal of
Synchrotron Radiation 22:828–838. DOI: https://doi.org/10.1107/S1600577515003513, PMID: 25931103

Erickson MF. 1991. Histologic estimation of age at death using the anterior cortex of the femur. American
Journal of Physical Anthropology 84:171–179. DOI: https://doi.org/10.1002/ajpa.1330840207, PMID: 22119313

Guatelli-Steinberg D. 2003. Macroscopic and microscopic analyses of linear enamel hypoplasia in Plio-
Pleistocene south african hominins with respect to aspects of enamel development and morphology. American
Journal of Physical Anthropology 129:309–322. DOI: https://doi.org/10.1016/s0002-9483(01)00086-8,
PMID: 12627527

Guatelli-Steinberg D, Huffman M. 2012. Histological features of dental hard tissues and their utility in forensic
anthropology. In: Crowder C, Stout S (Eds). Bone Histology an Anthropological Perspective. CRC Press. p. 91–
107. DOI: https://doi.org/10.1201/B11393-5

Gunz P, Neubauer S, Falk D, Tafforeau P, Le Cabec A, Smith TM, Kimbel WH, Spoor F, Alemseged Z. 2020.
Australopithecus Afarensis endocasts suggest ape-like brain organization and prolonged brain growth . Science
Advances 6:eaaz4729. DOI: https://doi.org/10.1126/sciadv.aaz4729

Maggiano IS, Maggiano CM, Clement JG, Thomas CD, Carter Y, Cooper DM. 2016. Three-dimensional
reconstruction of haversian systems in human cortical bone using synchrotron radiation-based micro-CT:
morphology and quantification of branching and transverse connections across age. Journal of Anatomy 228:
719–732. DOI: https://doi.org/10.1111/joa.12430, PMID: 26749084

Mani-Caplazi G, Schulz G, Deyhle H, Hotz G, Vach W, Wittwer-Backofen U, Müller B. 2017. Imaging of the human
tooth cementum ultrastructure of archeological teeth, using hard X-ray microtomography to determine
age-at-death and stress periods. Proceedings of SPIE.

Paparini D, Mayo SC, Gureyev TE, Miller PR, Wilkins SW. 2002. Simultaneous phase and amplitude extraction
from a single defocused image of a homogeneous object. Journal of Microscopy 206:33–40. DOI: https://doi.org/10.1046/j.1365-2818.2002.01010.x, PMID: 1200561

Ramachandran GN, Lakshminarayanan AV. 1971. Three-dimensional reconstruction from radiographs and
electron micrographs: application of convolutions instead of fourier transforms. PNAS 68:2236–2240.
DOI: https://doi.org/10.1073/pnas.68.9.2236, PMID: 5289381

Ricqlès AJ, Padian K, Horner JR, Fracillon-Vieillot H. 2000. Palaeohistology of the bones of pterosaurs (Reptilia:
archosauromorpha): anatomy, ontogeny, and biomechanical implications. Zoological Journal of the Linnean Society
129:349–385. DOI: https://doi.org/10.1002/zool.1096-3642.2000.tb00016.x

Tafforeau P, Smith TM. 2008. Nondestructive imaging of hominoid dental microstructure using phase contrast
X-ray synchrotron microtomography. Journal of Human Evolution 54:272–278. DOI: https://doi.org/10.1016/j.
Jhevol.2007.09.018, PMID: 18045654

Tang N, Le Cabec A, Antoine D. 2016. Dentine and Cementum Structure and Properties. In: Irish J. D, Scott G. R
(Eds). A Companion to Dental Anthropology. Wiley Blackwell. p. 204–222. DOI: https://doi.org/10.1002/9781118845486.ch115

van Aarle W, Palenstijn WJ, Cant J, Janssens E, Bleichrodt F, Dabravolski A, De Beenhouwer J, Joost Batenburg,
K, Sijbers J. 2016. Fast and flexible X-ray tomography using the ASTRA toolbox. Optics Express 24:25129–
25147. DOI: https://doi.org/10.1364/OE.24.025129

Vo NT, Drakopoulos M, Atwood RC, Reinhard C. 2014. Reliable method for calculating the center of rotation in
parallel-beam tomography. Optics Express 22:19078–19086. DOI: https://doi.org/10.1364/OE.22.019078

Vo NT, Atwood RC, Drakopoulos M. 2015. Radial Lens distortion correction with sub-pixel accuracy for X-ray
micro-tomography. Optics Express 23:32859–32868. DOI: https://doi.org/10.1364/OE.23.032859

Vo NT, Atwood RC, Drakopoulos M. 2018. Superior techniques for eliminating ring artifacts in X-ray micro-
tomography. Optic Express 26:28396–28412. DOI: https://doi.org/10.1364/OE.26.028396

Beaudet et al. eLife 2021;10:e64804. DOI: https://doi.org/10.7554/eLife.64804
Wadeson N, Basham M. 2016. Savu: a Python-based, MPI framework for simultaneous processing of multiple, N-dimensional, large tomography datasets. arXiv. https://arxiv.org/abs/1610.08015.