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A case of benign osteogenic tumour in *Homo naledi*: Evidence for peripheral osteoma in the U.W. 101-1142 mandible

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ABSTRACT

The reported incidence of neoplasia in the extinct hominin record is rare. We describe here the first palaeopathological analysis of an osteogenic lesion in the extinct hominin *Homo naledi* from Dinaledi Cave (Rising Star), South Africa. The lesion presented as an irregular bony growth, found on the right lingual surface of the body of the adult mandible U.W. 101-1142. The growth was macroscopically evaluated and internally imaged using micro-focus x-ray computed tomography (μCT). A detailed description and differential diagnosis were undertaken using gross and micromorphology, and we conclude that the most probable diagnosis is peripheral osteoma – a benign osteogenic neoplasia. These tumours are cryptic in clinical expression, though they may present localised discomfort and swelling. It has been suggested that muscle traction may play a role in the development and expression of these tumours. The impact of this lesion on the individual affected is unknown. This study adds to the growing corpus of palaeopathological data from the South African fossil record, which suggests that the incidence of neoplastic disease in deep prehistory was more prevalent than traditionally accepted. The study also highlights the utility of micro-computed tomography in assisting accurate diagnoses of ancient pathologies.

1. Introduction

We present a detailed case study and palaeopathological analysis of a mandibular exostosis present on the lingual aspect of the U.W. 101-1142 fossil specimen, initially identified by Laird and colleagues (2016) as a mandibular osteoma. This was recovered from the Dinaledi Chamber, Rising Star Cave, Cradle of Humankind, South Africa. Rising Star Cave is located within the dolomitic karst landscape of the Cradle of Humankind World Heritage Site, some 50 km outside of Johannesburg, South Africa (Fig. 1). Excavations at the site have, to date, yielded more than 1550 identifiable fossil elements (Berger et al., 2015; Randolph-Quinney, 2015). The fossils were derived from at least 15 individuals, a total likely to represent a small fraction of the fossils remaining in the chamber and awaiting excavation (Fig. 2). This discovery is the largest single fossil hominin assemblage found on the African continent to date (Berger et al., 2015; Randolph-Quinney, 2015). The context of the Naledi deposition in the cave has been described by Dirks and colleagues (Dirks et al., 2015, 2016), and the formation of the assemblage is interpreted as being due to deliberate body disposal by conspecifics (Dirks et al., 2015, 2016), a process known as funerary caching (after after Pettitt, 2011; Berger et al., 2017; Randolph-Quinney, 2015). Fossils from the Dinaledi Chamber have been attributed to the taxon *Homo naledi* (Berger et al., 2015; Laird et al., 2016). While highly primitive in terms of cranial capacity and body size, this taxon presents a mixture of primitive and derived characters that convincingly argue for inclusion in the *Homo* genus (Berger et al., 2015; Dembo et al., 2016; Laird et al., 2016; Schroeder et al., 2015).

The Dinaledi Chamber fossils have been shown to be late Middle Pleistocene in age. Based on optically stimulated luminescence (OSL) dating of the cave sediments, U-Th and palaeomagnetic dating of flowstones, and U-series and electron spin resonance (ESR) dating of

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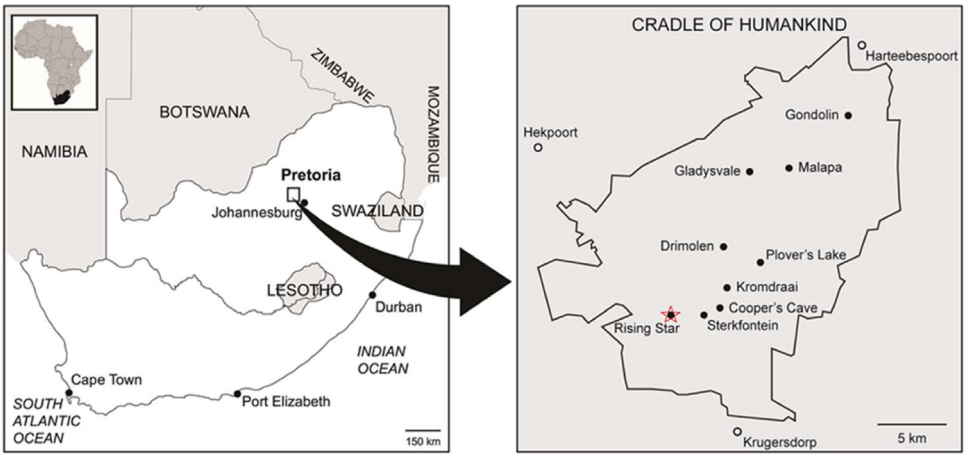

Fig. 1. Location of the Rising Star Cave system within the Cradle of Humankind, South Africa.

Fig. 2. Layout photograph of some of the Dinaledi Chamber fossils. The figure includes all of the material incorporated into the diagnosis of *Homo naledi*, and includes the holotype specimen, paratypes and referred material list in Berger and colleagues (2015). The fossil shown make up 737 partial or complete anatomical elements, many of which consist of several refitted specimens. Specimens not identified to element, such as non-diagnostic long bone or cranial fragments, are not shown. The 'skeleton' layout in the centre of the photo is a composite of elements that represent multiple individuals. The view is foreshortened and the table on which the bones are arranged is 120-cm wide for scale. Image, courtesy of John Hawks and taken with permission from Berger et al., 2015.

teeth, the skeletal remains from the Dinaledi Chamber were deposited between 236 ka and 335 ka (Dirks et al., 2017). This Middle Pleistocene date should not be viewed as representing first or last appearance of *Homo naledi*, whilst some researchers have suggested that the species may be of Lower Pleistocene origin or older, based on analyses of cranial morphology (Dembo et al., 2016; Thackeray, 2015). A second chamber within the Rising Star cave system has recently yielded further remains of *Homo naledi* (Hawks et al., 2017). This has been named the Lesedi Chamber, and has yielded the remains of at least three individuals which fall within the range of morphological variation exhibited by the Dinaledi Chamber fossils; for the moment the Lesedi Chamber fossils remain undated.

2. Materials

Specimen U.W. 101-1142 is an adult right mandibular fragment comprising the midpoint and proximal aspect of the body extending to the mandibular angle, including the RM_2 and RM_3, and a portion of the distal (inferior) ramus, excluding the coronoid, condyle processes and anterior mandibular body. This partial mandible has been attributed to *Homo naledi*; a detailed description of the morphology and metrics of the specimen can be found in Laird and colleagues (Laird et al., 2016). The specimen was recovered in a partially fragmented state, and reconstructed by Peter Schmidt. The largest fragment of U.W. 101-1142 preserves a damaged right corpus, RM_2, RM_3, and a portion of the right ramus. To this fragment, a piece of the gonial region and a small portion of the ramus have been refit (Fig. 3a and c). An isolated RM_1, U.W. 101-1304, fits into the preserved portion of the M_1 alveolus (Fig. 3f). Supporting their allocation to a single biological individual, the interproximal contact facets of U.W. 101-1304 and the U.W. 101–1142 M_2, match in size and shape. Other isolated teeth from the U.W. 101 assemblage may represent this individual as well, but their associations are less certain.

As judged by dental eruption and attrition, U.W. 101-1142/1304 is an adult. Further, though lacking dentine exposure, the M_3 cusp tips are blunted by wear, which corresponds to Smith's (1984) wear stage 2. The M_2 has tiny pits of dentine exposed over each of its buccal cusps; though, much of the occlusal fissure pattern remains (stage 3). The U.W. 101–1304 M_1 is worn and uncoalesced pits of dentin are exposed over each of the five cusps (stage 4) (Fig. 3c). Antemortem enamel chipping is also evident on all three molars. The allocation of U.W. 101-1142/1304 to *H. naledi* is supported by its dental morphology. For example, the molars have an $M_1 < M_2 < M_3$ size gradient, the hypoconulid on all molars is relatively large, all molars lack supernumerary cusps (Fig. 3f), the protostylid is present on M_2 and M_3 as a faint crest restricted to the mesiolingual corner of the crown, and a three-dimensional geometric morphometric analysis of the enamel-dentine junction shows that the U.W. 101–1142 M_2 falls into a unique region of phenotype space with the rest of the U.W. 101 molar teeth.

3. Methods

The specimen was evaluated macroscopically, and the morphology was compared to all other mandibular specimens of *Homo naledi* recovered to date. Initial external macro-photographic images were taken using a Canon 70D 20MP DSLR, with a 60 mm Canon EF f2.8 macro lens and ring-flash. Following macro-photography, images of the internal structure of the specimen were obtained using micro-focus X-ray computed tomography (μCt) at the Evolutionary Studies Institute of the University of the Witwatersrand. Scanning of the bone fragment

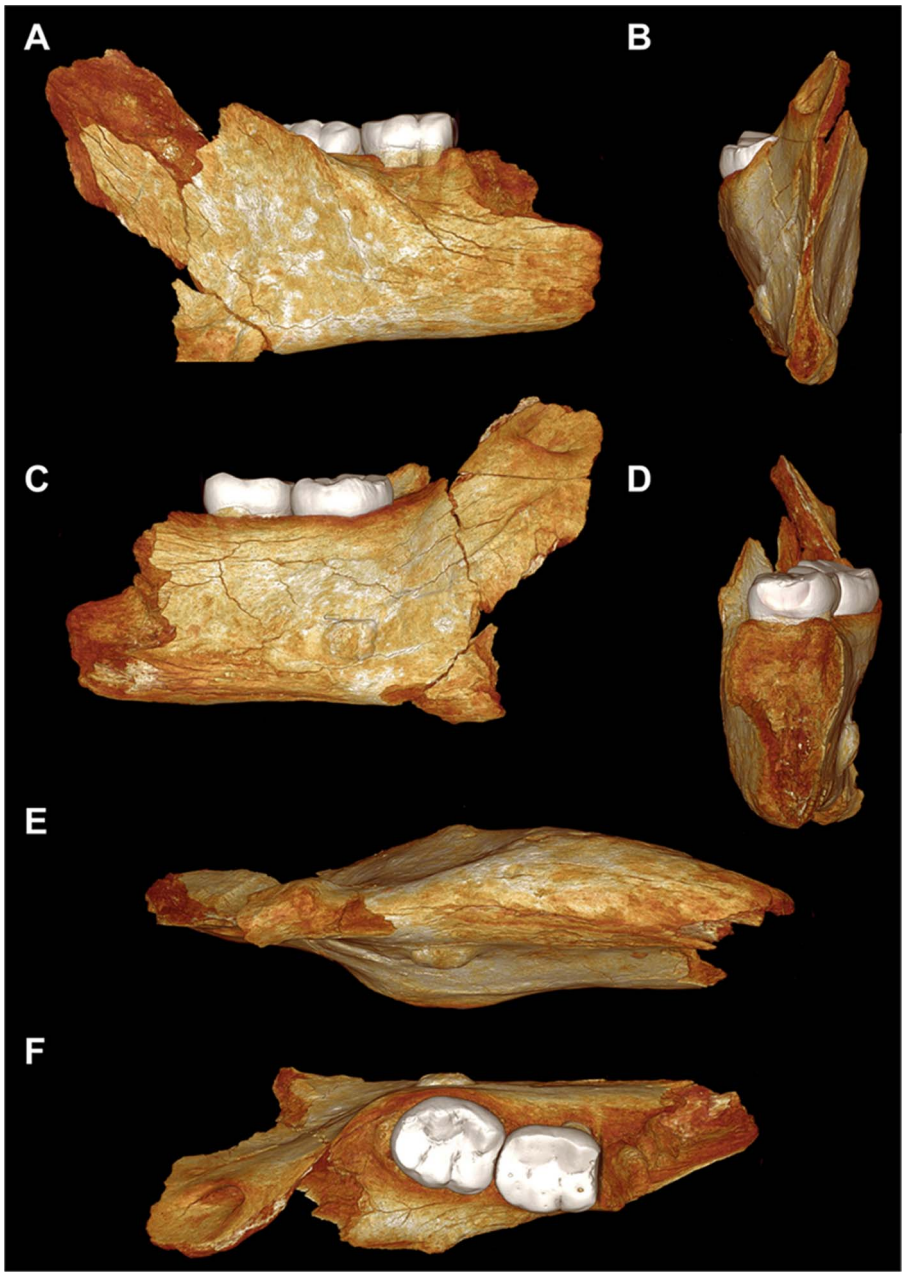

Fig. 3. External morphology of the U.W. 102-1142 mandible. (A) buccal (B) posterior (C) lingual (D) anterior (E) inferior and (F) occlusal views. All image derived from 3D surface rendering of micro-tomographic volume data.

was carried out by K.J. and L.K.D. using a Nikon XTH 225/320 LC µCT system. This was done using a confocal beam of X-rays produced using a potential difference of 60 kV. The source to specimen to detector distances were chosen to keep the fossil in the field of view and resulted in a resolution of 16 µm. Volume reconstruction was undertaken by K.J. using CT-Pro 3D, with the image volume output as a tiff stack. Subsequent imaging, with 2D orthoslice generation and 3D volume rendering was carried out by P.S.R-Q, L.K.D. and E.J.O. using Avizo Amira 5.4.5 (see Fig. 3 panel). Analysis of internal structure and external morphology was undertaken by E.J.O., P.S.R-Q., L.K.D. and J.S.S.

4. Results

The lingual surface of the body of the U.W. 101-1142 corpus displays an irregular bony growth on the corpus, noted in the formal description of the specimen by Laird and colleagues (Laird et al., 2016). This is externally visible as an irregularly-shaped bony mass attached directly to the right lingual cortex, directly below RM_3. The exostosis measures approximately 10 mm in diameter and is located 20 mm below the mylohyoid line, and 20 mm cranially from the inferior margin of the corpus. Macroscopically, the external surface of the exostosis appears relatively smooth and sub-rectangular to ovoid in shape, with rounded edges in the inferolateral quadrant and with a somewhat planar (flattened) surface along its superior edge. To the antero-superior aspect of the lesion can be seen a short vascular canal (Fig. 3c), which travels mesially, penetrating parallel to, and then diving obliquely into the cortex of the corpus (Fig. 4a), before connecting with the medulla (Fig. 4b).

Cross-sections (2D orthoslices) derived from micro-tomographic imaging (Fig. 6a–h – see Fig. 5 for guide to slice placement) indicate an irregularly shaped hemispherical, bi-lobular mass sessile dome-shaped, 1 cm diameter, sub rectangular to oval application to cortex with smooth convex surface, indicating slow if any enlargement in

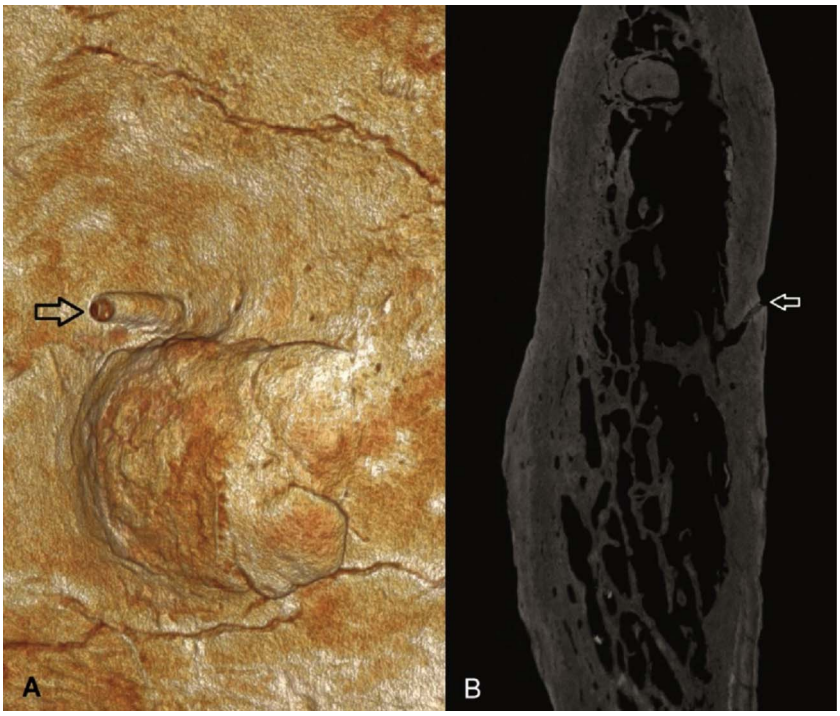

Fig. 4. Detailed image of vascular canal observed superior to the bony mass. This canal does not occur within the range of normal variation of *Homo naledi* and may be co-responsive with the formation of the lesion. The canal travels disto-mesially, penetrating parallel to, and then diving obliquely into the cortex of the corpus (surface rendered view 4a), before connecting with the medulla (orthoslice 4b).

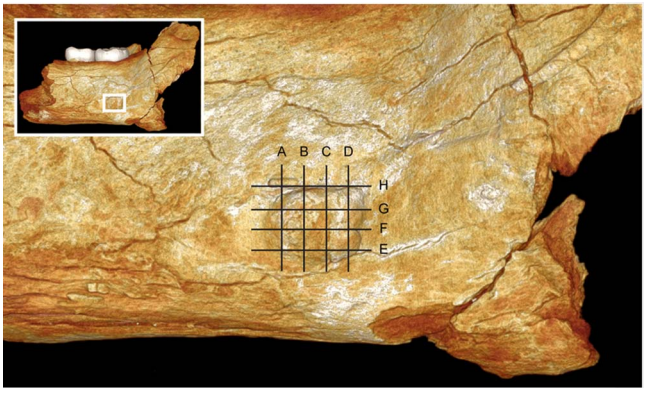

Fig. 5. Anatomical location of orthoslices A to H displayed in Fig. 6.

premortem time, which is integrated almost completely into the lingual cortex. The mass is dominated by a large primary lobe, with a smaller lobule occurring in the disto-inferior quadrant. The lesion is complete, with no post-mortem loss, except for a slight discontinuity caused by post-mortem cracking of the cortex in the inferolateral portion; this cracking can be seen penetrating the junction between the mass and the cortex in Figs. 6a–d.

The internal morphology of the mass is highly informative (Fig. 6a–h). The central region of the lesion exhibits a stratified convex lamella (radio-opaque laminations) in cross section (Fig. 6c and e) as in the common button osteoma which is most pronounced in the anterior half of the exostosis. Overall, the cortical bone and the margin of the lesion are contiguous to the extent that it is difficult to distinguish the cortex from the lesion, other than the slightly sclerotic and irregular internal morphology of the bone at the margin. There is no evidence of invasion by the mass sub-cortically into the medulla of the corpus, and instead the mass presents a lingual expansion of the cortex as seen in Fig. 6e–g. As noted above, a well-defined vascular canal is also present on the external cortex of the corpus, just antero-superiorly to the lesion (Fig. 6a and b). Whilst this does not penetrate the lesion directly, the walls of the canal share a similar pattern of radiopacity as seen in the outer edge of the lesion, and the presence of the canal may well be predicated on the presence and growth of the lesion. Such a vascular feature is not noted or identified in any other comparable mandibular specimen of *Homo naledi* (Laird *personal communication,* November 2016) and was not observed in non-pathological modern human mandibles in the Raymond A. Dart Collection (University of the Witwatersrand, sampled by E.J.O) and skeletal collections housed at the University of Central Lancashire (sampled by P.S.R-Q.).

4.1. Differential diagnosis

Diagnosis was undertaken using both palaeopathological and clinical diagnostic criteria (Ortner, 2003; Resnick, 1995; Roberts and Cox, 2003; Rothschild and Martin, 1993; Vigorita, 2008). The presence of reorganized sclerotic bone indicates an ante-mortem process, and the lesion cannot therefore be attributed to taphonomic, diagenetic, or pathology-mimicking effects or processes (Bloem and Kroon, 1993). The accumulated evidence for both osteogenic and osteosclerotic processes indicates that the pathological process was chronic, with no evidence of aggressive bone remodelling, cortical resorption, osteolysis, and sub-periosteal reactive processes (Aufderheide and Rodríguez-Martin, 1998; Bloem and Kroon, 1993). With specific regard to the specimen, the lesion offers no evidence of a healed bone fracture or any bone deformity, as a consequence of traumatic insult. Traumatic avulsion at a remote muscle insertion site with subsequent remodelling is possible (given the proximity of the lesion to the medial pterygoid muscle) though we consider this unlikely given the lobulated morphology of the lesion, and the lack of sub-periosteal reactive processes or osseous reaction within the surviving region of the medial pterygoid enthosite. There is no evidence of perilesional or endosteal inflammation of the mandibular bone cortex or associated osteolytic lesions on the jaw, ruling out any form of systemic infection or inflammatory diseases such as condensing osteitis, periodontal, periapical, or endodontal lesions, including mandibular osteomyelitis and Garre's sclerosing osteomyelitis (Nakano et al., 2008). Osteosarcoma is not comprised

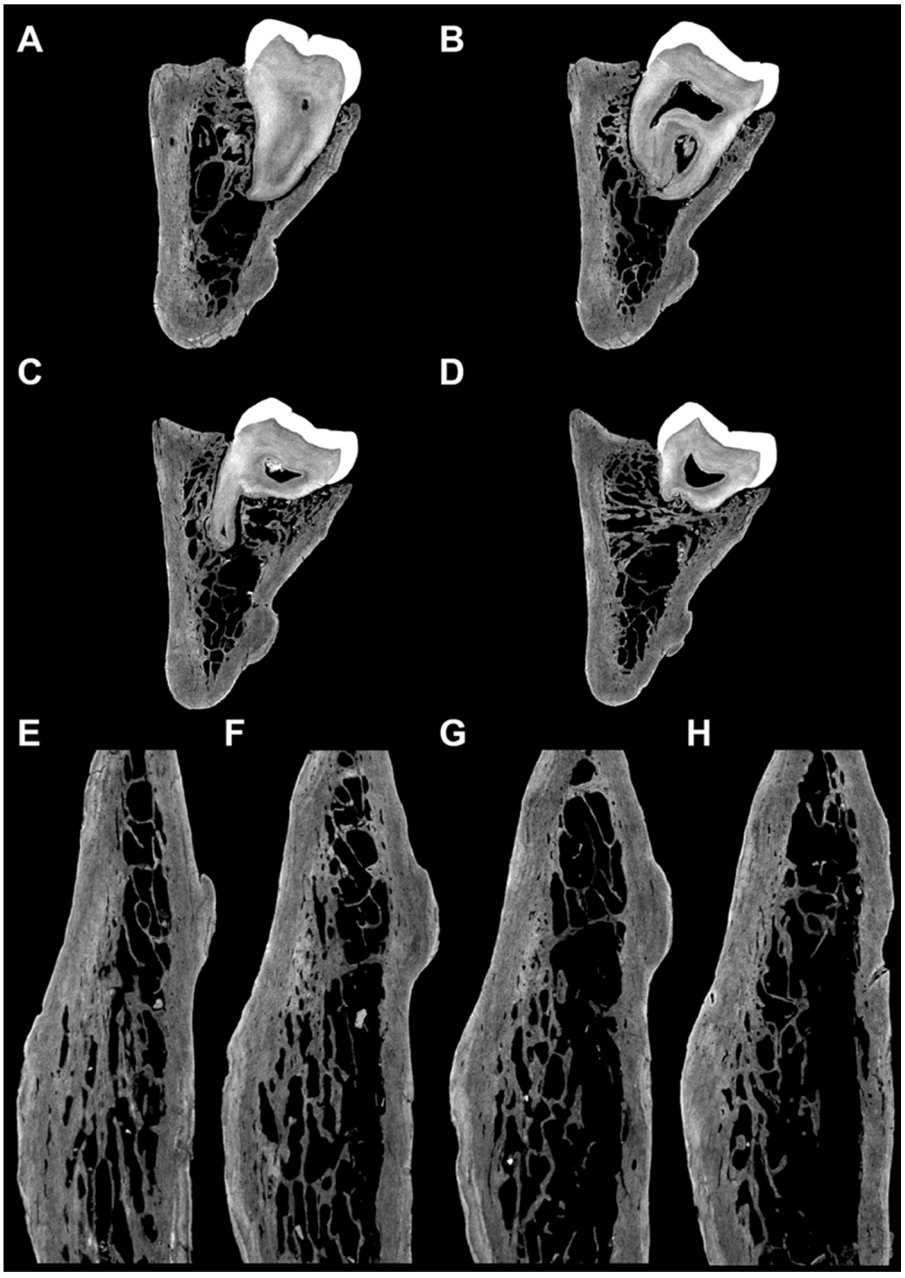

Fig. 6. Coronal (A to D) and transverse (E to H) micro-tomographic orthoslices through the U.W. 101-1142 mandible. See Fig. 5 for anatomical location of each slice.

of lamellar bone and the small size of the lesion is unrealistic and thus rules out osteosarcoma as a possible diagnosis (Mensforth et al., 2000; Strouhal et al., 1997; Suzuki, 1987; Unni and Dahlin, 1989).

The morphology and location of the lesion suggests that several bone-forming pathologies should be included in a differential diagnosis for this condition and include: osteochondroma, osteoid osteoma, mandibular osteoma, and mandibular torus (exostosis). Table 1 lists and details the diagnostic criteria

As there is no visible evidence of delineation with the bone cortex which shows total integration (Ragsdale, 1993), a generally smooth texture of the lesion under study indicates a strong possibility of mandibular osteoma (Baykul et al., 2003; Capasso, 1997; Durão et al., 2012; Fallahi Motlagh et al., 2015; Federspiel, 1924; Georgalas et al., 2011; Green and Boweran, 1974; Johann et al., 2005; MacLennan and Brown, 1974; Premužić et al., 2013; Roy, 2008; Sayan et al., 2002; Souza et al., 2015; Steinberg and George, 1989; Yadav et al., 2015) with secondary diagnosis of mandibular exostosis. Based on the observed gross pathological, micro-morphological, and location criteria, the two most likely diagnoses are mandibular osteoma (Baykul et al., 2003; Capasso, 1997; de Souza et al., 2015; Durão et al., 2012; Fallahi Motlagh et al., 2015; Federspiel, 1924; Georgalas et al., 2011; Green and Boweran, 1974; Johann et al., 2005; MacLennan and Brown, 1974; Premužić et al., 2013; Roy, 2008; Sayan et al., 2002; Steinberg and George, 1989; Yadav et al., 2015) or congenital mandibular torus (exostosis). Exostoses are hyperplastic bone protuberances occurring in mandibular and maxillary bone (Allan and Reid, 1967; Katz et al., 1993; Revington, 1984; Sanders and McKelvy, 1977; Smitha and Smitha, 2015). They can be trabecular or cortical in nature and mostly comprise mature bone. Generally, they are bilateral lesions, and we are unable to ascertain whether this is bilateral expression due to the absence of the left mandibular antimere. However, internal morphology, the location of the lesion (occurring below the mylohyoid line), and its relationship to the alveolus is inconsistent with such an exostosis. We consider it most likely that this specimen presents peripheral mandibular osteoma, and thus a condition of benign osteogenic neoplasia.

Table 1
Differential diagnostic options for the U.W. 101-1142 mandible.

Osteochondroma (mandibular)	A common benign bone tumour, also known as osteocartilaginous exostosis. It can be interpreted as a developmental irregularity; commonly asymptomatic, and if singular has a low malignancy potential. They are usually slow growing, and presents as a radiopaque mass with well-defined margins. Radiographic images have indicated exophytic growths measuring 3–4 cm. Osteocartilaginous exostosis (osteochondromas) are generated from a cartilage cap by enchondral ossification and present with a bony stalk-type protrusion; a smooth cortical plate develops with mature bone. The cartilage cap will stop its growth and is completely absorbed by the enchondral process. It is rare in the in the maxillofacial region due to intra-membranous growth of these bones, and tends to occur wherever bones grow through endochondral ossification; when seen in the mandible it most commonly affects the condylar and coronoid processes (Sanders and McKelvy 1977; Andrade et al., 2014).
Osteoid osteoma	A benign slow-growing bone-forming tumour. It usually originates in spongy bone but can also involve the cortex. Usually less than 2 cm in diameter. Presents characteristically with a lucent nidus framed with a thin fibrovascular rim surrounded by sclerotic tissues of host bone. The nidus may exhibit a central mineralised region. Radiologically seen as round or oval lesions less than 2 cm in diameter, with a 1–2 mm peripheral radiolucent zone in radiographs. They are usually cortical lesions, and can manifest anywhere in the bone. Up to 80% of cases are found in the long bones of the lower extremities. Other sites include the hands, feet, pelvis, vertebrae, and phalanges. Less than 1% of cases occur in the jaws (Infante-Cossio et al., 2016; Singh and Solomon, 2012; Greene et al., 1968; de Souza Dias and Frost 1974; Zulian et al., 1987; Radcliffe et al., 1998; Tochihara et al., 2001; Liu et al., 2002; Jones et al., 2006; An et al., 2013; Adouly et al., 2015; Da Costa et al., 2015).
Osteoma (of the jaw)	Types of mandibular osteoma include periosteal (peripheral), endosteal (central) or extra-skeletal (coming from soft tissue). Several different causes such as neoplastic, developmental and reactive have been inferred as possible etiologic factors for mandibular osteoma. These peripheral osteomas have been argued are not neoplastic because they are slow growing. Other researchers have reported them as a reactive condition caused by trauma, because peripheral osteomas typically present on the inferior border of the buccal aspect of the mandible which is an area susceptible to traumatic insult. Peripheral osteomas are usually located in close proximity to muscle attachments, suggesting muscle traction may be involved in their development (Roy 2008). Although common in crania, they are less common in the jaws, though they occur more frequently in the mandible than the maxilla. The lingual region of the mandibular body is one of the most frequent sites for this osteoma (Richards et al., 1986; Sayan et al., 2002). Radiographically they can present as a single, well defined, pedunculated (or not), oval or round mushroom-shaped radiopaque mass displaying a density resembling bone (Kaplan et al., 1994). A histologic similarity of "button osteomas" of calvarium and osteomas of mandible has been established. The frequency of button osteoma is similar in modern (37.6%) and archaeological (41.1%) populations, in blacks, whites, males, and females, and correlates with age. It is rare in nonhuman primates. The frequency of large osteomas (0.5-1.0 cm) was similar in young and old age groups. The demographic characteristics of button osteoma, mainly its high frequency among ancient and modern populations, its independence of sex and race, its scarcity in other primates, and the fact that its macro- and microstructure are indicative of an hamartoma, and not a neoplastic osteoma or post-traumatic exostosis. This suggests an evolutionary history to this condition (Eshed et al., 2002). Alternative locations for the presentation of osteomas include external auditory canal, orbits, temporal bone and pterygoid process (Soni and Bhargava 2014; Federspiel 1924; Green and Boweran 1974; MacLennan and Brown 1974; Steinberg and George 1989; Capasso 1997; Sayan et al., 2002; Baykul et al., 2003; Johann et al., 2005; Roy 2008; Georgalas et al., 2011; Durão et al., 2012; Premužić et al., 2013; de Souza et al., 2015; Fallahi Motlagh et al., 2015; Yadav et al., 2015). The World Health Organization (WHO) in its recent classification of diseases reports osteoma as a benign Aussies neoplasm, and specifically distinct from exostoses and tori, which are hamartoma, has been followed by several investigators (Agrawal et al., 2015). The published literature is contradictory on frequency of the condition. The lingual region of the mandible is considered one of the most common loci for mandibular osteoma (Richards et al., 1986; Sayan et al., 2002). According to Khandelwal et al. (2016), involvement of the mandibular lingual cortex is rare.
Tori or mandibular exostoses	Tori are amongst the most frequent benign jaw lesions (Platzek et al., 2014). Tori are outgrowths of bone projecting from the surface of the mandible or maxilla (Choi et al., 2012; Cortes et al., 2014; Igarashi 2016). They consist mostly of compact bone, and are homogenously mineralised. Mandibular tori typically form from the inner surface of the mandible, and are found near the premolars and distal to the molars. They are commonly found below the alveolus and above the mylohyoid muscle attachment (Sneck et al., 2009; Hassan et al., 2012). Some researchers however, disagree and note that torus mandibularis is also known from the lingual surface of the mandible and often located medial to molar roots (Ihunwo and Phukubye 2006). They are not commonly exhibited before 10 years old (Shah et al., 1992). They are known to occur bilaterally, with solitary tori more commonly observed than multiple occurrences and are known to present earlier in life (Axelsson and Hedegard, 1981). They are not commonly exhibited before 10 years old (Shah et al., 1992). Several studies have reported incidences of tori and exostoses, increase with age, with higher prevalence observed in the over 18 year old age group (Auškalnis et al., 2015). Tori are more commonly known to occur during mid-life (García-García et al., 2010). In both male and female, incidence of the two types of tori was the highest in the 35–65 year old group (Haugen, 1992). Some consist of marrow space and display trabeculations. In a clinical case study, patients presenting with torus mandibularis showed a much greater prevalence with characteristics such as a square-shaped jaw, sharp angular morphology ($P = .001$) and a normal mandibular cortex ($P = .03$). The subjects displaying an absence of torus mandibularis were more highly likely to have rounded mandibles with less sharp angular morphology and mandibular cortical erosion. The study concluded that parafunctional activity may be a possible cause of torus mandibularis by applying stress in the locus where the tori typically develop. This may infer that squarely-shaped mandibles, which are more prone to stress concentration, may be associated with a greater incidence of torus mandibularis (Cortes et al., 2014). This may have an interesting implication for this pathology in hominin mandibles in future studies.

5. Discussion

The hominin individual associated with U.W. 101-1142, most likely was affected by a peripheral osteoma, a benign osteogenic neoplasm. A neoplasm ('new-growth' or tumour) is defined as a mass of localised tissue growth, the cellular proliferation of which is no longer subject to the effects of normal growth-regulating mechanisms (Binder et al., 2014; Capasso, 2005; Retief and Cilliers, 2011; Weinberg, 1983). A neoplasm may be benign or malignant; in the case of malignancy they are often referred to as cancer (Aufderheide and Rodríguez-Martin, 1998; Ortner, 2003). The preserved signatures of neoplasms of any kind are rare in archaeological populations, and are extremely rare in the fossil record (Capasso, 2005), though there is building evidence for such conditions in the fossil record as recent publications attest. The earliest confirmed evidence of neoplastic disease, an osteoid osteoma, comes from a 300-million-year-old fossil fish (*Phanerosteon mirabile*) from the Devonian Period (Capasso, 2005; Ortner, 2003; Rothschild et al., 1999; Rothschild et al., 2003; Rothschild and Martin, 1993). The condition is also the first observed neoplasia in the hominin fossil record, with a case of vertebral osteoid osteoma from the MH1 skeleton of *Australopithecus sediba* from Malapa, South Africa, dated to 1.98 Ma (Randolph-Quinney et al., 2016). Osteoid osteoma also has been recognised in 24,000-year-old European mammoths (Leshchinskiy, 2012). The earliest evidence for malignancy (cancer) in the hominin record comes from Swartkrans, South Africa, with a case of parosteal osteosarcoma dated to c. 1.7 mya (Odes et al., 2016). Other reported cases of neoplasia (both benign and malignant) are rare in the fossil record, with the majority of cases in the human lineage dating from the Holocene (Capasso, 2005; Ortner, 2003; Rothschild and Martin, 1993).

Osteoma of the cranium, particularly of the vault, is widely reported from the palaeopathological record of the Holocene, with (less-frequent) mandibular cases noted (Capasso, 2005; Ortner, 2003; Rothschild and Martin, 1993). In non-human primates it is worth noting that benign osteomas have been observed in both gorilla

subspecies but have not been seen in either chimpanzees or orangutans (Lovell, 1990). Because the pathogenesis of osteoma is not fully resolved, some researchers regard it as a neoplasm whilst others deem it to be the consequence of a traumatic insult (Bloem and Kroon, 1993; Capasso, 1997; MacLennan and Brown, 1974; Roy, 2008). Both hamartomatous and neoplastic factors have been advocated, but no definite conclusion has been reported. Developmental, neoplastic and reactive causes have been attributed as possible etiologic factors (Capasso, 1997), though it is unlikely that peripheral osteomas are a developmental anomaly, as most cases occur in adults (MacLennan and Brown, 1974; Roy, 2008). The oncogenetic basis of this condition is for the present unresolved. Other benign osteogenic tumours display a clear genetic basis to expression. In osteoid osteoma for instance, cytogenetic chromosomal studies indicate that there is some degree of genetic basis to the condition. This includes duplications and deletions at 22q13.159, the locus of which reflects genes that play a role directly in osteogenesis (PDGF-B and ATF-4), and aberrant expression of transcription factors Runx2 and Osterix, both of which are master regulators of osteoblastic lineage differentiation (Baruffi et al., 2001; Selvarajah et al., 2010; Weinberg, 1983).

With regards to the U.W. 101-1142 specimen, clinical manifestations and effects on the individual may have been slight. Large tori have been known to present with small amounts of localised discomfort (Gil Tutor, 1999). From modern clinical studies it is known that osteoma is a slow growing lesion, which is often cryptic, though it may have caused other symptoms such as pain and localised swelling. The proximity of the lesion to the insertion of the medial pterygoid muscle, and the associated vascular involvement and sequestration of the cortex suggests the potential impact on normal function of the medial pterygoid, which may have had consequences for elevation of the jaw on the right side, as well as consequential discomfort of the right temporo-mandibular joint. This is in keeping with the classification of the condition. Many peripheral osteomas are in close proximity to muscle attachments (i.e. masseter, medial pterygoid, temporalis), and researchers have considered it possible that muscle traction may play a role in the development and expression of these tumours (Al-Yahya et al., 2015; Arzul et al., 2012; Baykul et al., 2003; Kaplan et al., 2008; MacLennan and Brown, 1974; Ogbureke et al., 2007; Roy, 2008).

This study illuminates the importance of the challenge of understanding ancient hominin neoplastic disease and other diseases, constrained by limited sample sizes versus the more abundant samples of modern clinical disease restricted studies of tumours in human specimens of skeletal remains, making definitive diagnoses difficult (Aufderheide and Rodríguez-Martin,1998; Capasso, 2005; Ortner, 2003). However, neoplastic disease has been observed by a number of past studies of benign and malignant bone tumours arising from the fossil record that extend into deep ancient time (Capasso, 1997, 2005; David and Zimmerman, 2010; Davies and Lineweaver, 2011; Odes et al., 2016; Randolph-Quinney et al., 2016; Retief and Cilliers, 2011; Roberts and Cox, 2003; Rothschild et al., 1999; Rothschild et al., 2003; Rothschild and Martin, 1993). The paucity of definitive neoplastic evidence in the archaeological and fossil record may well be put down to a number of factors such as preservational or sample size bias, poor imaging methods, or deficient analyses. Computed tomography, and micro-computed tomography in particular, has been widely suggested as the imaging method of choice when diagnosing bone neoplasms, where radiolucency and sclerosis are most often evidenced, and is especially useful when experiencing difficulty with dense bone material (Odes et al., 2016). Modern imaging techniques (such as micro-computed tomography or phase-contrast synchrotron tomography), and the use of carefully selected clinical skeletal comparatives have become exceedingly important tools in assisting with obtaining accurate diagnoses of ancient pathologies.

Authors' contributions

P.S.R.Q. and L.R.B. coordinated the research and incorporated case notes and observational data on U.W. 101-1142 that were provided by E.J.O, L.K.D. and J.S.S. J.K. and L.K.D. undertook the micro-tomographic scanning of the specimen, and primary reconstruction. Post-reconstruction rendering and slicing was carried out by P.S.R-Q, L.K.D. and E.J.O. Analysis of micro-tomographic results was undertaken by E.J.O., P.S.R-Q., L.K.D. and J.S.S., T.N.A. provided discussion of oncogenetics. All authors contributed equally to data acquisition and analysis and to editing.

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References

Adouly, T., Oubahmane, T., Adnane, C., Rouadi, S., Abada, R., Roubal, M., Mahtar, M., 2015. Bilateral osteoid osteoma of the mandible: an unusual case report. Int. J. Pediatr. Otorhinol. 10 (3), 56–58.

Agrawal, R., Agrawal, S., Bhargava, S., Motlani, M., Agrawal, R., 2015. An uncommon case of solitary peripheral osteoma in the mandible. Case Rep. Dent. 15 (Article ID 319738, 4 pages http://dx.doi.org/10.1155/2015/319738).

Al-Yahya, S.N.S.H., Wan Hamizan, A.K., Zainuddin, N., Arshad, A.I., Ismail, F., 2015. Mastoid osteoma: report of a rare case. EJENTAS 16 (2), 189–191.

Allan, I.M.B., Reid, W.H., 1967. Unilateral exostosis of the coronoid process of the mandible: a report of two cases. Br. J. Oral Surg. 5 (1), 20–24.

An, S.-Y., Shin, H.-I., Choi, K.-S., Park, J.-W., Kim, Y.-G., Benavides, E., Kim, J.-W., An, C.-H., 2013. Unusual osteoid osteoma of the mandible: report of case and review of the literature. Oral Surg. Oral Med. Oral Pathol. Oral Radiol. Endod. 116 (2), e134–e140.

Andrade, N.N., Gandhewar, T.M., Kapoor, P., Thomas, R., 2014. Osteochondroma of the mandibular condyle—report of an atypical case and the importance of computed tomography. J. Oral. Biol. Craniofac. Res. 4 (3), 208–213.

Arzul, L., Vincent, C., Mercier, J.M., 2012. Ostéome mandibulaire post-traumatique. Rev. Stomatol. Chir. Maxillofac. 113 (3), 169–172.

Auškalnis, A., Bernhardt, O., Putnienė, E., Šidlauskas, A., Andriuškevičiūtė, I., Basevičienė, N., 2015. Oral bony outgrowths: prevalence and genetic factor influence. Study of twins. Medicina (Mex) 51 (4), 228–232.

Aufderheide, A.C., Rodríguez-Martin, C., 1998. The Cambridge Encylopedia of Human Paleopathology. Cambridge University Press, Cambridge.

Axelsson, G., Hedegard, B., 1981. Torus mandibularis among Icelanders. Am. J. Phys. Anthropol. 54 (3), 383–389.

Baruffi, M., Volpon, J., Neto, J., Casartelli, C., 2001. Osteoid osteomas with chromosome alterations involving 22q. Cancer Genet. Cytogenet. 124, 127–131.

Baykul, T., Heybeli, N., Oyar, O., Doğru, H., 2003. Multiple huge osteomas of the mandible causing disfigurement related with Gardner's syndrome: case report. Auris Nasus Larynx 30 (4), 447–451.

Berger, L.R., Hawks, J., de Ruiter, D.J., Churchill, S.E., Schmid, P., Delezene, L.K., Kivell, T.L., Garvin, H.M., Williams, S.A., DeSilva, J.M., Skinner, M.M., Musiba, C.M., Cameron, N., Holliday, T.W., Harcourt-Smith, W., Ackermann, R.R., Bastir, M., Bogin, B., Bolter, D., Brophy, J.K., Cofran, Z.D., Congdon, K.A., Deane, A.S., Dembo, M., Drapeau, M., Elliott, M.C., Feuerriegel, E.M., Garcia-Martinez, D., Green, D.J., Gurtov, A., Irish, J.D., Kruger, A., Laird, M.F., Marchi, D., Meyer, M.R., Nalla, S., Negash, E.W., Orr, C.M., Radovcic, D., Schroeder, L., Scott, J.E., Throckmorton, Z.J.,

Tocheri, M.W., VanSickle, C., Walker, C.S., Wei, P., Zipfel, B., 2015. Homo Naledi, A New Species of the Genus Homo from the Dinaledi Chamber. eLife, South Africa, pp. e09560.
Berger, L.R., Hawks, J., Dirks, P.H.G.M., Elliott, M., Roberts, E.M., 2017. Homo naledi and Pleistocene hominin evolution in subequatorial Africa. eLife 6, e24234.
Binder, M., Roberts, C., Antoine, D., Cartwright, C., 2014. On the antiquity of cancer: evidence for metastatic carcinoma in a young man from ancient nubia (c. 1200BC). PLoS One 9, e90924.
Bloem, J.L., Kroon, H.M., 1993. Osseous lesions. Radiol. Clin. N. Am. 31 (2), 261–278.
Capasso, L., 1997. Osteoma: palaeopathology and phylogeny. Int. J. Osteoarchaeol. 7 (6), 615–620.
Capasso, L.L., 2005. Antiquity of cancer. Int. J. Cancer 113, 2–13.
Choi, Y., Park, H., Lee, J.-S., Park, J.-C., Kim, C.-S., Choi, S.-H., Cho, K.-S., Chai, J.-K., Jung, U.-W., 2012. Prevalence and anatomic topography of mandibular tori: computed tomographic analysis. J. Oral Maxillofac. Surg. 70 (6), 1286–1291.
Cortes, A.R.G., Jin, Z., Morrison, M.D., Arita, E.S., Song, J., Tamimi, F., 2014. Mandibular tori are associated with mechanical stress and mandibular shape. J. Oral Maxillofac. Surg. 72 (11), 2115–2125.
Da Costa, D.N.B., Almeida Júnior, P., De Melo, M.D.E.F.B., Da Fonte, J.B.M., Valois, R.B.V., De Albuquerque Júnior, R.L.C., 2015. Small osteoblastoma or osteoid osteoma of the mandible? Report of an atypical case. Oral Surg. Oral Med. Oral Pathol. Oral Radiol. Endod. 120 (2), e76.
David, R.A., Zimmerman, M.R., 2010. Cancer: an old disease, a new disease or something in between? Nat. Rev. 10, 728–733.
Davies, P.C.W., Lineweaver, C.H., 2011. Cancer tumors as Metazoa 1.0: tapping genes of ancestors. Phys. Biol. 8, a015001.
de Souza Dias, L., Frost, H.M., 1974. Osteoid osteoma – osteoblastoma. Cancer 33, 1075–1081.
de Souza, P.D., Leonhardt, F.D., Ahumada, N.G., Abrahão, M., Cervantes, O., 2015. Giant osteoma of the mandible. Braz. J. Otorhinolaryngol. 81 (1), 107–108.
Dembo, M., Radovčić, D., Garvin, H.M., Laird, M.F., Schroeder, L., Scott, J.E., Brophy, J., Ackermann, R.R., Musiba, C.M., de Ruiter, D.J., Mooers, A., Collard, M., 2016. The evolutionary relationships and age of Homo naledi: an assessment using dated Bayesian phylogenetic methods. J. Hum. Evol. 97, 17–26.
Dirks, P.H.G.M., Berger, L.R., Roberts, E.M., Kramers, J.D., Hawks, J., Randolph-Quinney, P.S., Elliott, M., Musiba, C.M., Churchill, S.E., de Ruiter, D.J., Schmid, P., Backwell, L.R., Belyanin, G.A., Boshoff, P., Hunter, K.L., Feuerriegel, E.M., Gurtov, A., Harrison, J.D., Hunter, R., Kruger, A., Morris, H., Makhubela, T.V., Peixotto, B., Tucker, S., 2015. Geological and taphonomic context for the new hominin species Homo naledi from the Dinaledi Chamber, South Africa. eLife 4, e09561.
Dirks, P.H.G.M., Berger, L.R., Hawks, J., Randolph-Quinney, P.S., Backwell, L.R., Roberts, E.M., 2016. Comment on deliberate body disposal by hominins in the dinaledi chamber, cradle of humankind, South Africa? J. Hum. Evol. 96, 149–153.
Dirks, P.H.G.M., Roberts, E.M., Hilbert-Wolf, H., Kramers, J.D., Hawks, J., Dosseto, A., Duval, M., Elliott, M., Evans, M., Grün, R., Hellstrom, J., Herries, A.I.R., Joannes-Boyau, R., Makhubela, T.V., Placzek, C.J., Robbins, J., Spandler, C., Wiersma, J., Woodhead, J., Berger, L.R., 2017. The age of Homo naledi and associated sediments in the Rising Star Cave, South Africa. eLife 6, e24231.
Durão, A.R., Chilvarquer, I., Hayek, J.E., Provenzano, M., Kendall, M.R., 2012. Osteoma of the zygomatic arch and mandible: report of two cases. Rev. Port. Estomatol. Cir. Maxilofac. 53 (2), 103–107.
Eshed, V., Latimer, B., Greenwald, C.M., Jellema, L.M., Rothschild, B.M., Wish-Baratz, S., Hershkovitz, I., 2002. Button osteoma: its etiology and pathophysiology. Am. J. Phys. Anthropol. 118 (3), 217–230.
Fallahi Motlagh, M., Janbaz, Y., Abaszade, A., 2015. Huge peripheral osteoma of the mandibular condyle: a case report. J. Oral. Maxillofac. Surg. Med. Pathol. 27 (6), 808–811.
Federspiel, M.N., 1924. A clinical report reganding a case of osteoma involving the maxilla. Int. J. Orthod. Oral. Surg. Radiogr. 10 (10), 654–655.
García-García, A.S., Martínez-González, J.M., Gómez-Font, R., Soto-Rivadeneira, Á., Oviedo-Roldán, L., 2010. Current status of the torus palatinus and torus mandibularis. Med. Oral Patol. Oral Cir. Bucal 15 (2), e353–e360.
Georgalas, C., Goudakos, J., Fokkens, W.J., 2011. Osteoma of the skull base and sinuses. Otolaryngol. Clin. N. Am. 44 (4), 875–890.
Gil Tutor, E., 1999. Torus mandibularis. Apropos a case. An. Otorrinolaringol. Ibero. Am. 26 (5), 457–460 (Spanish. PubMed PMID: 10568301).
Green, A.E., Boweran, J.E., 1974. An osteoma of the mandible. Br. J. Oral Maxillofac. Surg. 12 (2), 225–228.
Greene Jr., G.W., Natiella, J.R., Spring Jr., P.N., 1968. Osteoid osteoma of the jaws: report of a case. Oral Surg. Oral Med. Oral Pathol. Oral Radiol. Endod. 26 (3), 342–351.
Hassan, K.S., Alagl, A.S., Abdel-Hady, A., 2012. Torus mandibularis bone chips combined with platelet rich plasma gel for treatment of intrabony osseous defects: clinical and radiographic evaluation. Int. J. Oral Maxillofac. Surg. 41 (12), 1519–1526.
Haugen, L.K., 1992. Palatine and mandibular tori: a morphologic study in the current Norwegian population. Acta Odontol. Scand. 50 (2), 65–77.
Hawks, J., Elliott, M., Schmid, P., Churchill, S.E., d. Ruiter, D.J., Roberts, E.M., Hilbert-Wolf, H., Garvin, H.M., Williams, S.A., Delezene, L.K., Feuerriegel, E.M., Randolph-Quinney, P., Kivell, T.L., Laird, M.F., Tawane, G., DeSilva, J.M., Bailey, S.E., Brophy, J.K., Meyer, M.R., Skinner, M.M., Tocheri, M.W., VanSickle, C., Walker, C.S., Campbell, T.L., Kuhn, B., Kruger, A., Tucker, S., Gurtov, A., Hlophe, N., Hunter, R., Morris, H., Peixotto, B., Ramalepa, M., v. Rooyen, D., Tsikoane, M., Boshoff, P., Dirks, P.H.G.M., Berger, L.R., 2017. New fossil remains of Homo naledi from the Lesedi Chamber, South Africa. eLife 6, e24232.
Igarashi, Y., 2016. Frequency of mandibular tori in prehistoric and historic Japanese island populations. Quatern Int. 405, 87–100 (Part B).
Ihunwo, A.O., Phukubye, P., 2006. The frequency and anatomical features of torus mandibularis in a Black South African population. HOMO 57 (4), 253–262.
Infante-Cossio, P., Restoy-Lozano, A., Espin-Galvez, F., Gonzalez-Perez, L.-M., 2016. Mandibular osteoid osteoma. J. Emerg. Med pii: S0736-4679(16)30878-2. 10.1016/j.jemermed.2016.10.003.
Johann, A.C.B.R., Freitas, J.B.D., Aguiar, M.C.F.D., Araújo, N.S.D., Mesquita, R.A., 2005. Peripheral osteoma of the mandible: case report and review of the literature. J. Craniomaxillofac. Surg. 33 (4), 276–281.
Jones, A.C., Prihoda, T.J., Kacher, J.E., Odingo, N.A., Freedman, P.D., 2006. Osteoblastoma of the maxilla and mandible: a report of 24 cases, review of the literature, and discussion of its relationship to osteoid osteoma of the jaws. Oral Surg. Oral Med. Oral Pathol. Oral Radiol. Endod. 102 (5), 639–650.
Kaplan, I., Calderon, S., Buchner, A., 1994. Peripheral osteoma of the mandible: a study of 10 new cases and analysis of the literature. J. Oral Maxillofac. Surg. 52 (5), 467–470.
Kaplan, I., Nicolaou, Z., Hatuel, D., Calderon, S., 2008. Solitary central osteoma of the jaws: a diagnostic dilemma. Oral Surg. Oral Med. Oral Pathol. Oral Radiol. Endod. 106 (3), e22–e29.
Katz, J.O., Theisen, F.C., Mosby, E.L., 1993. Bony exostosis of the mandibular condyle. Oral Surg. Oral Med. Oral Pathol. Oral Radiol. Endod. 75 (6), 783–785.
Khandelwal, P., Dhupar, V., Akkara, F., 2016. Unusually large peripheral osteoma of the mandible–a rare case report. J. Clin. Diagn. Res. 10 (11), ZD11–ZD12. http://dx.doi.org/10.7860/JCDR/2016/21399.8807.
Laird, M.F., Schroeder, L., Garvin, H.M., Scott, J.E., Dembo, M., Radovčić, D., Musiba, C.M., Ackermann, R.R., Schmid, P., Hawks, J., Berger, L.R., de Ruiter, D.J., 2016. The skull of Homo naledi. J. Hum. Evol pii: S0047-2484(16)30136-1. 10.1016/j.jhevol.2016.09.014.
Leshchinskiy, S.V., 2012. Paleoecological investigation of mammoth remains from the Kraków Spadzista Street (B) site. Quatern Int. 276, 155–169.
Liu, C.J., Chang, K.W., Chang, K.M., Cheng, C.Y., 2002. A variant of osteoid osteoma of the mandible: report of a case. J. Oral Maxillofac. Surg. 60 (2), 219–221.
Lovell, N.C., 1990. Patterns of Injury and Illness in Great Apes. SIP, Washington, DC.
MacLennan, W.D., Brown, R.D., 1974. Osteoma of the mandible. Br. J. Oral Maxillofac. Surg. 12 (2), 219–224.
Mensforth, R.P., Way-Mosakowski, J., Zeman, K.E., 2000. A rare case of periosteal osteosarcoma of the mandible from the late archaic ward site (McL-11), McLean County, Kentucky. Am. J. Phys. Anthropol 22–227.
Nakano, H., Miki, T., Aota, K., Sumi, T., Matsumoto, K., Yura, Y., 2008. Garré's osteomyelitis of the mandible caused by an infected wisdom tooth. Oral Sci. Int. 5 (2), 150–154.
Odes, E.J., Randolph-Quinney, P.S., Steyn, M., Throckmorton, Z., Smilg, J.S., Zipfel, B., Augustine, T.N., de Beer, F., Hoffman, J.W., Franklin, R.D., Berger, L.R., 2016. Earliest cancer in the hominin record: 1. 7 milllion year old osteosarcoma from Swartkrans Cave, South Africa. S. Afr. J. Sci. 112 (7/8) (Art. #2015-0471.).
Ogbureke, K.U.E., Nashed, M.N., Ayoub, A.F., 2007. Huge peripheral osteoma of the mandible: a case report and review of the literature. Pathol. Res. Pract. 203 (3), 185–188.
Ortner, D.J., 2003. Tumors and tumor-like lesions of bone. Identification of Pathological Conditions in Human Skeletal Remains. D. J. Ortner, Amsterdam, AP, pp. 503–544.
Pettitt, P., 2011. The Palaeolithic Origins of Human Burial. Routledge, London.
Platzek, I., Schubert, M., Sieron, D., Laniado, M., 2014. Mandibular tori as an incidental finding in MRI. Acta Radiol. Open 3 (2) (2047981614522790).
Premužić, Z., Rajić Šikanjić, P., Mašić, B., 2013. Frontal sinus osteoma in a 16th century skeleton from Zagreb, Croatia. IJPP 3 (1), 54–58.
Radcliffe, S.N., Walsh, H.J., Carty, H., 1998. Osteoid osteoma: the difficult diagnosis. Eur. J. Radiol. 28 (1), 67–79.
Ragsdale, B.D., 1993. Morphologic analysis of skeletal lesions: correlation of imaging studies and pathologic findings. RAPL 6, 445–490.
Randolph-Quinney, P.S., Williams, S.A., Steyn, M., Meyer, M.R., Smilg, J.S., Churchill, S.E., Odes, E.J., Augustine, T., Taffreau, P., Berger, L.R., 2016. Osteogenic spinal tumor in Australopithecus sediba: earliest evidence for neoplasia in the human lineage. S. Afr. J. Sci. 112 (7/8) (Art. #2015-0470).
Randolph-Quinney, P.S., 2015. The mournful ape: conflating expression and meaning in the mortuary behaviour of Homo naledi. S. Afr. J. Sci. 111 (11/12) (Art. #a0131).
Resnick, D., 1995. Diagnosis of Bone and Joint Disorders. W.B. Saunders Company, Philadelphia, PA.
Retief, F.P., Cilliers, L., 2011. Breast cancer in antiquity. S. Afr. Med. J. 101 (8), 513–515.
Revington, P.J., 1984. 'Turret exostosis' of the coronoid process. Br. J. Oral Maxillofac. Surg. 22 (1), 37–41.
Richards, H.E., Strider, J.W., Short, S.G., Theisen, F.C., Larson, W.J., 1986. Large peripheral osteoma arising from the genial tubercle area. Oral Surg. Oral Med. Oral Pathol. Oral Radiol. Endod. 61 (3), 268–271.
Roberts, C., Cox, M., 2003. Health and Disease in Britain From Prehistory to the Present Day. Sutton Publishing, Stroud.
Rothschild, B.M., Martin, L.D., 1993. Paleopathology: Disease in the Fossil Record. CRC Press, Boca Raton, FL.
Rothschild, B.M., Witzke, B.J., Hershkovitz, I., 1999. Metastatic cancer in the Jurassic. Lancet 354, 398.
Rothschild, B.M., Tanke, D.H., Hebling, M., Martin, L.D., 2003. Epidemiologic study of tumors in dinosaurs. Sci. Nat. 90, 495–500.
Roy, I.D., 2008. Peripheral osteoma of mandible. Med. J. Armed Forces India 64 (4), 385–386.
Sanders, B., McKelvy, B., 1977. Osteochondromatous exostosis of the condyle. J. Am. Dent. Assoc. 95 (6), 1151–1153.
Sayan, N.B., Üçok, C., Karasu, H.A., Günhan, Ö., 2002. Peripheral osteoma of the oral and maxillofacial region: a study of 35 new cases. J. Oral Maxillofac. Surg. 60 (11), 1299–1301.
Schroeder, L., Scott, J.E., Garvin, H.M., Laird, M.F., Dembo, M., Radovčić, D., Berger,

L.R., 2015. Skull diversity in the Homo lineage and the relative position of Homo naledi. J. Hum. Evol pii: S0047-2484(16)30136-1. 10.1016/j.jhevol.2016.09.014.
Selvarajah, S., Zielenska, M., Squire, J., Park, P., 2010. Genetic Aspects of Bone Tumors. Bone Cancer. D. Heymann, Elsevier, London, pp. 161–170.
Shah, D.S., Sanghavi, S.J., Chawda, J.D., Shah, R.M., 1992. Prevalence of torus palatinus and torus mandibularis in 1000 patients. Indian J. Dent. Res. 3 (4), 107–110.
A. Singh, M.C. Solomon. (2012). Osteoid osteoma of the mandible: a case report with review of the literature. JDS (in press) http://dx.doi.org/10.1016/j.jds.2012.10.002.
Smith, B.H., 1984. Patterns of molar wear in hunter–gatherers and agriculturalists. Am. J. Phys. Anthropol. 63 (1), 39–56 ().
Smitha, K., Smitha, G.P., 2015. Alveolar exostosis–revisited: a narrative review of the literature. Saudi J. Oral. Dent. Res. 6 (1), 67–72.
Sneck, M., Scott, G.R., Leeper, K.L., 2009. Mandibular torus in the Greenlandic Norse. Am. J. Phys. Anthropol 243–243.
Soni, S., Bhargava, A., 2014. Revisiting peripheral osteoma of the mandible with case series and review of literature. Indian J. Otolaryngol. Head Neck Surg. 66 (2), 212–218.
Steinberg, H., George, C., 1989. Fracture-associated osteogenic sarcoma and a mandibular osteoma in two goats. J. Comp. Pathol. 100 (4), 453–457.
Strouhal, E., Vyhnanek, L., Horackova, L., Benesova, L., Nemeckova, A., 1997. A case of osteosarcoma in a late medieval-early modern skull from Kyjov (Czech Republic). Int. J. Osteoarchaeol. 7, 82–90.
Suzuki, T., 1987. Paleopathological study on a case of osteosarcoma. Am. J. Phys. Anthropol. 74, 309–318.
Thackeray, J.F., 2015. Estimating the age and affinities of Homo naledi. S. Afr. J. Sci. 11 (11/12) (#a0124).
Tochihara, S., Sato, T., Yamamoto, H., Asada, K., Ishibashi, K., 2001. Osteoid osteoma in mandibular condyle. Int. J. Oral Maxillofac. Surg. 30 (5), 455–457.
Unni, K., Dahlin, D., 1989. Osteosarcoma: pathology and classification. Semin. Roentgenol. 24 (3), 143–152.
Vigorita, V.J., 2008. Orthopaedic Pathology. Lippincott Williams & Wilkins, Philadelphia.
Weinberg, R., 1983. Oncogenes and the molecular biology of cancer. J. Cell Biol. 97, 1661–1662.
Yadav, S., Malik, S., Mittal, H.C., Puri, P., Duhan, A., 2015. Gigantic osteoma of the mandible—an unusual sequelae to dental caries. J. Oral. Maxillofac. Surg. Med. Pathol. 27 (4), 592–594.
Zulian, M.A., Kirk Vincent, S., Robert Hiatt, W., 1987. Osteoid osteoma of the mandibular ramus. J. Oral Maxillofac. Surg. 45 (8), 712–714.