

Supplementary material to: Odes EJ, Randolph-Quinney PS, Steyn M, Throckmorton Z, Smilg JS, Zipfel B, et al. Earliest hominin cancer: 1.7-million-year-old osteosarcoma from Swartkrans Cave, South Africa. *S Afr J Sci.* 2016;112(7/8), Art. #2015-0471, 5 pages. <http://dx.doi.org/10.17159/sajs.2016/20150471>

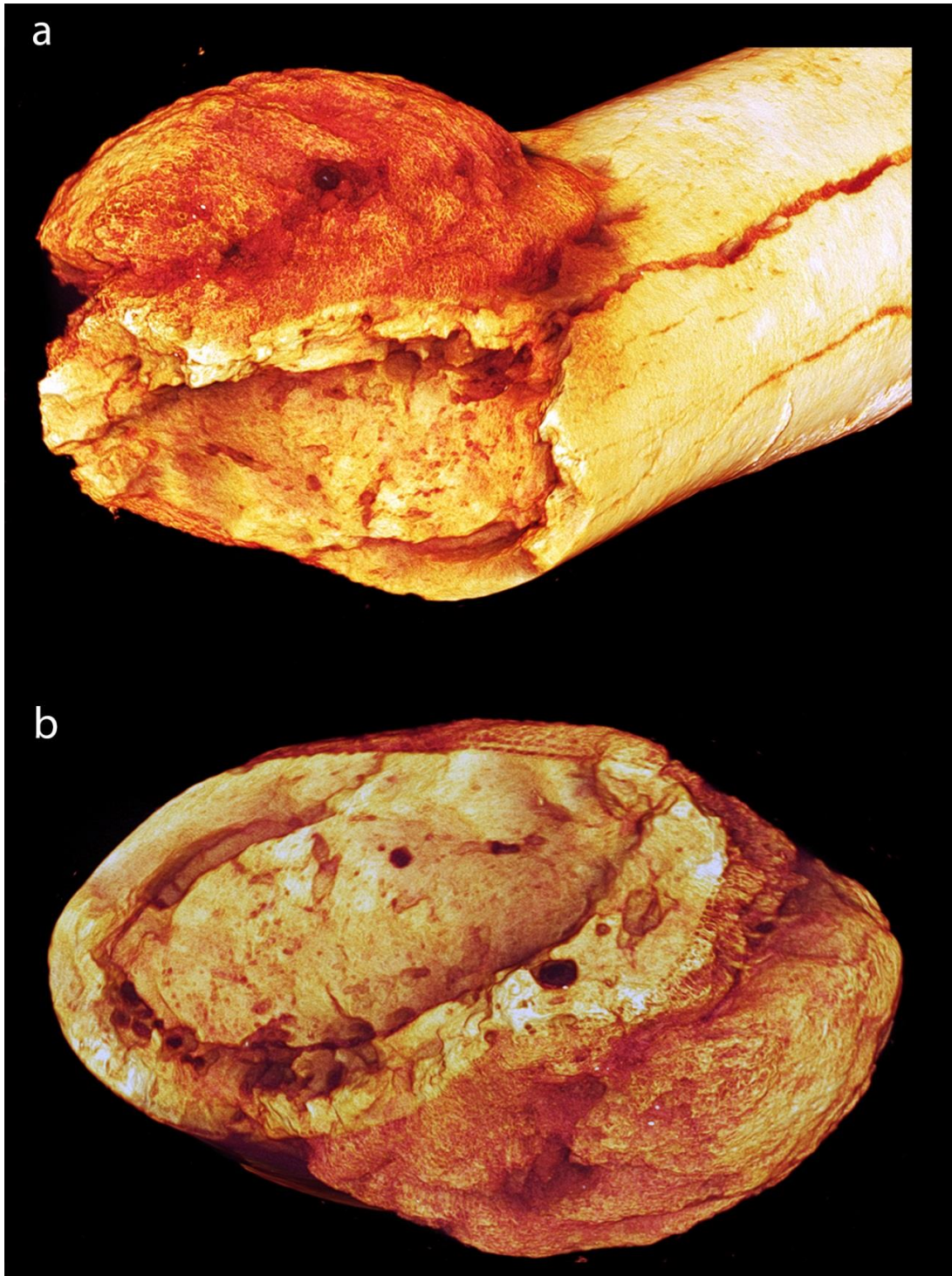


Figure 1: (a) and (b) surface rendered models (proximo-dorsal aspects), showing medullary bone infill and clear focalised cortical destruction near the periosteal margin in (b). Images by E.J.O.

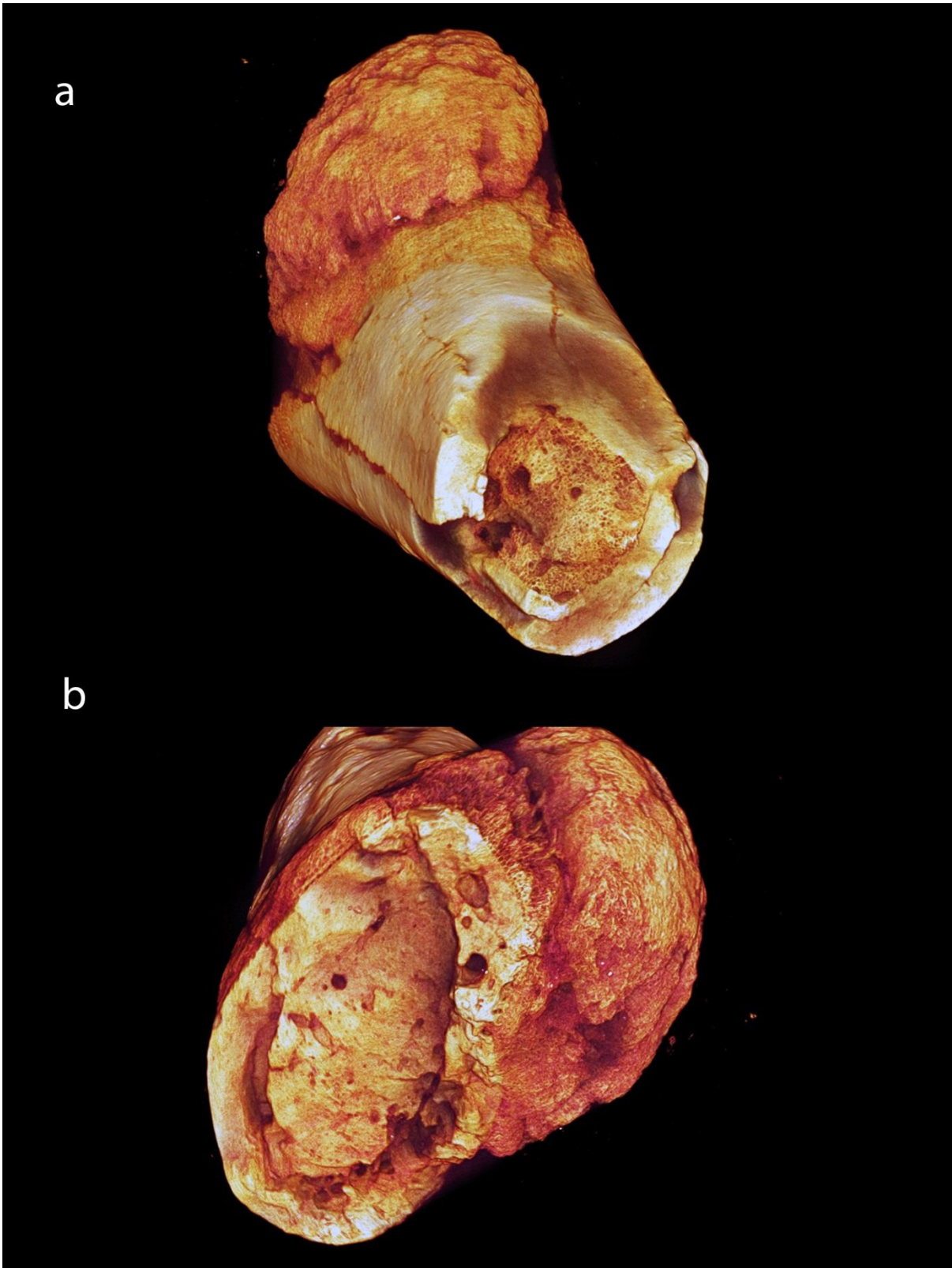


Figure 2: 5th metatarsal SK 7923: (a) and (b) surface rendered models (dorso-distal aspects), showing medullary spongy bone infill and clear focalised cortical destruction near the periosteal margin. Also evident on external cortical margin directly abutting malignant neoplasm is the characteristic hair on end bone reaction in (b). Images by E.J.O.

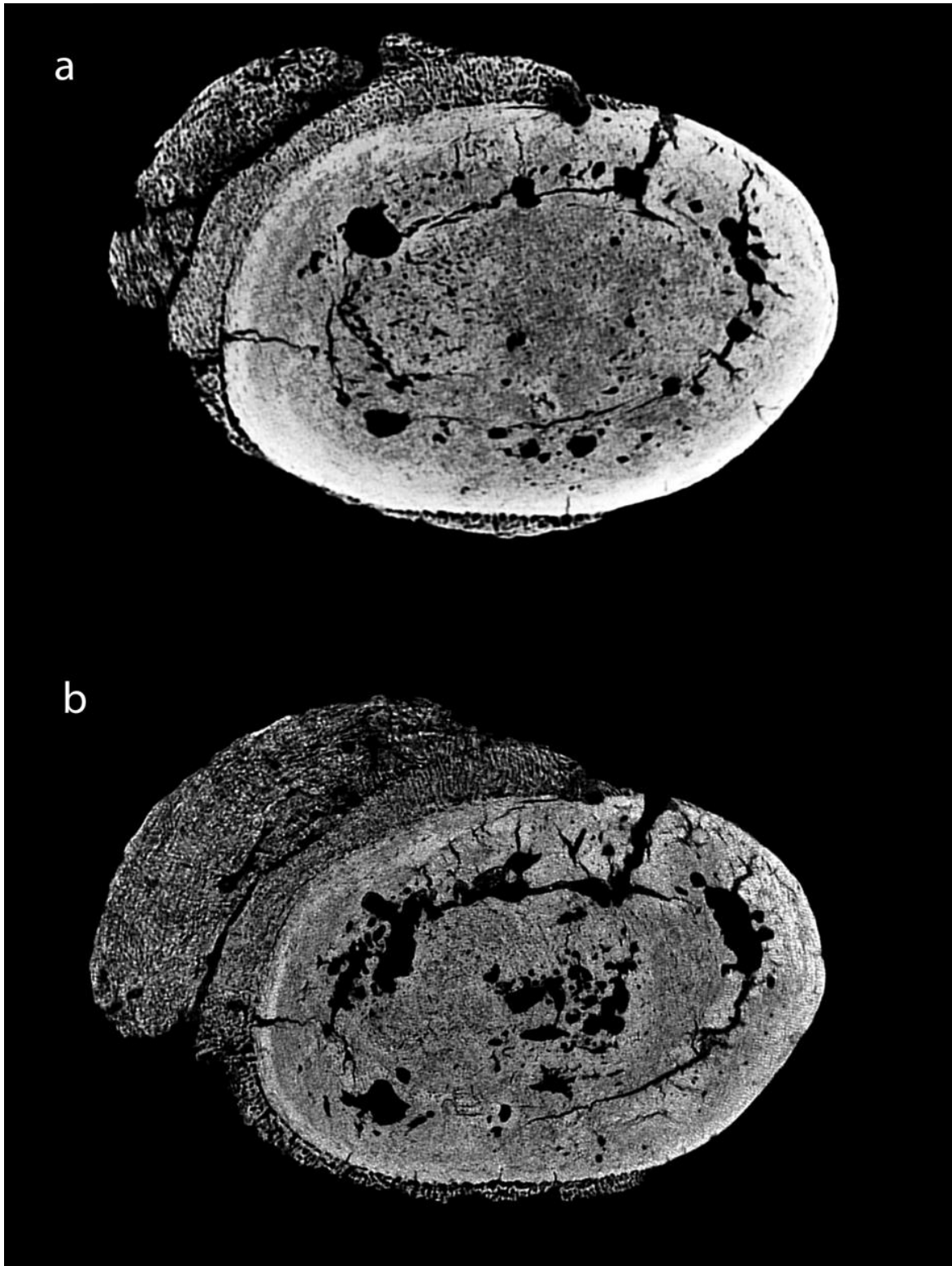


Figure 3: (a) and (b). Transverse micro-CT orthoslices through 5th metatarsal SK 7923. (a) The transverse orthoslice shows sclerotic cortical margin abutting the neoplasm. The sub-periosteal cortical invasion is clearly evident ventrally, with the medullary cavity mostly infilled with bone. In (b) the cortical bone abutting the neoplasm shows a sclerotic arc for the majority of the area under the neoplasm, and spicular hair on end reaction is evident proximally. Images produced by E.J.O. and P.S.R.Q.

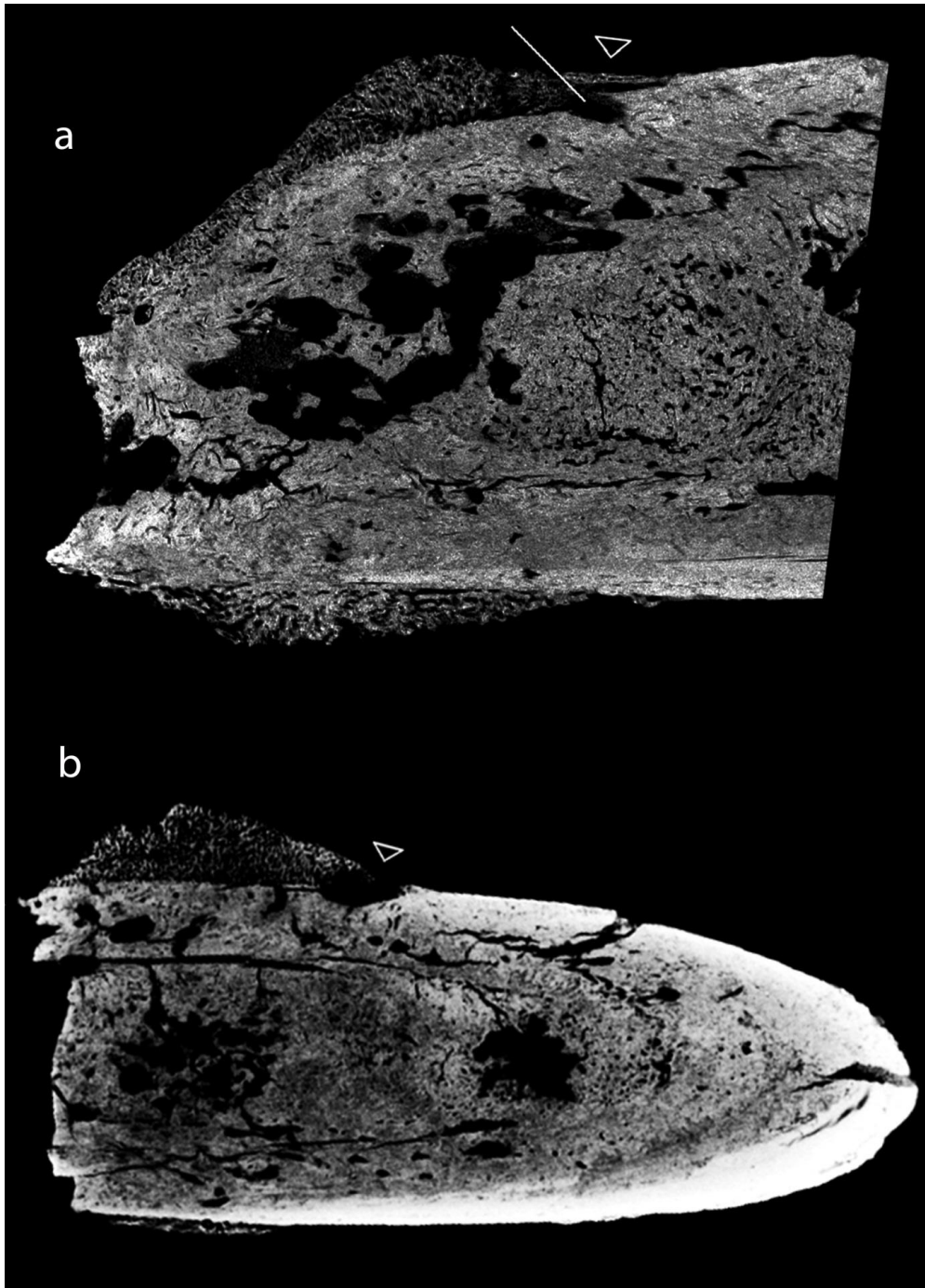


Figure 4: (a) and (b). Axial micro-CT orthoslices through SK 7923. Orthoslices taken at lateral aspect of the neoplasm. The posterior and ventral aspect shows sclerosis, especially in the cortical regions abutting the neoplasm. The central medullary cavity exhibits clear osteoblastic remodelled bone infill processes. In (b), the distal end of the lesion displays localised sub-periosteal invasion by the mass into the cortex. The cross-section shows that the ossified cauliflower-like mass is not completely fused or integrated with the cortex, but adheres to the cortical surface displaying an irregular spongy woven bone texture. The Codman triangle is clearly visible at the distal end of the cortical erosion, which appears sclerotic. The arrow in (a) denotes a Codman triangle; the oblique line denotes a clear example of invasion of cortical bone. The arrow in (b) illustrates invasion of the cortex. Images produced by E.J.O. and P.S.R.Q.

Table 1: Detailed differential diagnoses of Swartkrans hominin SK7923 metatarsal

Disease or condition	Pathological expression	Elements affected	Prevalence
Chondrosarcoma	<p>Chondrosarcomas are malignant cartilaginous neoplasms. This is a slow-growing tumour commonly found in tubular bone. Can occur de novo (primary) and may also develop on pre-existing benign cartilaginous neoplasms (secondary). May be located in the central region of a bone; can also be on the bone periphery; producing a 'saucer'-type defect in the cortical bone. Chondrosarcomas are large masses and can measure between 4 cm and 10 cm in size. They may exhibit a lytic pattern radiographically, or the production of a ring and arc feature, and may include intra-lesional calcifications. The tumour can exhibit regional bone destruction and an expanded cortical shell and trabeculation. A chondrosarcoma can be an extremely large tumour and lies on the surface of a flat or a long bone. Central osteochondromas pressure the cortex and lead to sclerotic margins or endosteal bone 'buttressing' in long bones. A spiculated or periosteal reactivity may be evident; soft tissue masses are sometimes also visible.</p>	<p>Frequently found in long bones (45%); femur (20%–35%); tibia (5%); upper limb (mostly proximal humerus) (10%–20%); pelvis (25%); ribs (8%); spine (7%) with thoracic most frequent: scapula (5%); sternum (2%); head and neck (including cervical spine) (7%); craniofacial (2%).</p> <p>Such tumours in hands and feet are rare and observed with caution. Location comprises 30%–50% of long bone shafts. A second form of chondrosarcoma affects the ribs, scapulae and pelvis.</p>	<p>This type of neoplasm represents 20%–27% of all primary malignant tumours. Presents typically in individuals in their forties and fifties. There is a male predominance of 1.5:1 to 2:1.</p>
Ewing's sarcoma	<p>Radiographical expressions typically exhibit poorly defined osteolytic lesions and a laminated periosteal reaction (57%). It consistently exhibits on a radiograph either as a neoplastic entity or as inflammation.</p> <p>Radiographic tumours are usually radiolucent, infiltrative, and exhibit a moth-eaten and/or permeative⁶ pattern of destruction. Lesion can be mottled, with a laminated periosteal reaction (57%). Occasionally presents with a spiculated hair-on-end response, Codman's triangles, or thick periosteal reaction. Its proliferative response often mimics osteomyelitis; also known to be sclerotic (40%).</p>	<p>Usually affects femoral bone and it is mostly found in central meta-diaphyseal or diaphyseal regions.</p> <p>Most common sites affected by this tumour are lower limb (45%), innominate (20%), upper limb (13%), ribs and axial skeleton (13%), and facial bones (2%).</p>	<p>A highly malignant primary tumour of childhood and young adulthood. ES accounts for 10%–15% of all primary bone tumours. Typically begins in the medullary cavity and invades the Haversian system. Incidence has been approximated at around 0.6 per million on a yearly basis. It usually occurs between 10–20 years of age. Approximately 13 per million are affected in the age bracket 0–24 years in the UK. Not commonly encountered in individuals over 25 years old. Male predilection (1.5:1).</p>

Disease or condition	Pathological expression	Elements affected	Prevalence
Osteochondroma	<p>The lesion comprises cortical and medullary bone, protruding from and continuous with underlying bone. Lesions can be sessile or pedunculated. Arcs and (rings) or flocculent calcification may be exhibited. In certain cases, some mineralisation of the cartilage cap and irregular subchondral bone can be evident. Aggressive structures may be seen, including bony destruction, large soft tissue and metastases, indicating possible malignancy.</p>	<p>Lower extremity long bones are most often affected (50%). Occur mostly above the knee (40%). Femur most affected bone (30%), distal regions being the most frequently involved; also tibia (15%–20%); small bones of the hand and foot (10%); scapula (4%); pelvis (5%); spine (2%). Long bone lesions mostly affect the metaphyseal regions, commonly projecting away from epiphysis. Diaphyseal involvement is rare.</p>	<p>Constitutes 10%–15% of all bone tumours, and 20%–50% of benign tumours.</p> <p>Symptomatic lesions occur mostly in young patients; 75%–80% present before 20 years old. Male predilection (approximately 1.6:1 to 3.4:1).</p>
Metastatic carcinoma	<p>Metastatic malignancy often simulates benign disease or primary malignancies. Generally, metastases lead to skeletal loss and bone formation. Loss can arise through either osteoclastic activity or enzymatic damage. Bone formation can arise within the neoplastic substrate or the adjacent bone reaction to the neoplasm, equivalent to callus development.</p> <p>Metastases can follow three different processes. They can be either lytic, sclerotic or a combination of sclerotic and lytic. Morphologically, metastases can be diffuse, focal or expansive. Bone metastases can be difficult to identify radiographically, because at least 30% to 50% bone loss is needed before density loss is observable⁹. Other examples are visible by cortical damage and evidence of sclerotic repair. Metastatic neoplasms generally exhibit little or no periosteal reaction.</p>	<p>Metastases usually found in pelvis, vertebrae, proximal femur, proximal humerus and cranium. Uncommonly found on knee and elbow.</p>	<p>Bone metastases make up 70% of malignant bone, with breast malignancy, renal cell carcinoma, lung and prostate malignancy accounting for about 80% of all bone metastases.</p>

Disease or condition	Pathological expression	Elements affected	Prevalence
Osteoblastoma	Osteoblastoma lesions are benign, mostly lytic, focally obliterative, and may be expansive. They appear as radiolucent defects and may present with internal ossification. They may have a sclerotic border or periostitis (50%). Cortical expansion and some destruction is common; a soft tissue mass may be present. Microscopic findings include irregular spicules of mineralised bone, eosinophilic osteoid, and woven bone rimmed by osteoblasts. The neoplasm forms osteoid and bone. Vascularity is high. Lesions are typically larger than 2cm.	Commonly found in the metaphysis and distal diaphysis of long bones; spine (up to 46%), and commonly involves the posterior cervical spine (up to 40%) or the sacrum (17%).	Osteoblastoma is a rare primary bone neoplasm; it represents approximately 1%–3% of all primary bone tumours ^{16, 17} . It affects mainly adolescents and young adults in the 2nd and 3rd decades of life, but does have a wide age range (6 to 75 years). It represents 1% of primary bone tumours. Predilection of male to female is 2.5:1.
Osteosarcoma	This type of primary malignant tumour typically shows a moth-eaten or permeated bone destruction pattern. It can exhibit cortical and medullary obliteration and some degree of tumour matrix mineralisation. It also exhibits wide zones of transition; presence of aggressive periosteal new bone reaction (which can include either a lamellated reaction, Codman’s triangle and/or spiculated sunburst-type reaction). Sometimes soft tissue masses are present. Most common form is central osteogenetic sarcoma, which could either be an osteoblastic or osteolytic lesion or a mix of both. Osteosarcoma has several categories depending on the focus within the bone, and histology and variation: intramedullary (80%); surface or juxta-cortical (10%–15%); and extra-skeletal (5%).	Typically occurs in the metadiaphyseal area of long bones, commonly the distal femur (40%); proximal tibia (16%); humerus (15%). Occurs less frequently in the mandible, maxilla, clavicle and ribs, os coxae, and vertebrae.	Accounts for approximately 20% of all primary bone neoplasms. ²⁰ They can be primary or secondary. Primary osteosarcoma typically occurs in the 10–20-year age group, with occurrence <20 years being 75%. Secondary osteosarcoma is prevalent in elderly individuals. Minor male predilection.
Low-grade osteogenic sarcomas	This group of low-grade tumours was first described by Dahlin and Unni (1977). It includes low-grade intramedullary and surface forms of osteogenic sarcoma (juxta-cortical osteosarcomas). Their incidence is not more than 5% of all osteogenic sarcomas. Diagnosis is difficult because of rarity and the complexity of the fibrous surface lesions. Represents less than 2% of all osteosarcomas. Usually exhibits large medullary sclerotic tumours at the end of long bones. Mixed sclerotic and lytic lesions can be detected. Periosteal new bone formation is rare, as is soft tissue extension. Macroscopically it appears as a slowly growing lesion; clearly distinct mass with erosion of the endosteum. In older lesions, cortical invasion can be seen.	Primary tumours exhibit in the metaphyseal areas of long bones, preferring the knee; secondary neoplasms have a preference for flat bones.	
Low grade intramedullary (central) osteogenic Sarcoma			

Source: Data derived from listed references.¹⁻²⁰

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