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Review Article

An Overview of X-Ray Findings of Bone Tumors

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Abstract

Based on certain radiographic features, benign and malignant bone tumors have a wide variety of appearances. Because a significant number of bone lesions are uncommon or rare, only a limited number of radiologists develop sufficient expertise to diagnose bone lesions and tumors accurately. In clinical practice, non-trained radiologists put a lot of effort into learning the characteristic imaging findings of various bone lesions and recalling; both of which are subjected to bias. Therefore, among general radiologists, the interpretation of most bone lesions can be variable, resulting in misdiagnosis and eventually suboptimal patient care and management. With the recent advances in imaging modalities of bone lesions, the role of computed tomography (CT) and magnetic resonance imaging (MRI) has been of great importance and value in reaching the correct diagnosis of bone tumors. Therefore, they are being considered now the core of residency training. Consequently, teaching about conventional radiographs, as well as, its usage in practice has been significantly limited, even though conventional radiographs remain the key to the diagnosis of bone tumors. This paper reviews the typical radiographic features of a wide variety of bone tumors in order to help radiologists minimize the list of differentials and reach an almost accurate single diagnosis.

Keywords: *X-Ray; Bone Tumors, Malignancy; Review*

Introduction

The radiographic approach in the diagnosis of bone tumors includes the analysis of a certain lesion in an organized manner, paying attention to specific radiographic findings, including the location, size, and number of lesions as well as the lesion margins, transition zones,

periosteal reaction patterns, mineralization, tumor matrix, cortical involvement, and whether or not soft tissue components are present [1,2].

Patients' age and determining whether the lesion is solitary or multiple are fundamental clinical information for the diagnosis of a wide range of bone lesions, as many tumors have a predilection for specific age groups [1]. However, this semiological diagnostic approach has neither the accuracy nor the capacity to arrive at a final accurate histological diagnosis. Meanwhile, this approach remains helpful in narrowing down the long list of differential diagnoses while indicating the most appropriate step taken from that point forward [1,3].

In this context, it is highly likely to reduce the number of differential diagnoses significantly through the application of this approach in concordance with the characteristic findings of conventional radiotherapy without the need for more advanced imaging modalities, such as computed tomography (CT) or magnetic resonance imaging (MRI). Typical examples include simple bone cysts and non-ossifying fibromas, which occasionally eliminate the need for further evaluation approaches other than conventional radiography [3].

This article reviews basic bone tumor semiology and highlighting their presenting findings on conventional radiographs. It will help radiologists better comprehend and recognize the semiology and characteristic presenting patterns of bone tumors on radiographs. Particularly, the following features of bone tumors will be discussed thoroughly: patients' age, tumor location, size and number, patterns of bone destruction, margins, tumor matrix, periosteal reaction (PR) and cortical involvement.

Methods

We performed an extensive literature search of the Medline, Cochrane, and EMBASE databases on 12 December 2019 using the medical subject headings (MeSH) terms. Papers discussing x-ray findings of bone tumors were screened for relevant information. There were no limits on date, language, age of participants or publication type.

Diagnostic approach of bone tumors based on sociodemographic and radiographic features

Tumor location and age are two of the most essential aspects in evaluating patients with bone tumors. Based on the availability of data regarding these two factors solely, the differential diagnosis of bone tumors could be narrowed down without even looking at any radiographic images. Furthermore, the knowledge of the specific radiographic findings of each tumor will subsequently help narrow the list even further with a high possibility of reaching a single correct diagnosis. These radiographic features are listed as follows: tumor location, size and number, margins and zone of transition, tumor matrix, periosteal reaction, and cortical involvement [2]. While these findings were originally reported with reference to the tumor lesions on conventional radiographs, they can also be applied to computed tomographic (CT) modality, however, this is not feasible in case of magnetic resonance imaging (MRI) [2].

Patient age

The majority of bone tumors have a predilection towards a certain age group [2]. For example, Ewing's sarcoma is common during the 1st two decades of life, whereas, multiple myeloma and metastases tend to present in patients older than 40 years of age [2,4]. Therefore, age is considered a cornerstone clinical variable during the assessment of bone tumors. Even though exceptions do exist, typical peak ages of various bone lesions should be given great attention in narrowing down the differential list (Table 1). The general distribution of aggressive and non-aggressive bone tumors according to age is presented in table 1 [2,5,6].

Tumor location

A wide range of bone tumors, regardless of being benign or malignant, frequently occur in a characteristic location in the skeleton (axial vs appendicular skeleton/ long vs flat bones); the highest incidence has been noted to occur in long bones of the limbs [6]. Within the long bones, the majority of tumors have a predilection for either the diaphysis, metaphysis, or epiphysis (Table 2), which are also correlated with certain age groups (Table 3) [2]. Meanwhile, there are certain tumors that tend to present at specific sites, giving more insight into accurate diagnosis (Table 4) [2].

Age (years)	Aggressive	Non-aggressive
0 - 10	Eosinophilic granuloma, Ewing's sarcoma, Hematologic malignancies, Neuroblastoma	Aneurysmal bone cyst (ABC), Eosinophilic granuloma, Simple bone cyst
10 - 20	Adamantinoma, Ewing's sarcoma, giant cell tumor (GCT), osteosarcoma	Adamantinoma, Aneurysmal bone cyst (ABC), Chondroblastoma, Chondromyxoid fibroma, Fibrous dysplasia, Nonossifying fibroma, Osteochondroma, Simple bone cyst
20 - 40	Chondrosarcoma, Periosteal osteosarcoma, Pleomorphic sarcoma	Enchondroma, Giant cell tumor (GCT)
> 40	Chondrosarcoma, Chondroma, Lymphoma, Metastases, Multiple myeloma (MM), Osteosarcoma (Paget's associated), Plasmacytoma, Pleomorphic sarcoma	Subchondral cyst, Intraosseous ganglion

Table 1: *The predilection of bone tumors based on patients' age [5].*

Age (years)	Diaphysis	Metaphysis	Epiphysis
< 20	Adamantinoma, eosinophilic granuloma, Ewing's sarcoma, fibrous dysplasia, lymphoma, osteoid osteoma	Aneurysmal bone cyst, chondromyxoid fibroma, enchondroma, nonossifying fibroma, osteochondroma, osteosarcoma, simple bone cyst	Chondroblastoma, infection
20 - 40	Adamantinoma, eosinophilic granuloma, Ewing's sarcoma, fibrous dysplasia, lymphoma, osteoid osteoma	Enchondroma, giant cell tumor, nonossifying fibroma, osteochondroma, osteosarcoma	Giant cell tumor, osteosarcoma
> 40	Fibrous dysplasia, metastases, myeloma	Lymphoma, metastases, myeloma, osteochondroma	Clear cell chondrosarcoma, Paget's disease, subchondral cyst

Table 2: *Differential diagnosis of bone tumors based on patients' age and tumor location [5].*

Location	Benign	Malignant
Epiphyseal		
	Chondroblastoma (skeletally immature patient)	Clear cell chondrosarcoma (exceedingly rare tumor)
	Giant cell tumor (skeletally mature patient)	
	Osteomyelitis (pyogenic: starts in the metaphysis and may spread to epiphysis if the person is 18 mo old; tuberculosis or fungus at end of the bone in skeletally mature person)	
	Paget disease	
	Intraosseous ganglion/geode (should have associated arthritis)	
	Osteochondral injury	

Metaphyseal		
Medullary	Simple (unicameral) bone cyst (centrally located)	Conventional osteosarcoma
	Aneurysmal (multicameral) bone cyst (eccentrically located; may be engrafted on other lesions such as giant cell tumor and chondroblastoma)	Chondrosarcoma
	Enchondroma (centrally located)	Metastatic disease
	Fibrous dysplasia	Myeloma (over age 40)
	Osteomyelitis (typical location for pyogenic infection in children 18 mo and adults)	Lymphoma
	Localized Langerhans cell histiocytosis	Malignant vascular tumors (very rare; angiosarcoma, hemangiopericytoma)
	Chondromyxoid fibroma (eccentrically located)	
Cortical	Fibrous cortical defect and nonossifying fibroma (lytic in children, fills in and involutes in adults)	Metastatic disease (especially lung)
	Osteoid osteoma (small lucent nidus with surrounding fusiform reactive sclerosis)	
Juxtacortical	Juxtacortical chondroma (arises from periosteum)	Periosteal osteosarcoma (arises from deep cambian layer of periosteum)
		Parosteal osteosarcoma (arises from a superficial layer of periosteum)
		Juxtacortical chondrosarcoma (arises from the periosteum)
Diaphyseal		
Medullary	Fibrous dysplasia	Ewing sarcoma (may also occur in the metaphysis and in flat bones: e.g. calvarium, pelvis, mandible, ribs; reflecting red marrow distribution)
	Localized Langerhans cell histiocytosis (may also occur in metaphysis and flat bones, e.g. calvarium, pelvis, mandible, ribs)	Lymphoma
		Myeloma (occurs in red marrow sites, e.g. axial skeleton and proximal aspects of humeri and femora)
		Metastatic disease (may be medullary or cortical)
		Malignant vascular tumors (very rare; angiosarcoma, hemangiopericytoma)
Cortical	Ossifying fibroma (ie, osteofibrous dysplasia or Campanacci lesion)	Adamantinoma (mixed lytic and sclerotic lesion occurring almost exclusively in anterior cortex of tibia; tibia may be bowed; look for satellite lesion in tibia or adjacent fibular involvement)
		Metastatic disease (especially lung)

Table 3: *Typical locations of bone lesions [2].*

Tumor	Site
Adamantinoma	Anterior cortex of tibia
Osteofibrous dysplasia	Anterior cortex of tibia
Epidermal inclusion cyst	Terminal tuft of phalanx
Glomus tumor	Terminal tuft of phalanx
Periosteal desmoid	Posterior cortex of distal femur
Parosteal osteosarcoma	Posterior cortex of distal femur
Chordoma	Clivus, vertebral bodies, sacrum
Hemangioma	Vertebral bodies
Simple bone cyst	Calcaneus
Intraosseous lipoma	Calcaneus (may have focal calcification)
Osteoblastoma	Posterior elements of spine
Aneurysmal bone cyst (ABC)	Posterior elements of spine

Table 4: *Specific sites of a limited number of selected tumors [2].*

Tumor size

The size of the bone tumor lacks the ability to accurately predict the actual diagnosis or bone lesion, even though it has been reported that lesions with a size of 6 cm or more are more likely to be malignant bone tumors [6]. Moreover, the diagnostic criteria based on tumor size could be of value in differentiating between osteoid osteoma and osteoblastoma: there are various thresholds reports, with 1.5 cm being the most commonly noted [6].

Margins and patterns of bone destruction

Till the current time, the Lodwick-Madewell classification remains very helpful in determining the biologic activity of a tumor by assessing the bone response on radiographs and, thus, can help differentiate benign from malignant lesions [7-10]. Due to the slow bone response, a slowly-growing lesion will give the bone enough time to create a solidified osseous tissue around the lesion site. On the other hand, a rapidly-growing lesion will result in a more disorganized response [10-12]. This classification refers to lytic lesions, which categorizes them into 5 subtypes: type IA, type IB, type IC, moth-eaten (type II), and permeative (type III) (Figure 1).

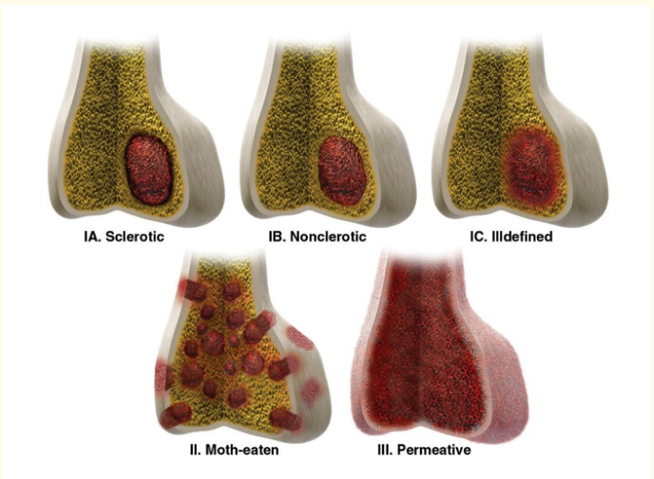

Figure 1: *Drawings showing margin classification system of primary bone tumors. Type I margins are round or oval and typically correspond to less-aggressive (benign) or less-advanced malignancies than moth-eaten (type II) or permeative (type III) fields of osteolysis. Margin classification system provides general guidelines for determining aggressive from nonaggressive lesions. Information such as patient age, bone affected, and location of the tumor in bone is also critical for assessing the identity of primary bone tumors.*

Type IA lesions, geographic well-defined lesions with sclerotic margins, are typical for slowly- or non-growing lesions, such as non-ossifying fibroma, simple bone cyst, fibrous dysplasia, intraosseous ganglion, and lipoma (Figure 2) [4,6,13]. Meanwhile, the observation of the inner and outer margins of the sclerotic rim provides a diagnostic value during the differentials. Clear-cut inner and ill-defined outer margins are usually indicative of osteomyelitis, avascular necrosis, and eosinophilic granuloma. On the other hand, clear-cut inner and outer margins are commonly observed in osteomyelitis, slowly-growing malignant tumors, benign tumors, and tumor-like lesions [2,4]. Moreover, mottled sclerosis can be noted in both malignant and benign tumors [4].

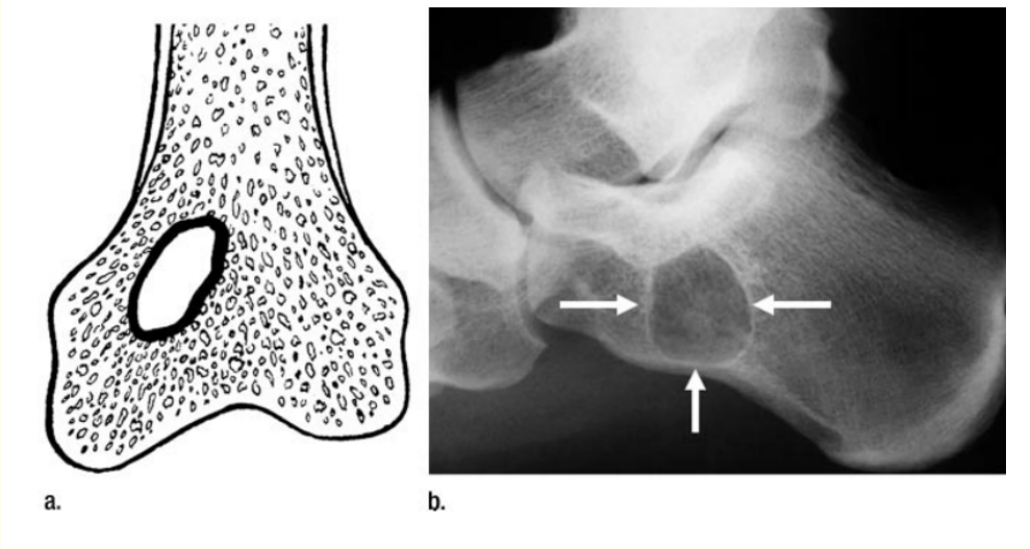

Figure 2: *Type 1A geographic lesion. (a) Diagram shows well-defined lucency with a sclerotic rim (Adapted from Madwell., et al.) [10]. (b) Lateral radiograph shows intraosseous lipoma of the calcaneus, with a sclerotic rim (arrows).*

Type IB lesions, geographic well-defined lesions without sclerotic margin, are better detected in areas with cancellous bone. These lesions are commonly cartilaginous or fibrous. In certain circumstances, endosteal scalloping may be the only presenting sign of an existing type IB lesion in the diaphysis of long bones. Common benign examples include enchondroma, giant cell tumor (GCT), eosinophilic granuloma, and fibrous dysplasia, even though multiple myeloma and certain low-grade sarcomas are present in this category [6].

Type IC lesions, geographic lesions with distinct margins, are suggestive of infiltration and increased activity. Examples include enchondroma, GCT, sarcomas, and metastases [6].

Type II lesions have moth-eaten patterns and typically indicate more aggressiveness. They are defined by multiple ovoid lesions parallel to the long axis of the bone, with a diameter ranging from 2 to 5 mm. Usually, type II lesions infiltrate more rapidly with consequent indistinct endosteal scalloping. Common examples of this group of lesions include metastases, multiple myeloma, chondrosarcomas, osteosarcomas, and lymphomas [6,14].

Type III lesions, known permeative, are the most aggressive subtype. It is defined by the presence of multiple ill-defined oval lesions, with a wide zone of transition, cortical involvement, and a soft tissue mass. Frequently, it is seen in malignant conditions, including metastases, multiple myeloma, lymphoma, Ewing's sarcoma, osteosarcoma, and high-grade chondrosarcomas [4,6].

The shape of the margin is also of diagnostic value in shortlisting the differentials of bone tumors. For example, a lobulated contour may be noted in malignant conditions, including chondrosarcoma, chondroma, and adamantinoma. This can also be noted in benign tumors, including enchondroma, chondroblastoma, and chondromyxoid fibroma [13,15-17].

Opacity, mineralization and tumor matrix

On conventional radiographs, bone tumors may be classified into lytic, sclerotic, or mixed lesions with typical opacity. However, a minimum of 30% lysis is required to become evident on radiographs [18]. For example, GCT and simple bone cysts are lytic; bone islands are sclerotic; adamantinomas are commonly mixed.

Lucency and sclerosis linked with true neoplasms are commonly due to the stimulation of osteoclasts or osteoblasts, respectively. In certain circumstances, the destructive process may lead to sequestration of a fragment of the bone within the lytic region; such sequestrum may be noted in both benign and malignant lesions [8].

Meanwhile, the trabecular pattern present in the lesion is the clue to its diagnosis. For instance, aneurysmal bone cysts and desmoplastic fibromas might have a honeycomb appearance, while Paget's disease may have coarsened trabeculae. On the other hand, a hemangioma within the long bones may have a sunburst or spoke-and-wheel pattern of trabeculation, whereas, the same entity within a vertebral body will have a vertically-oriented, coarsened, corduroy trabecular pattern [2].

That being said, mineralization of the tumor matrix can also affect the radiographic opacity of a bone tumor. Tumor matrix commonly describes the type of tissue of the tumor, such as osteoid, chondral, fibrous, or adipose, all of which are radiolucent. Meanwhile, mineralization refers to the calcification of the tumor matrix. This concept is essential to understand, as the pattern of mineralization can also be a valuable clue to the type of the matrix and, thus, the final diagnosis. However minimal or faint mineralization is best assessed through CT [19-21] while MRI is useful in defining medullary lesions and soft tissue extensions [12,20].

Periosteal reaction

The appearance of periosteal reaction is an important radiographic finding, which helps characterize bone tumors. Solid or unilamellated periosteal reaction is referred to as a non-aggressive appearance, indicating that the underlying tumor is slowly-growing and is giving the bone an opportunity to wall the lesion off (Figure 3). On the other hand, a multilamellar or 'onionskin' appearance is suggestive of an intermediate aggressive process, such as one that waxes and wanes or one that the bone is continuously trying to wall off but cannot (Figure 4) [22,23].

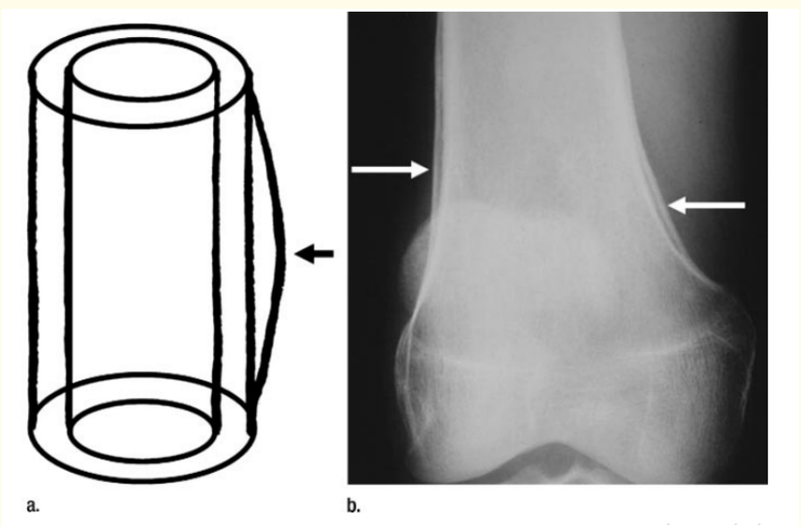

Figure 3: *Unilamellated periosteal reaction. (a) Diagram shows a single layer of reactive periosteum (arrow). (Adapted from Ragsdale., et al.) [23]. (b) Anteroposterior radiograph of the knee in a patient with hypertrophic osteoarthropathy shows thick unilamellated periosteal reaction (arrows).*

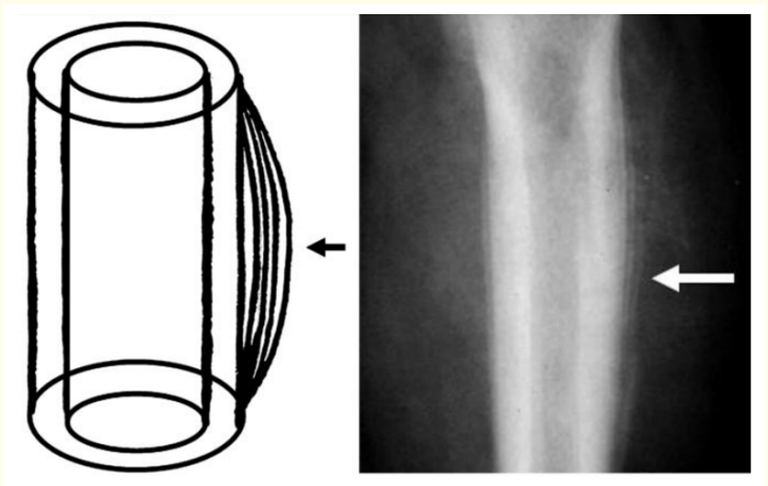

Figure 4: *Multilamellated periosteal reaction. (a) Diagram shows multilamellar, or 'onionskin', periosteal reaction (arrow). (Adapted from Ragsdale., et al.) [23]. (b) Anteroposterior radiograph in a patient with osteosarcoma shows multilamellar periosteal reaction (arrow) in the proximal portion of the femur.*

Meanwhile, interruption, or regional disruption, of either uni- or multi-lamellated periosteal reaction is suggestive of an aggressive process that has infiltrated through the periosteum. A speculated, or 'hair-on-end' appearance or sunburst pattern, is the most aggressive appearance, which is significantly suggestive of malignancy (Figure 5) [2]. The presence of Codman triangle, the elevation of the periosteum away from the cortex, with an angle formed elevated periosteum and bone meet together (Figure 6). Even though the Codman triangle is commonly associated with conventional osteosarcoma, any aggressive activity that elevates the periosteum might result in this characteristic appearance, certain benign entities, such as infection and subperiosteal hematoma can also have this appearance [2]. That being said, in certain circumstances, the periosteal reaction may be the result of pathologic fracture through the bone tumor and not related to the tumor itself, as in the case of simple bone cysts [2].

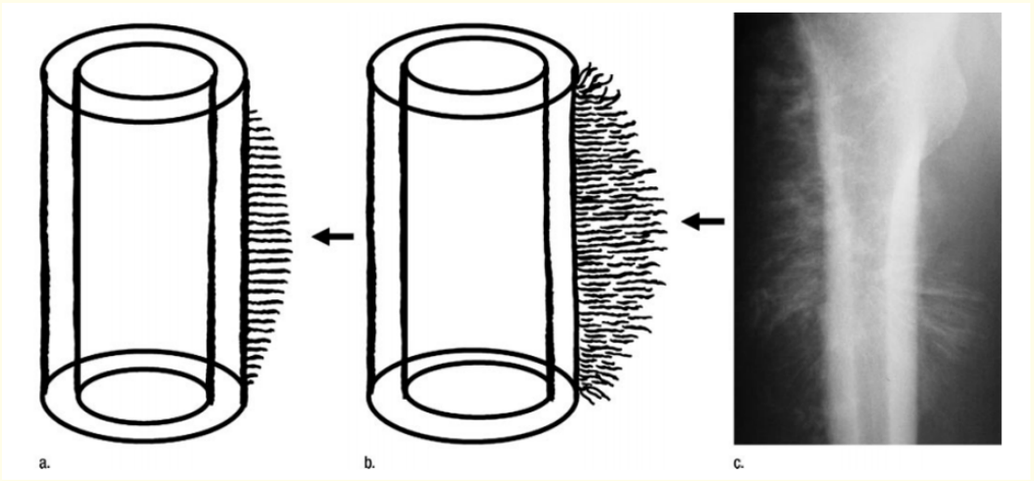

Figure 5: *Perpendicular periosteal reaction. (a) Diagram shows spiculated, or 'hair-on-end', periosteal reaction (arrow). (b) Diagram shows radial, or sunburst, periosteal reaction (arrow). (Adapted from Ragsdale., et al.) [23]. (c) Anteroposterior radiograph in a patient with osteosarcoma shows marked perpendicular periosteal reaction in the proximal portion of the femur. (Image courtesy of Marcia Blacksin, MD, University of Medicine and Dentistry of New Jersey, Newark, NJ).*

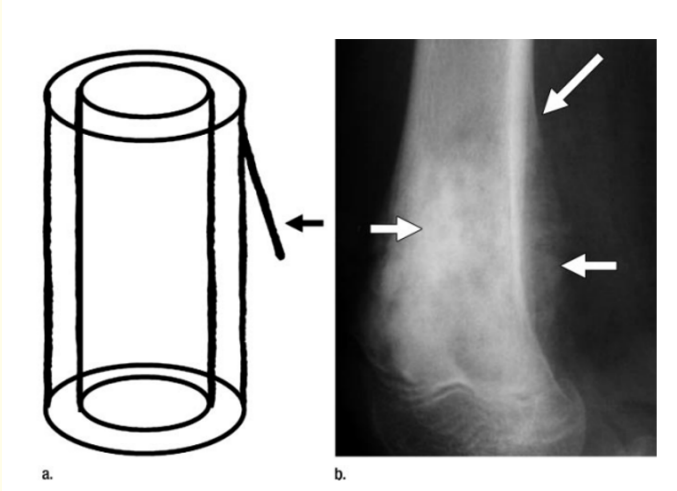

Figure 6: *Codman triangle. (a) Diagram shows elevated periosteum (arrow) forming an angle with the cortex. (Adapted from Ragsdale., et al.) [23]. (b) Lateral radiograph in a patient with osteosarcoma shows the elevated periosteum forming Codman triangle (long arrow). Notice the tumor-induced new bone formation (short arrows).*

Cortical involvement

The cortex is made of osseous tissue around a Haversian canal, which is surrounded by an inner and an outer fibrovascular layer, namely the endosteum and the periosteum. In this regard, certain aspects should be taken into consideration when discussing cortical involvement, such as scalloping, thickening, and destruction.

Scalloping refers to the erosion of the bone as a result of a lesion [24]. In most cases, it is endosteal scalloping, referring to a medullary tumor. It can be noted in both benign and malignant bone tumors, such as chondrosarcoma, enchondroma, and fibrous dysplasia [2,13,24-26]. That being said, outer scalloping has been reported to occur as a result of periosteal osteosarcoma or juxtacortical chondrosarcoma [17]. Meanwhile, the degree of endosteal scalloping can reflect if a lesion is more likely to be benign or malignant [27]. When the radiologist is uncertain between an enchondroma and low-grade chondrosarcoma, an erosion of more than two-thirds of the cortical thickness is more likely to be the result of the latter [16,28].

Cortical thickening can be noted in several types of osteosarcoma, Ewing's sarcoma, osteochondroma, central chondrosarcoma, and osteoid osteoma [17,29,30]. It usually distinguishes between chondrosarcoma and enchondroma: a sign of malignancy in long bones [31]. On the other hand, cortical thinning can also be noted in certain cases, as in clear cell chondrosarcoma or hemangioendothelioma [17].

Cortical destruction is suggestive of malignancy in both short and long bones [31]. According to Lodwick's classification, a partial or no cortical penetration would fall into subtypes IA or IB, whereas complete penetration would fall into the category IC or higher [8,9]. This can be noted in various types of lesions, with non-ossifying fibroma, fibrous dysplasia, ABC, Ewing's sarcoma, GCT, and osteoblastoma being the most notable ones [17,25,28,29,32-34]. In terms of differentiation between enchondroma, chondrosarcoma, or atypical cartilaginous tumor, cortical destruction is more likely to occur in the second category [25,27,28]. It should be noted that when cortical destruction is associated with a soft tissue mass, then the diagnosis of sarcoma is most likely until proven otherwise [17].

Benign bone tumors mimicking malignant radiographic features

Even though cortical disruption and periosteal reaction are characteristic radiographic findings in malignant bone tumors, there are certain conditions when these findings can be noted in non-malignant tumors. Therefore, it's of great importance to notice and immediately recognize the certain imaging patterns that are present in benign tumors but are indicative of malignant etiology, as to provide a certain diagnosis and adequately orientate the approach [35]. A summary of the main imaging findings that can be noted in benign lesions mimicking malignant ones is presented in table 5.

Conclusion

Besides the availability of advanced imaging modalities like CT and MRI along with their ever-increasing number of detectors and strength of the magnetic field, the diagnostic approach towards a bone tumor or a tumor-like lesion remains dependent upon conventional radiographs. By paying attention to the age of the patient and recognizing the characteristic locations and radiographic features of bone lesions, the interpreter will be able to reach a shortlist of differential, if not a single correct, diagnosis.

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Conflicts of Interest

No conflicts related to this work.

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