

# Bone Tumors of the Jaw – the “Blind Spot” for Radiologists Experienced with Tumors? – Part II

## Kiefertumoren – der „blinde Fleck“ des tumorversierten Radiologen? – Teil II

### Authors

Thomas Grieser<sup>1</sup>, Edgar Hirsch<sup>2</sup>, Ninette Tödtmann<sup>3</sup>

### Affiliations

- 1 Department of Diagnostic and Interventional Radiology and Neuroradiology, University Hospital Augsburg, Augsburg, Germany
- 2 Dentomaxillofacial Radiology, Leipzig University, Leipzig, Germany
- 3 Department of Oral and Maxillofacial Surgery, University Hospital Augsburg, Augsburg, Germany

### Keywords

jaws, odontogenic and non-odontogenic tumours, odontogenic and non-odontogenic dysplasias

received 14.5.2024

accepted 20.8.2024

published online 2024

### Bibliography

Fortschr Röntgenstr

DOI 10.1055/a-2416-1282

ISSN 1438-9029

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Georg Thieme Verlag KG, Rüdigerstraße 14, 70469 Stuttgart, Germany

### Correspondence

Dr. Thomas Grieser

Department of Diagnostic and Interventional Radiology and Neuroradiology, University Hospital Augsburg, Augsburg, Germany

thomas.grieser@gmx.com

 Deutsche Version unter: <https://doi.org/10.1055/a-2416-1282>.

### ABSTRACT

**Background** Primary bone tumours of the jaw are rare tumoral entities and do substantially differ from other bone tumours of the human body with respect of their frequently encountered unusual radiological appearances. The reason for that may be confined to the co-existence of two closely neighbored but different anatomical structures (i. e., tooth-forming apparatus and jaw bones with adjacent gingiva) and some tumour pathologies which are nearly exclusively encountered in

the jaw bones only (e. g., ameloblastoma, ossifying fibroma, ghost cell carcinoma).

This paper would like to highlight some basic principles of the diagnostic approach and possibilities of radiological differentiation of such tumour-suspicious changes within the gnathic system are elucidated and discussed.

**Method** The paper presented here is substantially based on the most recent classification of odontogenic and maxillofacial tumours (5<sup>th</sup> edition, 2022) which serves as a scaffold for the selection of typical tumour entities. Due to the educational character of this paper, only important jaw tumours worth mentioning and their characteristics are subject to be extracted from the literature and further discussed.

The main focus was put onto both the description of radiological tumoral appearance and the rational selection of a radiological diagnostic work-up. In order to better visualize this difficult field of tumour entities, much attention has been paid on a comprehensive pictorial essay.

**Conclusions** For radiologists, it is their foremost task to detect, describe, and to classify bone tumours of the jaw when they are found intentionally or accidentally, resp. A close cooperation with their clinical partners is of utmost importance to gain information about patient's history and clinical presentation. It is readily reasonable that radiologists are mostly able to provide only a suggestion of the presented tumour entity but this expert opinion would be very helpful to further narrow down the list of potential differential diagnoses (e. g., differentiation of a cyst vs. solid tumour osteolysis, identification of jaw osteomyelitis vs. tumoral infiltration, recognizing of secondary tumour involvement of the jaw).

### Key Points

- primary bone tumours of the jaw are very rare, moreover difficult to differentiate radiologically, and do need therefore histological proof;
- profound knowledge about tumour characteristics (location within the jaw, relationship to the tooth, bony destructive pattern) may allow a rough orientation and classification;
- matrix-forming tumours and dysplasias of the jaw facilitates their radiological differentiation and classification;
- in contrary, osteolyses should be thoroughly scrutinized for the more frequent gnathic cysts in differentiation of rather rare solid primary tumours;

- an interdisciplinary round-table discussion amongst well-experienced maxillofacial surgeons and specialized radiologists may be appropriate to avoid severe misinterpretations.

#### Citation Format

- Grieser T, Hirsch E, Tödtmann N. Bone Tumors of the Jaw – the “Blind Spot” for Radiologists Experienced with Tumors? – Part II. *Fortschr Röntgenstr* 2024; DOI 10.1055/a-2416-1282

## ZUSAMMENFASSUNG

**Hintergrund** Primäre Kiefertumoren stellen einerseits seltene Tumorentitäten dar und weichen andererseits hinsichtlich ihres differenteren und oft ungewohnten radiologischen Erscheinungsbildes von den vom übrigen Skelett bekannten, typischen radiologischen Knochentumormerkmalen ab. Ursachen sind zum einen die eng benachbarte Koexistenz zweier ontogenetisch differenter anatomischer Strukturen (zahnbildender Apparat und Kieferknochen nebst Gingiva), zum anderen einiger, nahezu exklusiv am Kiefer anzutreffender Tumorentitäten (z. B. Ameloblastom, ossifizierendes Fibrom, Schattenzellkarzinom).

Die vorliegende Arbeit möchte daher auf einige Grundprinzipien der diagnostischen Herangehensweise und radiologischen Differenzierung tumorverdächtiger und dysplastischer Veränderungen am gnathischen System eingehen und erläutern.

**Methode** Die vorliegende Arbeit stützt sich maßgeblich auf die aktuelle WHO-Klassifikation odontogener und maxillofazialer Tumoren (5. Auflage, 2022), entlang welcher ausgesuchte und typische Tumorentitäten besprochen werden. Aufgrund des edukativen Charakters der Arbeit werden dabei

lediglich wichtige und erwähnenswerte Tumoren und deren Charakteristika aus der Literatur extrahiert und diskutiert. Der Fokus liegt hier auf der Beschreibung radiologischer Tumormerkmale bzw. der sinnvollen Auswahl des radiologischen Instrumentariums. Der besseren Veranschaulichung wegen wird auf umfangreiches Bildmaterial Wert gelegt.

**Schlussfolgerungen** Dem Radiologen fällt die Aufgabe zu, Kiefertumoren zu detektieren, zu beschreiben und einzuordnen. Die notwendige Kenntnis von Anamnese und klinischer Symptomatik setzt eine enge Zusammenarbeit mit den klinischen Partnern voraus. In vielen Fällen wird man sich der Diagnose nur annähern können, was aber für die Eingrenzung möglicher, in Frage kommender Entitäten schon hilfreich sein kann (z. B. Differenzierung Zyste vs. solide Tumorosteolyse, Abgrenzung Kieferosteomyelitis gegen Tumordinfiltration, Erkennen einer sekundären Tumorbeteiligung des Kiefers).

#### Kernaussagen

- Primäre Kiefertumoren sind sehr selten, bildgebend schwer zu differenzieren und verlangen daher eine histologische Abklärung;
- Kenntnis typischer Kiefertumormerkmale (Lage, Zahnbezug, Destruktionsmuster) erlaubt eine grobe Eingruppierung;
- matrixbildende Kiefertumoren und Dysplasien erleichtern die radiologische Diagnostik und Einordnung;
- Osteolysen hingegen sollten sorgfältig hinsichtlich häufiger Zysten und selteneren soliden Tumoren differenziert werden;
- die interdisziplinäre Fallbesprechung unter erfahrenen Kieferchirurgen und Radiologen kann grobe Fehleinschätzungen vermeiden.

## Bone and cartilage tumors of the jaw

### Fibro-osseous tumors and dysplasias

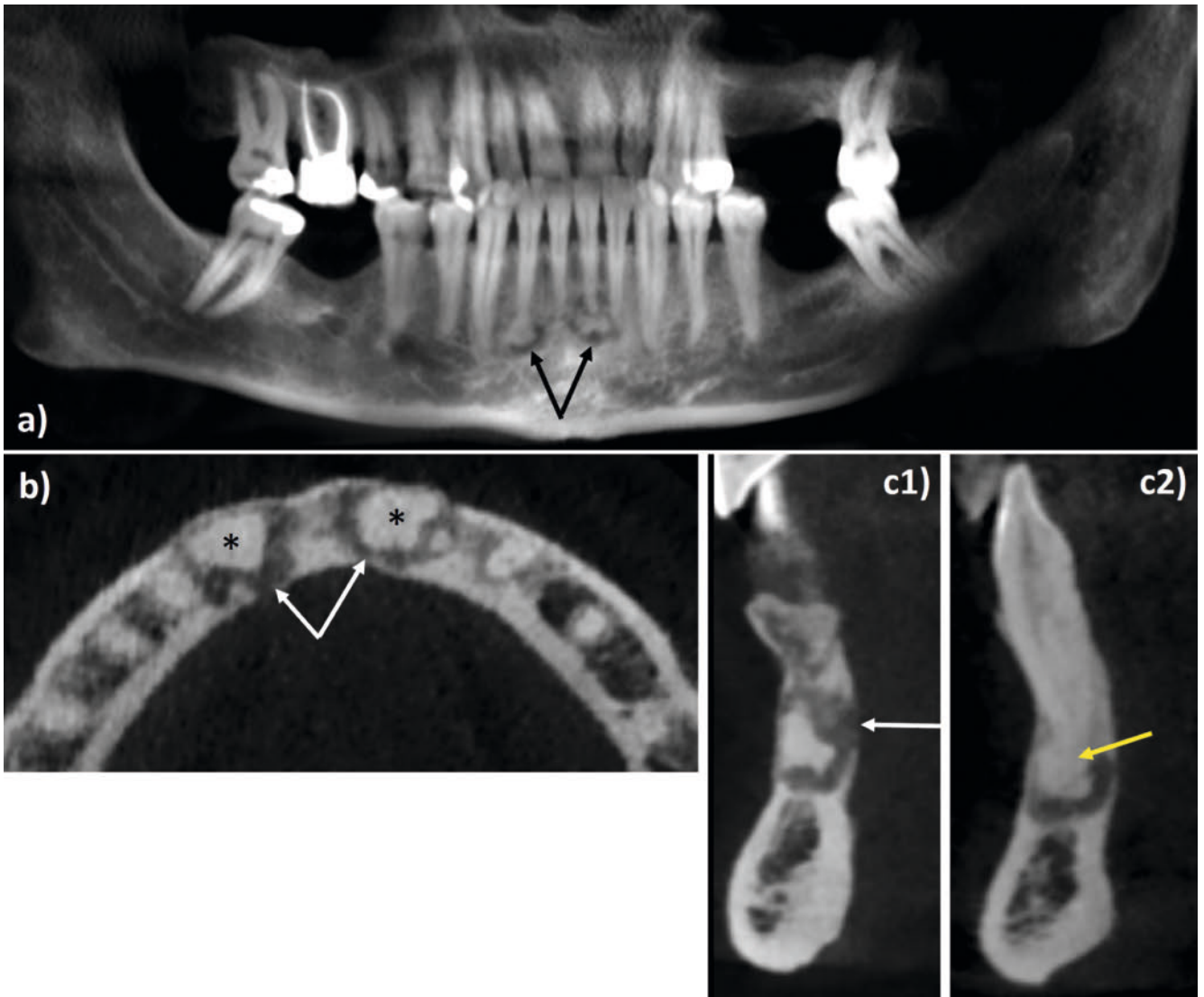
This group includes the most common benign fibro-osseous lesion, the cemento-ossifying (or cemento-osseous) dysplasia. This category has previously been divided into three subtypes: periapical, focal, and florid. A fourth subtype has now been added to the current 2022 classification: familial florid cemento-osseous dysplasia [1].

The cemento-ossifying dysplasia is a self-limiting disease and not a tumor. The radiopaque lesions, which are on average 0.5–1.5 cm in size, are primarily seen in the mandible, with over 90% occurring in women. The most common periapical location in the anterior region of the mandible (70%) has its origin in the periodontal ligament at the apical foramen of the tooth root, where cemental proliferation occurs (► **Fig. 1**). The focal forms of cemento-osseous dysplasia affect the posterior parts of the mandible, whereas the florid subtype affects several quadrants of the jaw [2]. Radiologically, the mature forms of cemento-ossifying dysplasia (stage III) are easily diagnosed by their radiopaque structure at the

root tip; however, the early stages I and II of cemento-osseous dysplasia are much more difficult to diagnose, as they appear lytic (stage I) or predominantly lytic with central cementoblastic opacity (stage II). Here, differential diagnostic difficulties arise in distinguishing between radicular cysts and sometimes also (cemento-)ossifying fibroma. The latter represents a true neoplasia, while cemento-ossifying dysplasia is considered a reactive lesion that may be expansive and thus space-occupying, but usually does not destroy the tooth root or the surrounding bone [3].

A compilation of typical hard tissue-forming jaw lesions is provided in **Table 6** and **Fig. 12** in Part 1 of this article.

Also discussed here is fibrous dysplasia (FD) which belongs to this group of the jaw. FD is a mesenchymal tumor of the bone (formerly called tumor-like lesion), which accounts for about 7% of all benign bone tumors [4]. Pathogenetically, FD is caused by a somatic mutation of the gene encoding stimulating G protein (activating GNAS1 gene mutation), which prevents lamellar maturation of the bone, but instead stops at the stage of woven bone with its typical vertebral structure [5]. The consequences of this bone immaturity are not only reduced bone strength (e.g. curvature of the long tubular bones), but also a more or less significant



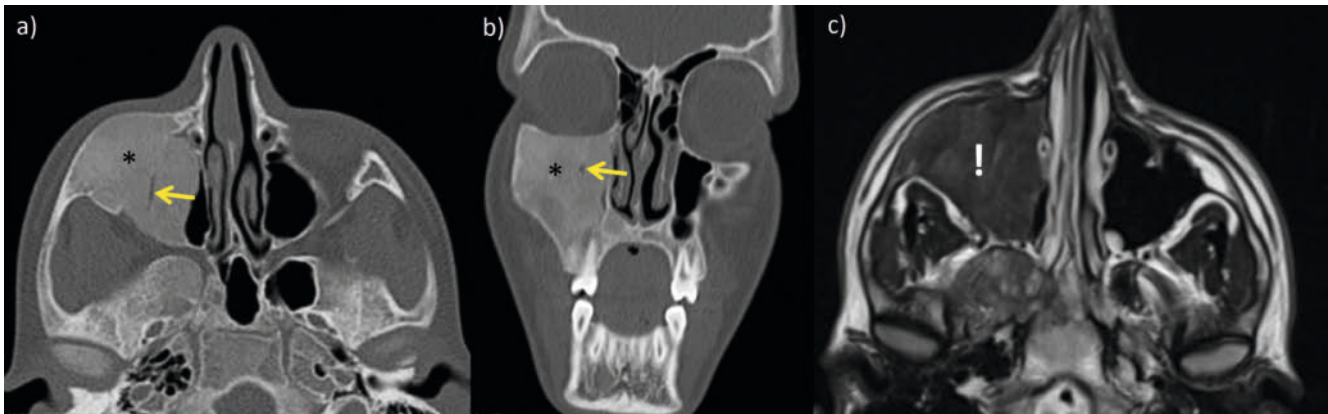
► **Fig. 1** Cemento-osseous dysplasia. 46-year-old patient, asymptomatic incidental finding, normal vitality of the mandibular anterior teeth: **a** DVT panoramic reconstruction with apical hard substance foci at 31 and 42 (arrows); **b** DVT, axial layer below root tips: the hard substance (\*) is surrounded by an irregular lysis margin (arrows); **c1**) DVT, sagittal reformation: perifocal lysis margin around the hard substance with degradation of the lingual cortex (white arrow); **c2**) topographical relationship of the hard substance to the root tip (yellow arrow).

increase in bone volume. This in turn has a direct impact on the facial skull, the third most common site of manifestation of FD after the femur and tibia (up to 27%), as it can lead to restrictions of the orbits and bony nerve canals, especially the optic canal [6]. In the craniofacial form, the maxilla is slightly more frequently affected than the mandible. Radiologically, the enlargement of the affected maxillary or mandibular bone section is noticeable, although the bone itself is not destroyed (► **Fig. 2**). The plain X-ray (OPG) usually shows blurred lesion margins; the lesion itself ideally has a ground glass-like matrix, but often it also appears lytic or mixed lytic-sclerotic. Due to the impaired bone maturation and the subsequent woven bone formation, native computed tomography (or DVT) detection of the so-called ground-glass matrix is highly specific for FD, in most cases even pathognomonic, which makes invasive sample collection for diagnostic purposes unnecessary. This is particularly important to note, as MRI is usually un-

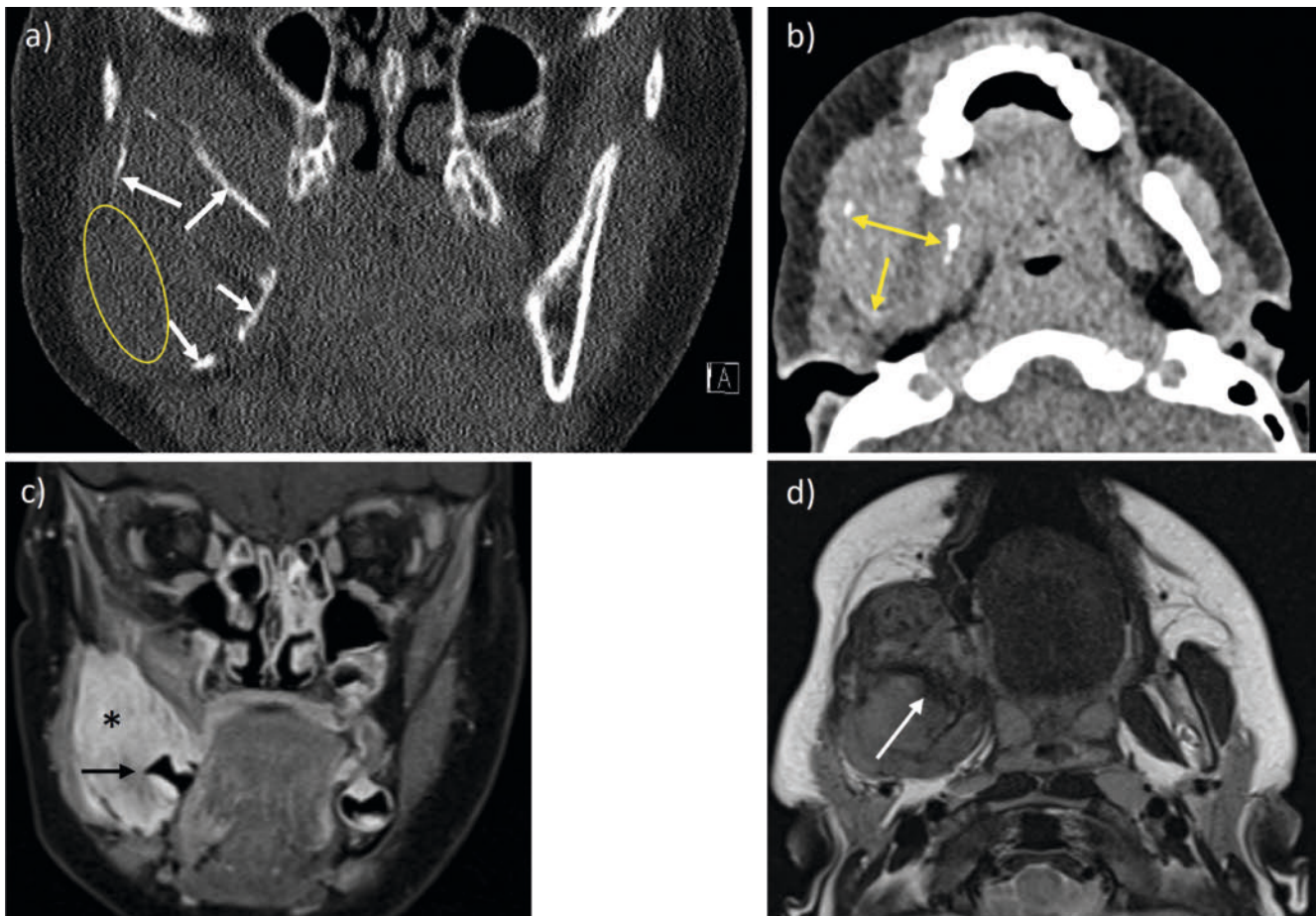
able to provide this specific evidence, or cannot provide it reliably, but should prompt a native CT scan, if there is a suspicion of this. However, diagnostic problems arise in those cases of FD where the ground-glass aspect is not prominent or is even missing. This is the case in purely lytic or severely sclerosed forms of FD. Here, there is a differential diagnostic proximity to (cemento-)ossifying fibroma, cemento-ossifying dysplasia and central giant cell granuloma, but also to sclerosing osteomyelitis and (low-grade) osteosarcoma [7].

### Benign, non-odontogenic maxillofacial bone and cartilage tumors

In addition to well-known tumors such as osteoblastoma, chondroblastoma, and chondromyxoid fibroma, this group also in-



► **Fig. 2** Fibrous dysplasia. **a+b** unenhanced CT axial and coronal: dense ground glass (\*), which occupies the right maxillary sinus, including the infraorbital nerve (yellow arrows); **c** MRI: T2 TSE: the striking signal hypo-intensity (!) specifically indicates the high calcium and collagen content of the lesion.



► **Fig. 3** Desmoplastic bone fibroma. 3-year-old girl. **a+b** native CT, bone (coronary) and soft tissue window technique (axial): intraosseous tumor with considerable expansion and neocortical formation in the ramus area (white arrows); the lateral cortical bone is completely destroyed (oval); **c** T1 fatsat with contrast-enhancement cor: homogeneous tumor enhancement (\*), displacing the tooth germ (arrow) **d** axial T2 TSE: the right-mandibular tumor is noticeably low in signal intensity, which indicates a high collagen fiber content (arrow).

► **Table 1** Overview of some important jaw lesions with radiopaque matrix (selection). based on: [20].

Entity	Age/Gender	Radiological signs	Topographical location
Cemento-osseous dysplasia (focal; periapical; florid)	> 50 years/female/ African American	focal lytic to radiopaque, non-expansive source of infection, lytic rim (halo)	along one or more roots: focal: posterior; periapical: anterior; florid: multiple
Osteoma	no predilection	smooth-edged radiopaque lesion without halo; mature bone	posterior mandible preferred
Osteoblastoma	2 <sup>nd</sup> –3 <sup>rd</sup> decade/ male	solitary osteolytic lesion with radiopaque, intralesional foci; MRI: Perifocal edema	mostly lower jaw, sometimes near the tooth apex
Cementoblastoma	2 <sup>nd</sup> –3 <sup>rd</sup> decade/no predilection	round, well-demarcated, radiopaque lesion at the root with lysis margin	always in connection with the root! mostly 1st mandibular molar
Odontoma	Children and young people	usually an incidental finding, but can hinder tooth eruption; compound type: “many small teeth” in lysis; complex type: amorphous, radiopaque structure with narrow border	Only tooth-bearing areas affected: compound → anterior maxilla, complex → posterior mandible
Ossifying fibroma (central)	2 <sup>nd</sup> –4 <sup>th</sup> decade/ female	sometimes large expansive lesion, solitary, well-demarcated: mostly mixed lytic-sclerotic lesion	Mandible
Calcific. cyst. odont. tumor/ calcific odontogenic cyst	2 <sup>nd</sup> –3 <sup>rd</sup> decade/ no predilection	Expansive tumor: well-demarcated, unicameral cyst with radiopaque contents of varying sizes. Density; CAVE: May be confused with apical periodontitis	anterior region of maxilla and mandible; mostly incisor/canine area
Osteosarcoma	Between 30 <sup>th</sup> –50 <sup>th</sup> year of life/male	Swelling, pain, numbness, loosening of teeth osteodestructive, sometimes subtle (widened periodontal space), restless mixed lytic-sclerotic image; CT: malignant periosteal reaction	Maxilla and mandible: Mandible: Molar region preferred; CAVE maxilla: Tumor can completely evade the OPG (DVT/CT)!
Osteomyelitis (OM) (different genesis, also CNO)	no predilection; CNO: Children and young people	acute osteomyelitis often radiologically “mute” subacute/chron. OM: inhomogeneous, osteolytic/-sclerotic Bone image; CT/DVT: mostly solid periosteal reaction CAVE: Tumor mimicker!	Mandible preferred; CAVE: Maxilla OM barely visible in OPG (therefore extensive use of DVT or CT is necessary)

cludes entities whose biological behavior and radiological appearance give rise to controversial considerations in the direction of aggressive, even malignant tumor entities, which is particularly true for desmoplastic bone fibroma. Except for the latter, these will not be discussed below and reference is made to the relevant literature [8, 9, 10, 11, 12, 13, 14].

The osteoma is clearly benign, also called enosteoma, compacta island, or bone island. Similar to odontoma, this is actually a hamartoma. In the jaw, a distinction is made between central (intraosseous), peripheral (periosteal or subgingival) osteoma, and extraskeletal soft tissue osteoma; the latter is very rare.

Osteomas of the jaw do not differ radiologically from those of the rest of the skeleton (high native density > 1,000 HE, pseudopodia-like projections at the edges) [15]. In terms of differential diagnosis, osteomas are sometimes indistinguishable from odontomas, but it is more important to differentiate them from osteoplastic metastases (breast cancer, prostate cancer), although in such cases generalized skeletal metastases are usually already present. Metastases can sometimes be unmasked as osteosclerotic lesions during chemotherapy.

The multiple occurrence of osteomas is known to be observed in Gardner syndrome (familial polyposis coli); however, the skull and jaw do not represent a specific site of involvement in osteopikilosis. Instead, what are known as tori occur on the jaw, exostosis-like cortical hyperostoses, which are typically found on the lingual side of the mandible (torus mandibularis), less frequently on the roof of the hard palate (torus palatinus). Morphology and topography characterize these lesions with sufficient diagnostic certainty.

Osteochondromas or cartilaginous exostoses, although they represent the most common benign bone-cartilage lesions of the human skeleton (about one third of all benign bone lesions), are very rare in the maxillomandibular region, which may be due to the different embryological origin of the facial bones: they arise from desmal (intramembranous) ossification (almost all bones of the rest of the skeleton follow the endochondral ossification mode). An exception is the temporomandibular joint, which develops via endochondral ossification, which is why mandibular osteochondromas are still most frequently found there [16, 17]. A special differential diagnostic entity of the temporomandibular joint is its synovial (osteo-)chondromatosis, which represents a

cartilaginous metaplasia of the synovium (primary form) [18]. Secondary osteochondromatosis is the consequence of long-standing temporomandibular joint arthrosis, but less frequently it also occurs post-arthritically.

The rare desmoplastic bone fibroma, in contrast – as in all other skeletal regions – it represents a diagnostic challenge because it grows locally in an osteodestructive manner and therefore appears like a malignancy. MRI reveals an inhomogeneous T2 image that mainly contains strongly hypointense “dark” areas that correspond to collagen fiber-rich, i. e. fibrous components,

which is a very defining radiological feature in MRI imaging for desmoplastic bone fibroma [14] (► Fig. 3). Finally, it should be remembered that desmoplastic bone fibroma is nothing other than the intraosseous variant of soft tissue fibromatosis of the desmoid type [19].

► Table 1 shows a compilation of radiopaque jaw lesions.

In addition, ► Table 2 and ► Fig. 4 show some specifics of the maxilla.

#### Note

1. Non-odontogenic, benign bone tumors of the jaw do not differ from those of the rest of the skeleton; the most common is fibrous dysplasia.
2. Due to dentogenic hard tissue proliferation of the jaw, the differentiation of bone-dense but non-odontogenic lesions is much more difficult than in the rest of the skeleton.

► Table 2 Overview of location and age frequency of tumors of the maxilla. Primary odontogenic tumors of the maxilla are rare, therefore there are hardly any large isolated reports on the above-mentioned distributions with regard to entity, topography, and age. Nevertheless, it is worth emphasizing the exclusive occurrence of the adenomatoid odontogenic tumor in the anterior maxillary region, which is obviously a specific feature (in red). Based on: [21].

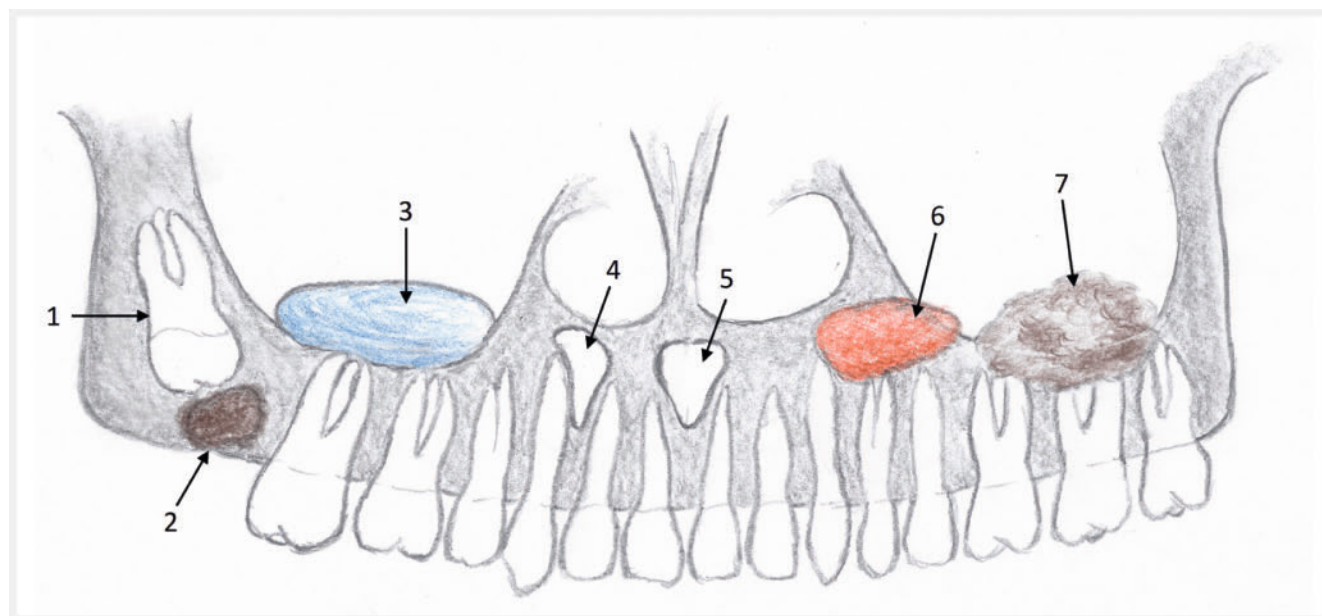
Entity	Topography	Preferred age
Ameloblastoma	Anterior and posterior maxilla	20 <sup>th</sup> –40 <sup>th</sup> year of life.
Adenomatoid odontogenic tumors	Anterior maxilla	10 <sup>th</sup> –20 <sup>th</sup> year of life.
Odontoma	Anterior and posterior maxilla	10 <sup>th</sup> –30 <sup>th</sup> year of life.
Osteosarcoma	posterior maxilla	30 <sup>th</sup> –50 <sup>th</sup> year of life.

## Malignant primary jaw tumors

### Malignant odontogenic tumors

These include several carcinomas (e.g. odontogenic shadow cell carcinoma, sclerosing odontogenic carcinoma) as well as odontogenic carcinosarcoma and sarcoma; they are all extremely rare. Due to their relative frequency, only ameloblastic carcinoma and odontogenic clear cell carcinoma will be discussed in more detail here.

The ameloblastic carcinoma does not represent a mere malignant variant of ameloblastoma, as presented in the 2017 classification, but forms a separate entity, which is histologically similar



► Fig. 4 Typical cystic and tumorous lesions of the maxilla. 1 – retained 18 due to a barrier to eruption; 2 – compound odontoma in the region 18 (shown here: barrier to eruption!); 3 – mucoid retention cyst (mucocele): typically originating from the maxillary sinus; 4 – globulomaxillary cyst: classic interradicular position between 2<sup>nd</sup> and 3<sup>rd</sup>, often spreading both roots; 5 – nasopalatine cyst (ductus incisivus cyst): always median interradicular; 6 – adenomatoid odontogenic tumor: typically located in the anterior maxilla, often in connection with a retained tooth in this region; 7 – osteosarcoma (note the root resorptions!).

to ameloblastoma [1]. Although less than 1% of all odontogenic tumors, ameloblastic carcinoma accounts for 30% of all malignant odontogenic tumors.

Radiologically, a mostly large, expansive osteolysis is seen in the (posterior) mandible (located there to over 80%), which has sharp edges but, if large enough, practically erodes the local cortex completely. Adjacent tooth roots are also destroyed and not relocated. Matrix mineralization is largely absent. MRI does not provide any specific diagnostic clues; the avid contrast enhancement is, as expected, heterogeneous and shows necrotic areas [22].

In addition to the high local recurrence rate of 40%, it is worth emphasizing the fact that ameloblastic carcinoma has a high pulmonary metastasis rate of 33%, which is actually more typical for sarcomas, while regional cervical lymph node metastasis amounts to “only” 13%. Unfortunately, even with complete surgical resection, the 5-year survival rate is relatively poor at about 70% and drops to less than 20% in the presence of metastases [23].

Odontogenic clear cell carcinoma received its name due to its striking histological similarity to renal clear cell carcinoma when it was first described in the 1980s [24]. Molecular genetics have now confirmed the high prevalence of ESWR1 gene rearrangement (80%), which actually represents a typical translocation for sarcomas (especially Ewing’s sarcoma) [25].

In contrast to ameloblastic carcinoma, odontogenic clear cell carcinoma is radiologically much less clearly demarcated in the bone, perforates the cortex, and more frequently grows into the periosteal soft tissue. The mandible is similarly frequently affected (approximately 75%) as in ameloblastic carcinoma. The recurrence rate is strikingly high at 40%; with curettage alone it is as high as 87% [26].

Sclerosing odontogenic carcinoma and odontogenic shadow cell carcinoma are extremely rare and ultimately represent surprising histological diagnoses that can only be guessed at due to their aggressive radiological pattern of destruction [27, 28, 29, 30].

### Note

1. Since malignant odontogenic carcinomas are very rare, the radiologist will hardly ever be confronted with them, especially since specific radiological characteristics are missing.
2. Considering other malignancies in the jaw region (e. g. squamous cell carcinoma, metastases), the radiologist should pay attention to and critically evaluate general criteria for malignancy: root destruction, but sometimes only root tip resorption, and radiologically aggressive growth (Lodwick IC and higher). If clinical symptoms such as pain, especially paresthesia, occur, then this calls for the utmost alertness.

► **Table 3** provides some radiological malignancy criteria for gnathic lesions.

### Malignant, non-odontogenic maxillofacial bone and cartilage tumors

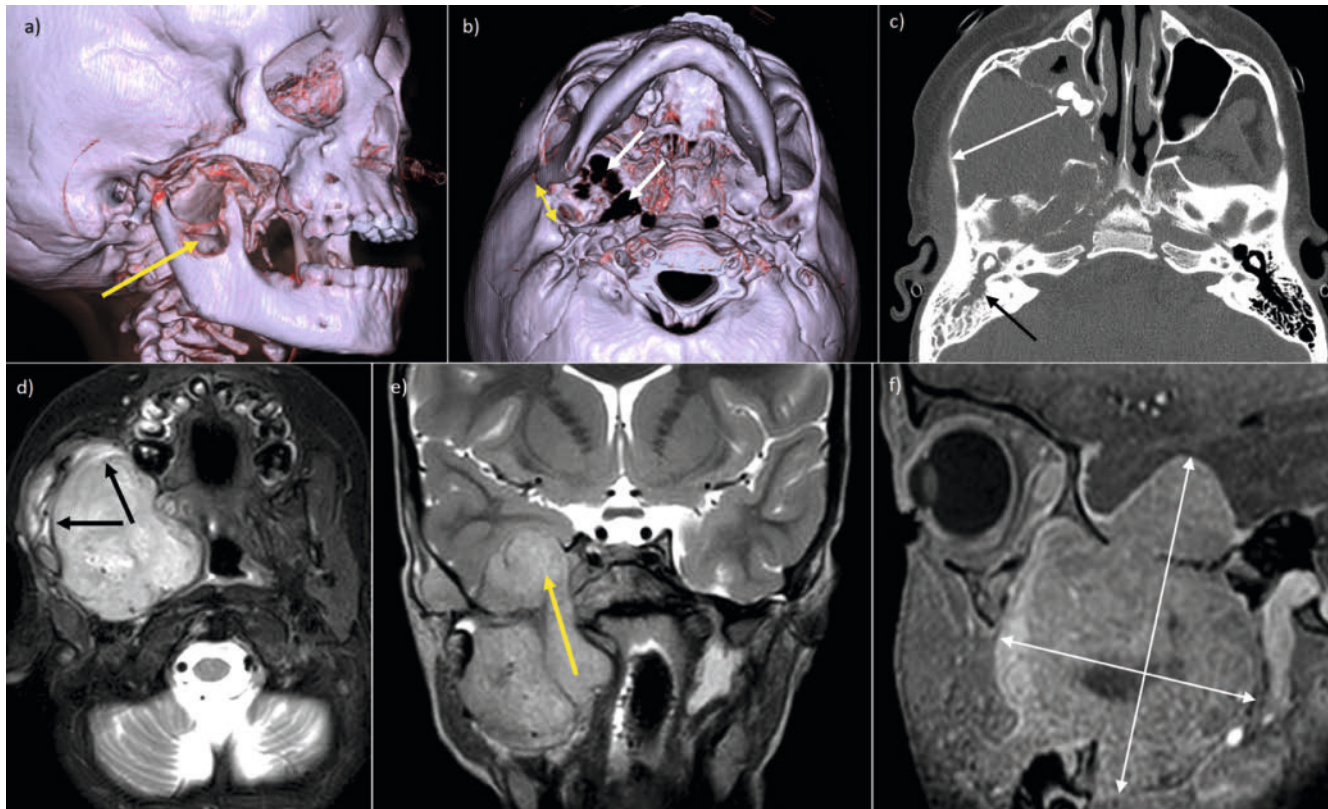
This includes, in particular, osteosarcoma of the jaw, which will be discussed in more detail; chondrosarcoma and its subtypes, as well as the newly added rhabdomyosarcoma with TFCP2 rearrangement, are only mentioned here [1] (► **Fig. 5**).

Osteosarcoma of the jaw accounts for only 1% of all malignant tumors of the head and neck region. Nevertheless, it is a fairly common malignant primary maxillofacial bone tumor, accounting for 6–10% of all osteosarcomas [31]. Patients are usually 10–20 years older than patients in childhood and adolescence with long tubular bone osteosarcoma; although the mandible is usually affected, the maxilla appears to be affected more frequently in men [32].

Maxillofacial osteosarcoma is also characterized by its osteoid production; as in the rest of the skeleton, its histological subtypes are differentiated into osteo-, chondro- and fibroblastic osteosarcomas, depending on the predominant malignant sarcoma cell type [33]. Low-grade central osteosarcoma (LGCO), which is difficult to diagnose histologically and is difficult to differentiate from benign bone lesions, especially fibrous dysplasia, is very rare in the jaw (only 1–2% of all jaw osteosarcomas) [34]. However, this and

► **Table 3** Selected malignancy criteria for gnathic bone lesions. The table should be understood in such a way that the radiological signs suspicious for malignancy listed here may also be based on benign entities. Criteria for radiation-based imaging (X-ray, DVT, CT) were taken into account. The above criteria apply primarily to lytic-destructive processes. However, if radiation-based imaging shows matrix elements, the possibility of a specific diagnosis is usually opened up.

Gnathic element	Radiological sign	Comments/benign DD
Tooth root, root tip	Destruction	History of dental root resection?
Parodont (periodontal gap)	Enlargement (Garrington sign)	Periodontitis/periodontitis marginalis
Lamina dura (dental alveolus)	Destruction	Inflammation (periodontitis, osteomyelitis)
Tooth-bearing bone	Cortical penetration/perforation	Osteomyelitis, Langerhans cell histiocytosis
Bone	Matrix-free osteolysis	CAVE before making hasty decisions: Cysts!
Tooth-bearing bone environment	Soft tissue tumor	Abscess, chronic fibrovascular inflammation
Jaw periosteum	“Onion skin”, spiculae, Codman triangle (interrupted periostectomy)	Osteomyelitis of the jaw, osteo(radio)necrosis



► **Fig. 5** Rhabdomyosarcoma in the right pterygoid region in a 5½-year-old girl. **a** CT with VRT and SSD imaging: Destruction of the mandibular notch (arrow); **b** View from below: lateral luxation of the mandibular head and empty articular fossa (double arrow) with extensive destruction of the medial. Skull base (white arrows); **c** the tumor fills the entire infratemporal fossa with luxation of a molar into the maxillary sinus (double arrow) and tube obstruction and fluid retention in the mastoid and tympanic cavity (black arrow); **d** T2 fs axial: signal-(cell-)rich tumor with perifocal muscle edema (black arrows); **e** T2 fatsat cor: Illustration of intracranial tumor spread into the middle. Cranial fossa (arrow); **f** T1 THRIVE with contrast medium: moderately avid tumor (double arrows) with central necrosis (\*), clearly visible pyramidal intracranial (extraaxial) tumor spread.

the peripheral osteosarcomas (parosteal, periosteal, and surface osteosarcoma), which also occur in less than 5% of cases of the jaw, are not discussed further here; only the possible radiological confusion of a parosteal osteosarcoma with benign gnathic bone tumors (osteoma, osteochondroma) is mentioned in this article [35].

Radiologically, osteosarcomas of the jaw do not differ in principle from those of the rest of the skeleton, but their appearance is completely uncharacteristic: it ranges from clearly defined osteolyses that look like cysts to irregularly defined, moth-eaten bone defects to severely sclerotic lesions, where the diagnosis of osteosarcoma is most likely due to matrix formation [36].

CT can help with non-overlapping matrix analysis with detection of irregular, often punctate intralesional calcifications, or ossifications as well as cortical destruction, destruction of the lamina dura (bone lamella of the dental alveolus) and root resorption, while spiculated and interrupted periosteal reactions (sunburst phenomenon, hair-on-end appearance) are typical for osteosarcoma, but are less common in the jaw. In addition, some osteosarcomas are largely free of radiologically detectable matrix calcification (► **Fig. 6**).

MRI can capture the entire extent of the osteosarcoma into adjacent bony and soft tissue structures and thus provide valuable information for local tumor staging (determination of resection

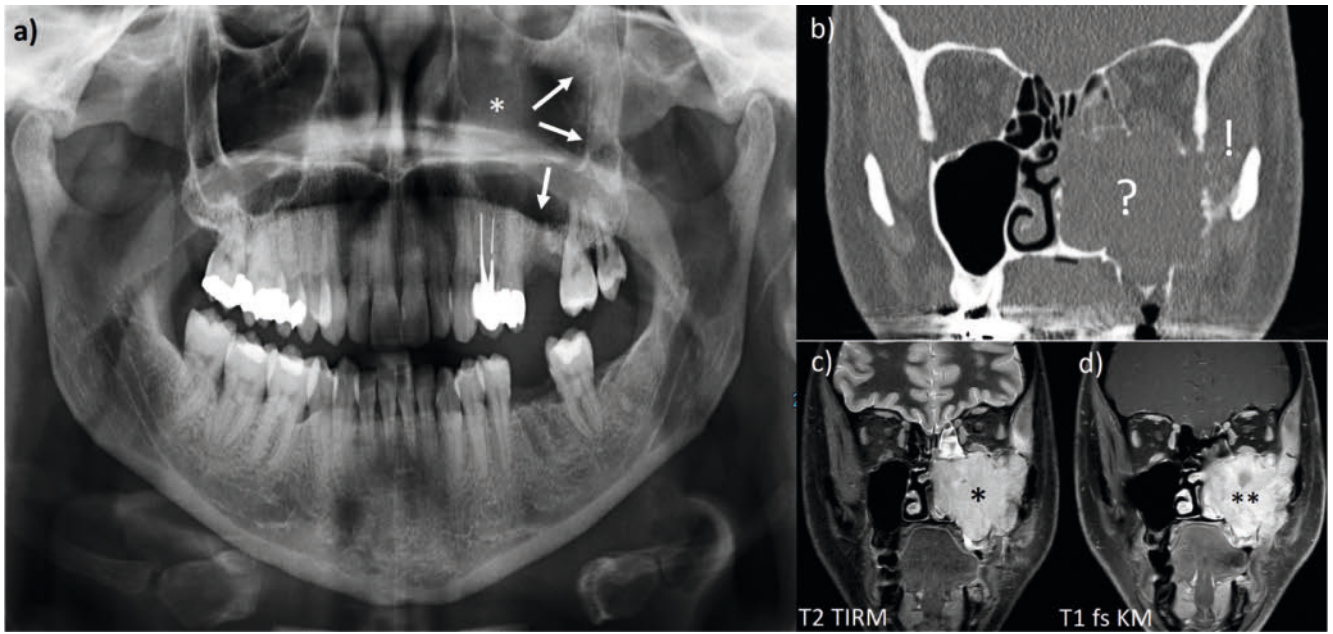
margins). This serves less to detect nasal or paranasal involvement than to detect possible orbital, frontobasal, and sphenooptic infiltration from the maxilla, as well as enoral, oropharyngeal, and temporomandibular enlargement of the tumor. It is generally accepted that the extent of sarcomatous tumors, especially in the upper jaw, is usually massively underestimated! [36].

The differential diagnosis is not trivial, since neither clinical nor radiological findings can contribute decisively to the identification of an underlying osteosarcoma. In particular, the much more common chronic osteomyelitis of the jaw can cause considerable differential diagnostic problems in the differentiation of a malignant bone tumor (see below). Chondrosarcoma and fibrosarcoma are also among the differential diagnoses, while the highly differentiated osteosarcoma presents difficulties in distinguishing it from fibrous dysplasia and ossifying fibroma. Late malignancies in the form of postradiogenic osteosarcomas in the jaw region are frequently seen after irradiated ENT carcinomas [37].

However, there are some notable features that distinguish osteosarcoma of the jaw from that of the long tubular bones [38]:

1. Patients with osteosarcoma of the jaw are 10–20 years older than those patients who typically develop osteosarcomas of the lower extremities in childhood or adolescence;
2. In contrast to osteosarcomas of the extremities, osteosarcomas of the jaw are more frequently low-grade osteosarcomas,





► **Fig. 6** Osteosarcoma of the maxilla. 40-year-old man with left-sided pain, stuffy nose and numbness over the central midface on the left. **a** OPG: apart from a slight sinus maxillary thickening on the left (\*), only the blurring of the lateral and caudal bony border is noticeable (arrows); **b** native CT, coronal reformation: extensive bone-destructive tumor without matrix calcification (?), only in the lateral border area are delicate matrix calcifications visible (!); **c+d** MRI: T2 TSE: striking signal-intense, i. e. proton-rich tumor (\*) with an avid, only slightly heterogeneous enhancement (T1 fs contrast-enhanced) (\*\*). Courtesy of Prof. Dr. I.-M. Nöbauer-Huhmann, Med. University of Vienna, Radiology.

which means a significantly lower degree of biological aggressiveness, making overall survival more favorable than with osteosarcomas of the extremities;

3. However, osteosarcomas of the jaw have a higher recurrence rate due to the difficult anatomical resection conditions, especially in the maxilla;
4. In contrast, distant metastases are significantly less common in jaw osteosarcomas than in extremity osteosarcomas.

► **Table 4** provides an overview of systematic radiological tumor matrix analysis.

## Langerhans cell histiocytosis of the jaw

Langerhans cell histiocytosis (LCH) represents a neoplastic proliferation of what are known as Langerhans cells, which occur as dendritic mononuclear cells primarily in the skin, mucous membranes, lymph nodes, and also in the bone marrow. The main age of manifestation is childhood and adolescence, but even toddlers can be affected by LCH. The gnathic system is affected in 10% of all LCH cases, and the mandible is by far the most common site of manifestation [39]. There, two types of involvement are distinguished: the more common alveolar type (affects the tooth-bearing process of the alveolar mandible) and the intraosseous type (affects mainly the ramus mandibulae).

Regarding the radiological appearance, every medical student has probably been shown the image of the so-called “floating teeth”, i. e. a large alveolar osteolysis in the lower jaw in which one or more teeth appear to “float”. This image, however, is as pa-

thognomonic as it is very rarely encountered! Rather, the X-ray image (OPG) can show all forms of destruction from a well-defined geographic osteolysis of Lodwick grade IA/B to the moth-eaten pattern of Lodwick grade II with regard to the LCH lesion pattern. In this respect, a wide differential diagnostic spectrum is available, ranging from odontogenic or non-odontogenic cysts to aggressive, even malignant jaw tumors; the most important (and most common) differential diagnosis, however, remains mandibular osteomyelitis [40].

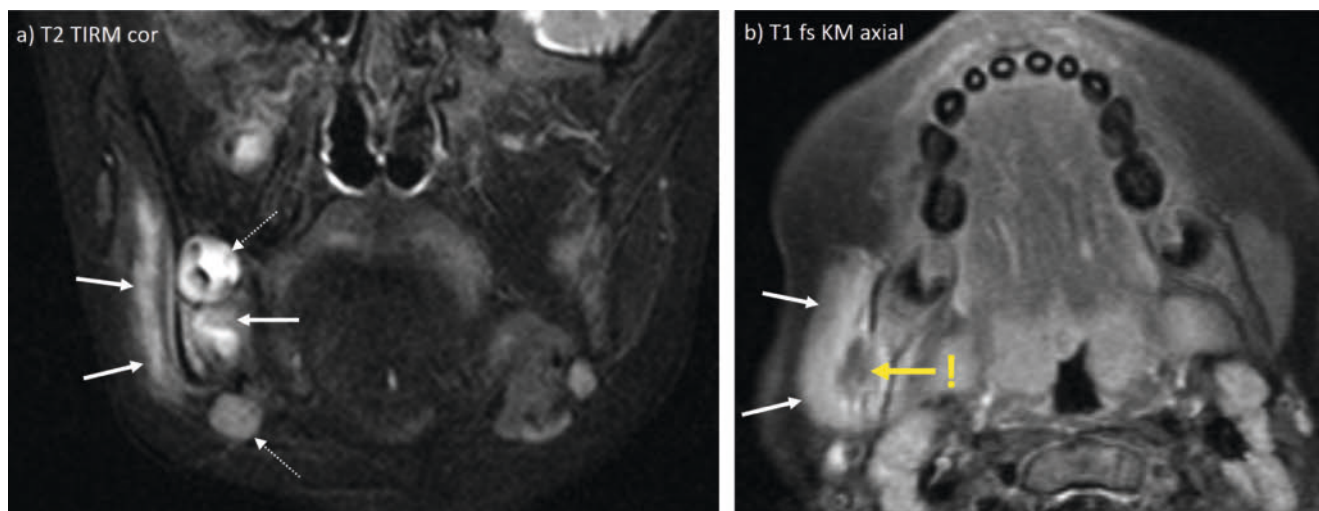
The CT typically shows unresponsive osteolysis with sometimes extensive cortical destruction of the jaw, which in turn would be more typical for a LCH and would speak against a – much more common – osteomyelitis. However, if periosteal reactions occur (solid or lamellar, but also interrupted forms), osteomyelitis is a serious differential diagnosis; in children, however, it could also be Ewing’s sarcoma. If intralésional calcifications are present (which would be atypical for LCH), osteosarcoma must also be considered, although jaw osteosarcomas tend to develop later, i. e. in the 20<sup>th</sup> to 40<sup>th</sup> year of life [41].

MRI also has a low discriminatory power in LCH compared to osteomyelitis: first, LCH causes a perifocal edema (in the bone, but also periosteally and in the soft tissue surrounding it) just like osteomyelitis, and second, tumorous soft tissue expansion is absent in both entities. In addition, liquid areas suspected of being abscesses that do not show contrast enhancement are also observed in LCH (► **Fig. 7**). If LCH occurs near the temporomandibular joint, there is a risk of confusion with septic temporomandibular arthritis. A differential diagnostic criterion, however, is the detection of dislocation of tooth buds or tooth roots, which is only found in LCH, but not in osteomyelitis [42]. It should be kept

► **Table 4** Analysis of radiopaque lesions in the jaw (X-ray matrix).

Radiological appearance	Probable entity	Comments
bone density: solitary, focal, without tooth reference	Osteoma, (cartilage) exostosis, torus	Confusion with odontoma, cementoma
very radiopaque (also heterogeneous), solitary, compact or irregular, related to the tooth	Odontoma (complex or compound)	often in the direction of tooth eruption; especially in children and adolescents
slightly less radiopaque, located at the root (tip)	Cementoblastoma, cemento-osseous dysplasia	pay attention to the existing periodontal gap!; DD chronic periapical periodontitis
diffuse sclerosis, ill-defined, with or without reference to the tooth root	Osteomyelitis, periodontitis	Clinic!, pay attention to uninterrupted periosteal reaction; CAVE: Malignant
irregular sclerosis with very dense bone sections (often alveolar ridge)	Bone sequestrum	primary inflammatory, secondary to bisphosphonates, postradiogenic
disseminated or irregular sclerosis foci with bone destruction, also extraosseous	Osteosarcoma	very rare, and can therefore be confused with the more common osteomyelitis; watch for periosteal reaction (spicules, discontinuous)
fibrous matrix: frosted glass-like appearance, "swollen" bone	Fibrous dysplasia, ossifying fibroma; other bone fibromas*	Biopsy in the "classic" frosted glass pattern is obsolete ("leave-me-alone")
irregular, popcorn-like calcifications with/without bone destruction	Chondrosarcoma	very rare; more common dys- or meta-plastic calcifications in other tumors

\* Fibromas and collagen fiber-rich tumors can exhibit metaplastic calcifications of varying degrees and therefore appear matrix-like.



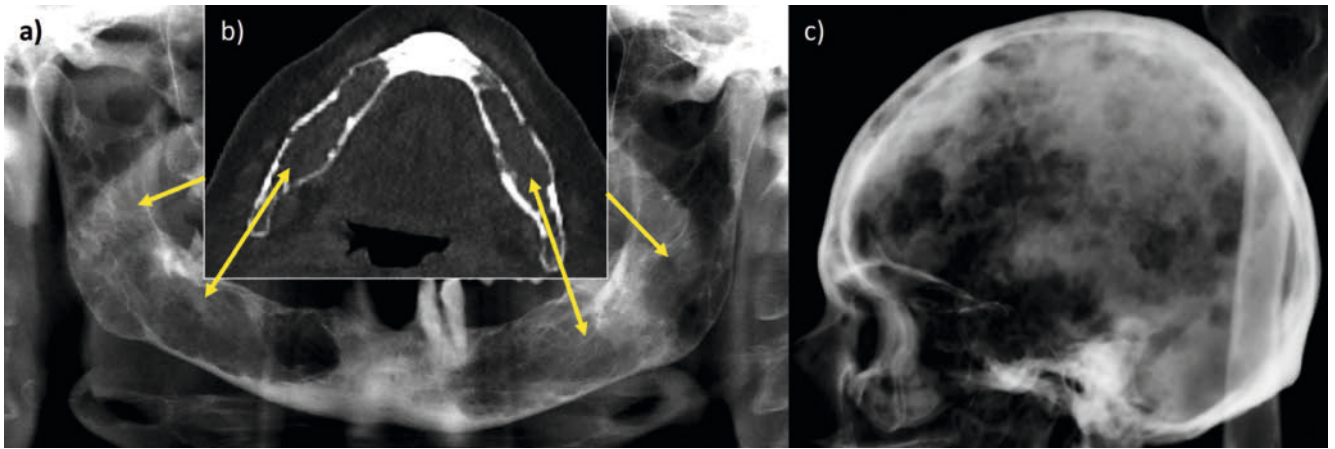
► **Fig. 7** Langerhans cell histiocytosis. A child with involvement of the right angle of the mandible region. **a** MRI: T2 TIRM cor: Illustration of both intraosseous bony and extraosseous soft tissue edema in the masseter muscle (arrows); dental follicle and submandibular lymph node (dashed lines). arrows); **b** T1 fatsat contrast-enhanced axial: clear contrast enhancement in the distended masseter muscle without actual tumor detection (white arrows), but here the outer cortical destruction can be clearly seen with missing intralesional contrast enhancement (yellow arrow + !): this finding would have been suitable for differential diagnosis with both a CNO and an Ewing sarcoma! Courtesy of Prof. Dr. M. Uhl, Freiburg i. Br.

in mind that clinical presentation and usual laboratory findings can hardly or only poorly differentiate between these two entities.

## Other malignant tumors of the jaw region and metastases

At this point we also have to talk about Ewing's sarcoma of the jaw, because it provides numerous clinical and radiological over-

laps with osteomyelitis and Langerhans cell histiocytosis: about 3% of all Ewing sarcomas occur in the maxillofacial region; mostly in the mandible [43]. Ewing's sarcoma has now been assigned to a separate tumor category (what are known as undifferentiated small round cell sarcomas of bone and soft tissue; 5<sup>th</sup> edition, WHO Soft Tissue and Bone Tumors, 2020 [44]). As a rapidly growing medullary tumor, Ewing's sarcoma shows all radiological signs of an aggressive, malignant tumor with a moth-eaten or permeative destruction pattern, although the true extent of the sur-



► **Fig. 8** Multiple myeloma. 63-year-old woman with known multiple myeloma and extensive skeletal involvement. **a** OPG: almost the entire mandible with the exception of the symphysis shows extensive, matrix-free osteolysis (arrows and double arrows); **b** axial CT slice through the mandible shows the medullary myeloma involvement (double arrows); **c** VRT from CT: “Shotgun skull”: typical multiple osteolyses in multiple myeloma.

rounding soft tissue tumor infiltration can only be determined with MRI. Only the detection of an extrasosseous soft tissue tumor component puts the radiologist on the diagnostic trail of a Ewing sarcoma. Conversely, such tumor masses are not necessarily found in Ewing sarcomas. Focal, irregular, or sharply defined geographic osteolyses also occur and mimic odontogenic processes such as periapical inflammation [45]. In the author’s experience, gnathic Ewing sarcoma always represents a diagnostically unexpected surprise.

The same applies to lymphoma of the jaw, which, with an incidence of only 0.6%, is a distinct rarity for primary non-Hodgkin lymphomas [46]. Because of this rarity, gnathic bone lymphomas are often misinterpreted as infections and mistreated. As with all other lymphoma manifestations that primarily or secondarily affect the bone, they can radiologically mimic virtually all pathological appearances, so that there are no typical pathomorphological criteria that would anticipate lymphoma involvement [47].

The (solitary) plasmacytoma of the jaw, the involvement of the jaw in multiple myeloma (► **Fig. 8**), and also the secondary metastatic involvement of the jaw are not the subject of discussion in this article, but should be mentioned because they are of clinical relevance.

Solitary plasmacytoma of the jaw occurs (approximately 12–15%) predominantly in the mandible and especially in the regions of increased hematopoiesis, i. e. in the angulus and ramus mandibulae as well as in the molar section of the corpus mandibulae [48]. These are radiologically unreactive osteolyses, untreated without any marginal sclerosis. Plasmacytomas can completely degrade the compacta and then develop extensively in an extraosseous location. The MRI shows this soft tissue expansion quite reliably, but does not allow a specific diagnosis. As a result, the biopsy confirmation of a plasmacytoma usually represents an unexpected surprise, since radiological confusion with odontogenic and non-odontogenic cysts is quite possible [49].

In contrast, involvement of the jaw in multiple myeloma usually poses little diagnostic problem, because the underlying disease is usually already known and the viscerocranium including the jaw

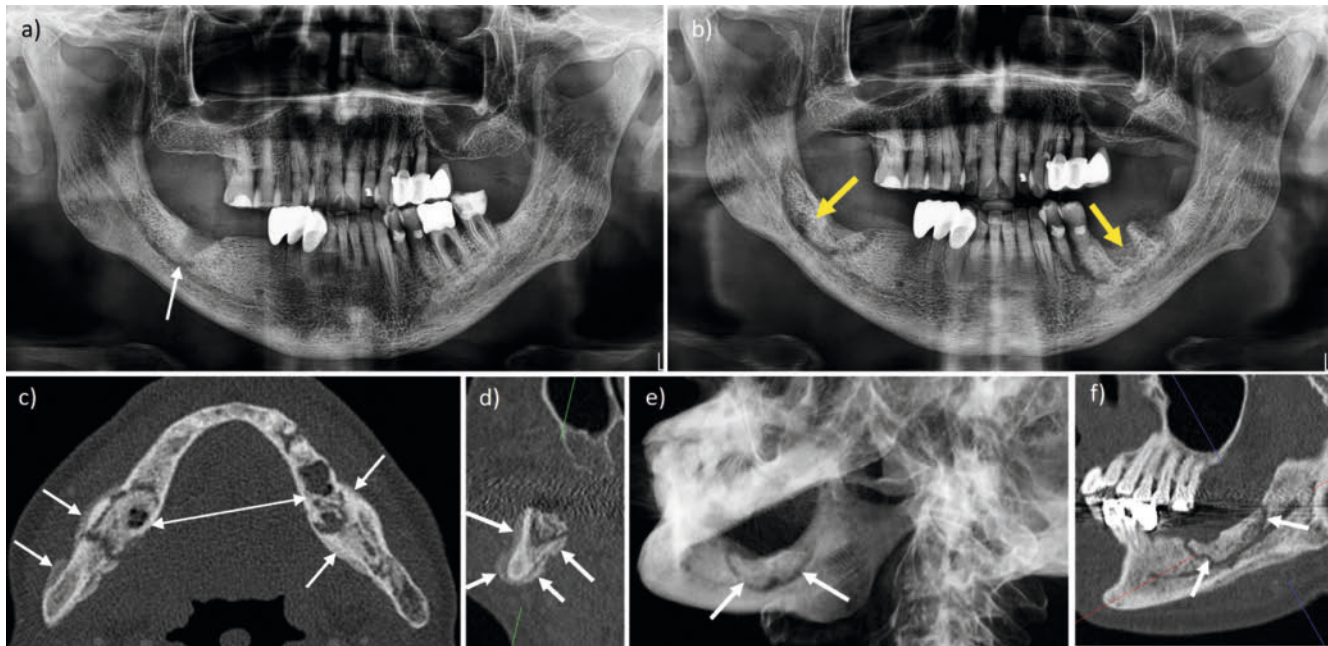
is also affected as part of the whole-body formation, so that involvement of the jaw is noticeable in the form of small to medium-sized, unresponsive osteolyses. However, there are case reports in which the gnathic manifestation of multiple myeloma was the first clinical symptom of malignant systemic disease [50]. The approximate incidence of maxillo-mandibular involvement in multiple myeloma is unknown. What must be particularly emphasized, however, is the fact that jaw osteonecrosis is a typical and feared complication in the treatment of multiple myeloma with bisphosphonates (BP): depending on the study, approximately 10% of these patients developed BP-induced osteonecrosis of the jaw during their treatment (or even afterwards) [51, 52]. The same applies analogously to BP-treated metastases, especially in breast cancer patients and prostate cancer patients (► **Fig. 9**).

This leads to a brief discussion of secondary, i. e. metastatic tumors of the jaw: histologically, most metastases are adenocarcinomas (61%); in women, they are breast cancer metastases (41%), and in men, they are lung cancer metastases (22%) [53]. In descending order of frequency, this includes metastases of renal, prostate, thyroid, colorectal, and gynecological carcinoma of the lower abdomen, but also of malignant melanoma and soft tissue sarcomas, although this order and composition varies according to the study and region [54, 55]. In the mandible, the molar region of the corpus and the ascending ramus of the mandible are most frequently affected (which is known as the M-shaped distribution; [56]). A certain peculiarity is maxillary metastases in children with neuroblastoma of the adrenal glands [57].

Since metastases of the oral cavity, including the jaw, are the first manifestation of undetected malignancies in up to 30% of cases, it is particularly important for the radiologist to carefully search the maxillo-mandibular region for conspicuous patterns of destruction [58].

#### Note

1. The gnathic system – like any other region of the human skeleton – can be the site of manifestation of malignant systemic diseases.



► **Fig. 9** Bisphosphonate-induced osteonecrosis of the jaw. 79-year-old patient with multiple myeloma and long-term bisphosphonate therapy. **a** OPG: edentulous posterior tooth area of right mandibular with beginning osteonecrosis demarcation (arrow); **b** OPG, 4 months later: clear osteonecrosis demarcation on both sides (left after extractions 36 and 37); **c** axial CT: Illustration of bilateral osteonecrosis (double arrow) with periosteal reactions (arrows); **d** CT, radial section: solid periosteal reaction (arrows) as an expression of chronic inflammation (osteomyelitis); **e+f** VRT from CT and sag. MPR from CT: clear illustration of sequestering osteonecrosis (arrows).

## 2. The radiological pattern of destruction of the jaw does not differ in principle from that of the rest of the skeletal involvement pattern. However, this is usually not expected for the lower jaw or is often simply overlooked for the upper jaw.

### Jaw osteomyelitis

Finally, it is important to talk about a final, non-tumorous entity that deserves attention due to its diagnostic mimicry of jaw tumors and their differential diagnostic significance: osteomyelitis of the jaw.

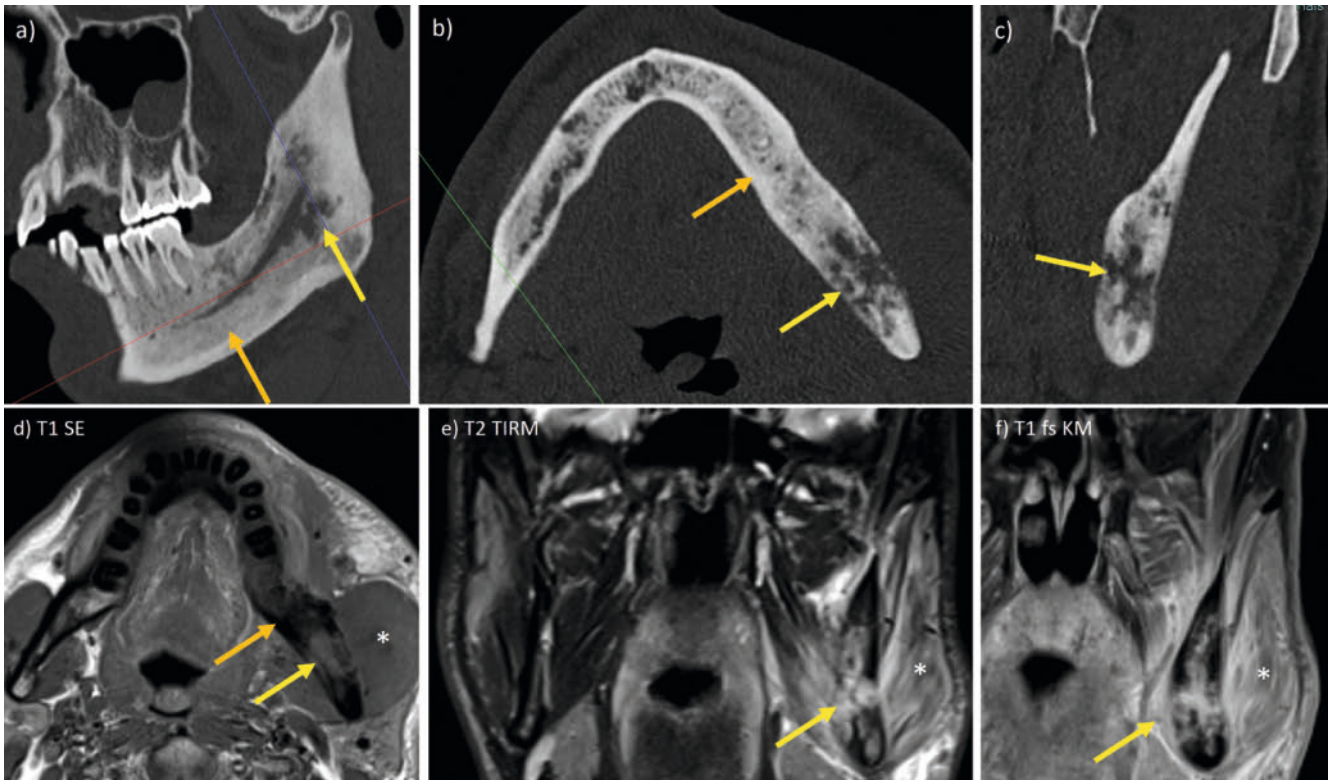
The lower jaw is usually affected. Regardless of its origin – dental, exogenous after trauma, surgery or other dento-gingival manipulation, as well as hematogenous – acute osteomyelitis is distinguished from its chronic form (after more than 1 month duration). While acute osteomyelitis (without abscess formation) can usually be suspected either from anamnesis or identified clinically (but in case of doubt it can also be detected by imaging using MRI; ► **Fig. 10**), radiation-based imaging diagnostics (OPG, DVT, CT) are of great importance in the diagnosis of chronic jaw osteomyelitis [59]. Typical for chronic osteomyelitis are sclerosing bone marrow changes in the sense of an osteosclerotic-osteolytic mixed picture. A particular problem is also posed by bisphosphonate-induced osteonecrosis, which is usually infected and therefore also belongs to the spectrum of chronic osteomyelitis (► **Fig. 10**).

Equally important are the periosteal reactions that occur, which – apart from cortical thickening – can consist of solid, monolamellar periosteal shells, but also of multilamellar perios-

teal “onion shell patterns”, although they must not be interrupted. The latter would strongly indicate an aggressive bone tumor, just as mixed osteosclerotic-osteolytic forms can be found in a number of ossifying dysplasias and fibromas, but also in odontogenic carcinomas and especially in maxillofacial sarcomas [60].

Of course, functional imaging such as bone scintigraphy and SPECT/CT has a sensitivity of almost 100%, which OPG does not reach by far, but the specificity is low. The negative predictive value of 100% according to a meta-analysis is useful in that it can be used to exclude chronic osteomyelitis from the outset if it is not present [61]. FDG-PET/CT, on the other hand, has its place in all forms of metabolically avid solid neoplasm, usually in addition to MRI, in order to identify vital tumor areas for diagnostic biopsy [62]. In addition, MRI is also useful in identifying osteomyelitis complications such as abscesses and fistulas (if not already visible sonographically), while bone sequestra can be better diagnosed by CT or DVT. The differentiation of inflammatory granulation tissue in osteomyelitis and soft tissue tumor tissue, however, remains a domain of MRI and must be “extracted” by biopsy in ambiguous cases [63].

At this point, we would like to point out a very special form of chronic osteomyelitis, the non-bacterial (NBO) or chronic non-bacterial osteomyelitis (CNO), also known as CRMO (chronic recurrent multifocal osteomyelitis). This typically occurs in childhood and adolescence, and is an autoimmune-mediated bone inflammation caused by a misguided antigen-antibody response, often of parainfectious origin following previous infections [64]. These forms of osteomyelitis occur primarily in the mandible and often present as “dramatic” findings in cross-sectional imaging



► **Fig. 10** Mandibular osteomyelitis. 46-year-old patient with acute pain and swelling of the left mandible. **a–c** MDCT with sagittal, axial and coronal reformations: moth-eaten bone destruction in the left angulus area (yellow arrows) with simultaneous sclerosis of the medullary cavity of the left corpus mandibulae (orange arrows): acute exacerbation of chronic osteomyelitis. **d–f** MRI: the “bright” intraosseous areas represent the florid osteomyelitis (yellow arrows) with periostitis, while the “dark” areas (orange arrow in **d**) represent chronic sclerosing osteomyelitis. Extensive muscle edema in the pterygoid muscles and the masseter muscle (\*), but no soft tissue abscess: acute exacerbation of chronic osteomyelitis.

(CT, MRI) with significant cancellous, cortical and periosteal thickening, as well as surrounding soft tissue edema (► **Fig. 11**) [65]. Abscesses are not found, but bony defects and erosions may be present. A soft tissue portion should not be visible! The most important differential diagnosis in childhood, in addition to Langerhans cell histiocytosis, is Ewing’s sarcoma [66].

A special entity known in dental and maxillofacial surgery with as yet unknown etiology is the so-called primary or diffuse sclerosing osteomyelitis of the jaw (historically also known as Garré osteomyelitis), which proves to be largely resistant to therapy; there is no evidence of bacterial infections, osteonecrosis, or fistulas [67]. Whether this is actually an independent entity or whether it should rather be attributed to an autoinflammatory genesis like CNO or SAPHO syndrome remains to be seen at present.

#### Note

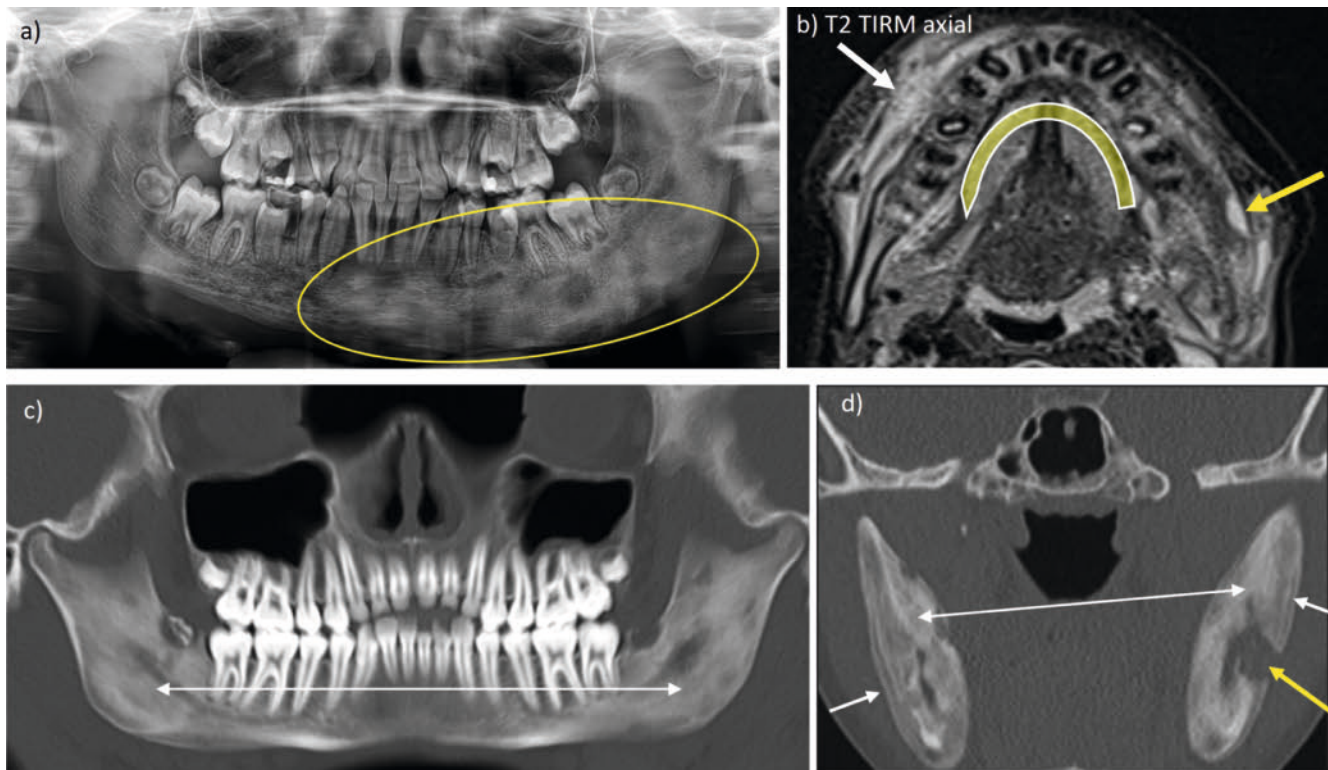
1. Jaw osteomyelitis is a significant and problematic tumor mimicker. Their partially aggressive destruction pattern can imitate and simulate (highly) malignant bone tumors.
2. Since jaw osteomyelitis is common, whereas malignant tumors are very rare, carefully weighing the diagnostic approaches represents a particularly demanding challenge. The key concepts here are overtreating (for osteomyelitis) and overlooking (for malignant tumors).

## Summary and conclusions for practice

Gnathic tumors of the bone or in the bone are rare; they represent only 2% of all bone tumors in the human body. In addition, there is the unique dual feature that, as a result of the teeth, in addition to bone tumors, there are also odontogenic tumors and dysplasias in the jaw bone, the appearance and diagnostic classification of which are, on the one hand, challenging due to their exclusivity, and on the other hand, they overlap with non-odontogenic pathologies. In this regard, knowledge of the pathomorphological aspect and the relationship to the tooth or periodontium in odontogenic tumors and dysplasias plays a crucial role (e.g. cemento-ossifying dysplasia and fibroma, odontoma, cementoblastoma).

In addition, odontogenic cysts are a common finding in the jaw, which sometimes makes their exact topographical classification on the OPG difficult (due to superposition). In addition to the common radicular cysts, especially at the root tip, and the follicular cysts around the crowns of impacted teeth, there are a number of other cysts in the jaw, knowledge of which is important in distinguishing them from cystic tumors (e.g. follicular cyst vs. ameloblastoma). While ameloblastoma is the most common benign epithelial odontogenic tumor, ossifying fibroma is the most common benign mesenchymal odontogenic tumor.

Primary malignant bone tumors of the jaw are fortunately very rare (e.g. ameloblastic carcinoma), but they pose a risk because they are associated with very non-specific symptoms and ambiguo-



► **Fig. 11** Two cases with chronic non-bacterial osteomyelitis. Top row: 10-year-old symptomatic girl with asymmetric left-sided mandibular swelling. Bottom row: 13-year-old girl with left-sided jaw pain and swelling. **a** OPG: mixed lytic-sclerotic bone changes in the left mandible, extending beyond the symphysis (oval); **b** MRI: T2 TIRM axial: the inflammation spreads over the entire mandible (curved arrow) with a focal structure suspicious for an abscess on the left (yellow arrow) and perimandibular soft tissue edema on the left (white arrow); **c** the curvilinear reconstruction from the CT shows extensive bilateral involvement of chronic osteomyelitis (double arrow); **d** craniofacial CT, coronal reformation: both posterior mandible sections show diffuse multi-sclerosis (double arrow) and a clear solid periosteal reaction (white arrows) that is broken through in one place (yellow arrow); no abscess formation!.

ous radiological image characteristics (e. g. osteosarcoma), and they are therefore often initially overlooked or misinterpreted or confused with other, much more common pathologies; examples of this would be jaw osteomyelitis, but also tumors that spread to the jaw secondarily, such as squamous cell carcinoma of the oral mucosa, which are a much more common cause of tumorous bone destruction of the jaw.

The jaw also contains two entities, the aforementioned ossifying fibroma and the giant cell granuloma, which are normally not or only rarely found elsewhere in the human body. Of course, the jaw bones are also home to the other known bone tumors and dysplasias (e. g. osteochondroma, fibrous dysplasia), as well as bony changes in systemic diseases such as brown tumors in hyperparathyroidism as opposed to cherubism, multiple myeloma, but also metastases, so that ultimately the gnathic system represents a mirror of human pathology.

With a few exceptions (leave-me-alone lesions, e. g. osteoma, osteochondroma, fibrous dysplasia), histological confirmation of tumorous lesions of the jaw in qualified correlation with appropriate imaging should therefore be the obligatory procedure to confirm the diagnosis.

## Acknowledgement

The corresponding author would like to express his sincere thanks for their expert advice and the provision of photographic material to Professor Dr. I. M. Nöbauer-Huhmann, Vienna, PD Dr. J. Henkelmann, Leipzig, PD Dr. M. Probst, Munich, Professor Dr. F.W. Roemer, Erlangen, Professor Dr. M. Uhl, Freiburg i. Br.

## Conflict of Interest

The authors declare that they have no conflict of interest.

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