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Bone Tumors of the Jaw – the "Blind Spot" for Radiologists Experienced with Tumors? – Part I

Kiefertumoren – der „blinde Fleck" des tumorversierten Radiologen? – Teil I

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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 excusively 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 (5th 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 foremast 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 upmost 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

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ZUSAMMENFASSUNG

Hintergrund Primäre Kiefertumoren stellen einerseits seltene Tumorentitäten dar und weichen andererseits hinsichtlich ihres differenten 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 Tumorinfiltration, 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.

Introduction

Primary bone tumors of the jaw are rare: they account for only about 2 % of all bone tumors in the human body [1]. Due to their rarity and the technically "remote" location of the gnathic system, in-depth knowledge about such tumors is not widespread, except in specialist circles that deal with gnathic bone tumors. In addition, maxillomandibular bone tumors differ in many ways from bone tumors in the rest of the body. This will be discussed further in the following section.

What makes bone tumors of the maxillofacial region special is that two fundamentally different primary tumor entities occur in close anatomical and topographical proximity to each other: this includes, on the one hand, the more common odontogenic tumors and dysplasias, and on the other hand, the much rarer non-odontogenic tumors of the jaw.

Embryologically, these two groups of tumors are recruited from different germ layers [2]: while the odontogenic tumors, like the teeth, arise from the ectodermal dental lamina, the non-odontogenic bone tumors of the jaw arise from the mesoderm, as do the primary bone tumors of the "rest" of the human body. Furthermore, there are special embryological forms of tumor formation, such as cartilage tumors from the Meckel cartilage, the first branchial arch from which the mandible arises [3].

In the following, we will discuss the two primary tumor groups of the jaw mentioned above, the odontogenic tumors and the non-odontogenic primary bone tumors; we will also discuss some typical odontogenic dysplasia forms and important differential diagnoses (e. g. osteomyelitis). A summary overview is provided in ▶ **Table 1**.

In addition, there are also a large number of other tumors that do not belong to either group, such as the squamous cell carcinomas that occur frequently in the oral cavity or the adenocarcinomas that grow into the jaw from the surrounding area, but rarely also lymphomas and multiple myeloma as well as secondary tumors (metastases).

Fortunately, most odontogenic tumors are benign and predominantly represent hamartomatous malformations; odontogenic carcinomas and sarcomas are extremely rare – the most common of these is still ameloblastic carcinoma.

However, it must be pointed out that the majority of malignant tumors involving the upper and lower jaw are carcinomas

▶ **Table 1** Abbreviated presentation of the new WHO classification of odontogenic and maxillofacial bone tumors from 2022, as discussed below. *removed from the current 2022 classification* (adapted and modified from [4]).

Category	Subcategory	Entities (selection)
Jaw cysts	further subdivisions were omitted in the current classification	radicular cysts, follicular cysts, odontogenic keratocysts; calcifying odontogenic cysts; fissural cysts
Odontogenic tumors	benign epithelial odontogenic tumors	Ameloblastoma, calcifying epithelial odontogenic tumor; odontogenic tumors (adematoid, squamous), ameloblastoma
	benign mixed epithelial and mesenchymal odontogenic tumors	Odontoma, ameloblastic fibroma
	benign mesenchymal odontogenic tumors	(Cemento)ossifying fibroma, cementoblastoma, odontogenic fibroma, odontogenic myxoma
	Malignant odontogenic tumors	ameloblastic carcinoma, sclerosing odontogenic carcinoma, odontogenic shadow cell and clear cell carcinoma
Giant cell lesions and bone cysts		central and peripheral giant cell granuloma, cherubism; aneurysmal and simple bone cysts
bone and cartilage tumors	fibro-osseous tumors and dysplasias	(cemento-)ossifying dysplasia, fibrous dysplasia; Segmental odontomaxillary dysplasia, ossifying fibromas (juvenile trabecular and psammomatoid)
	benign maxillofacial bone and cartilage tumors	Osteoma, osteochondroma, osteoblastoma (osteoid osteoma removed) Chondroblastoma, chondromyxoid fibroma; desmoplast. bone fibroma
	malignant maxillofacial bone and cartilage tumors	Osteosarcoma of the jaw, chondrosarcoma family; Rhabdomyosarcoma with TFCP2 rearrangement
hematolymphoid tumors, solitary plasmacytoma		*Lymphomas (primary bone lymphomas, secondary lymphoma involvement.) leukemic bone involvement; plasmacytoma/multiple myeloma*

that infiltrate the jaw from the surrounding area and destroy it [5]. We are talking about squamous cell carcinomas of the oral cavity (accounting for 90% of all tumors in this region), squamous cell and adenocarcinomas of the maxillary sinuses and the nasal cavity, as well as adenocarcinomas of the surrounding salivary glands, which can destructively penetrate the neighboring bony structures of the maxilla and mandible (▶ **Fig. 1**) [6]. These tumors as well as other tumor entities (e.g. extraosseous lymphomas, soft tissue sarcomas, neurogenic tumors, skin tumors, etc.) that do not originate in the gnathic system are ***not*** subject of the following discussion. An exception are maxillomandibular bone metastases, which will be briefly discussed at the end of the article.

Note

1. **Odontogenic tumors are rare and mostly represent benign or hamartomatous entities.**
2. **Much more frequently, however, the jaw region is infiltrated by malignant tumors (carcinomas) from the surrounding area.**

The current WHO classification of odontogenic and maxillofacial bone tumors from 2022

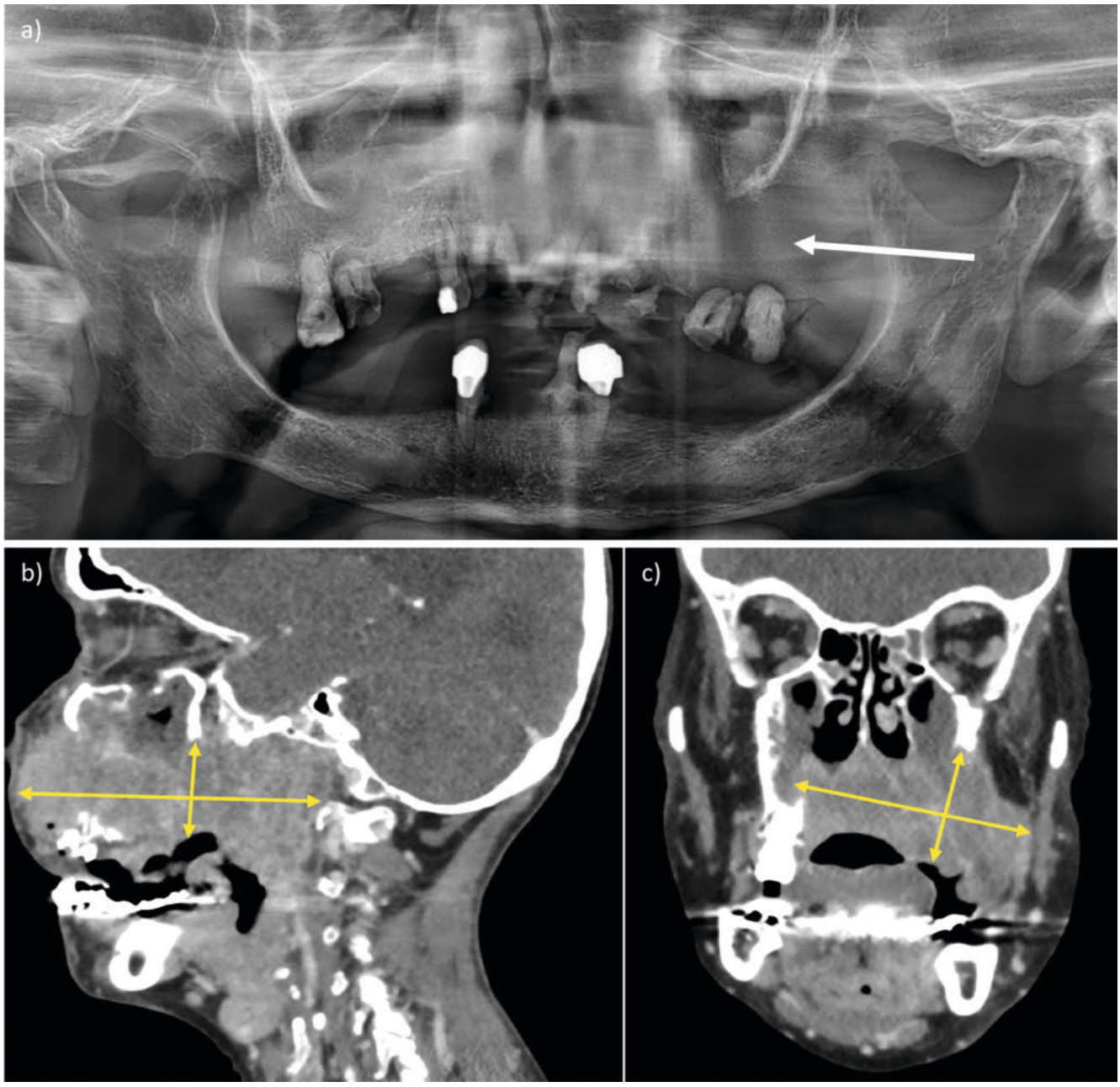
After the revision of the 3rd edition of the WHO classification of jaw tumors from 2005 was valid for over a decade before it was replaced by the 4th edition in 2017, the "brand new" 5th edition followed just five years later, in early 2022 [4]. This significant acceleration of the revision sequence is an expression of an exponential growth of molecular and genetic knowledge on the development of bone tumors of the jaw, which should quickly be incorporated into an adapted nomenclature against the background of a potential or already proven clinical benefit.

However, this article does not address the often very delicate innovations that are only relevant for specialists [7].

▶ **Table 1** therefore provides a deliberately shortened and selected overview of the current classification. It is intended to provide an overview of the multitude of different tumor entities, although in the following discussion only a part of them can be discussed in more detail, which also has a certain practical relevance.

Radiological differentiation and overview of bone tumors of the jaw

For reasons of space, this information was compiled and summarized in table format. The sensible and rational use of the radiological diagnostic armamentarium is shown in ▶ **Table 2**, and ▶ **Table 3** highlights the advantages and disadvantages (pros and cons) of the radiological (and nuclear medicine) imaging procedures mentioned above. A diagnostic algorithm for



▶ **Fig. 1** Oro-naso-palato-pharyngeal carcinoma (squamous cell carcinoma) with complete destruction of the left maxilla. 55-year-old patient with long-term nicotine and alcohol abuse. **a** OPG: in addition to a desolate dental status in the upper jaw and residual teeth in the lower jaw, obliterated bony structures can be seen in the upper jaw (arrow): Artifact or real? **b+c** Contrast-enhanced head and neck CT, sagittal, and coronal MPR: extensive tumor destruction of almost the entire maxilla with considerable enlargement beyond the anatomical upper jaw borders (double arrows).

radiologists based on the so-called "KISS principle" for jaw lesions is presented in **Infobox 1**.

Since it may be difficult for radiologists who are unfamiliar or only slightly familiar with jaw lesions to orient themselves in the multitude of jaw lesions, summary table overviews and graphic sketches of typically encountered entities are included in the individual chapters.

INFOBOX 1

Lesion analysis of the jaw according to the KISS principle ("keep it simple and straight").

Please note that the diagnosis resulting from the description or the comparison with existing empirical knowledge remains a suspected diagnosis until histopathological confirmation, which is particularly fraught with uncertainty in the jaw due to the duality of bone and teeth.

▶ **Table 2** "What do I do when?" – Compendium of the use of imaging diagnostics on the jaw for radiologists.

Modality	Indication/display options/limitations
OPG	The orthopantomogram (OPG) is a workhorse: it can provide a necessary overview; relationship of osteolytic/radiopaque lesions to the teeth; matrix analysis possible; location of the lesion in the jaw, but no exact topographical assignment, disturbing superprojection, especially in the upper jaw (limited destruction analysis).
DVT	Deep vein thrombosis (DVT) is another workhorse: it is necessary for all conspicuous or unclear jaw lesions, in order to clarify the relationship to the tooth and the surrounding jaw bone; exact destruction and matrix analysis is possible; local spread diagnostics in the bone (neighboring structures); however: it lacks soft tissue contrast, its ability to diagnose expansion is limited.
CT	Computed tomography is basically similar to DVT, but CT allows for surrounding diagnostics (staging) and soft tissue assessment thanks to contrast medium application (differentiation between cyst/necrosis/abscess/avid tissue); it is highly susceptible to metal artifacts.
MRI	Magnetic resonance imaging is rarely used on the jaw (no bone imaging, susceptible to artifacts from metal and air-containing spaces); it is useful for: acute osteomyelitis diagnostics, cyst diagnostics (especially differentiation between keratocysts and ameloblastoma; ABC); it also can be used to diagnose expansion with regard to permeative tumor infiltrations (bone, soft tissue).
Sonography	Sonography can be used for abscess diagnostics; in experienced hands, it can also provide: detection of cortical destruction with/without soft tissue tumor components; periosteal assessment in children; lymph node characterization (inflammatory vs. malignant); does not provide bone assessment.
Bone scintigraphy	Bone scans are useful for (chronic) osteomyelitis diagnostics with/without sequestrum; not suitable for tumor diagnostics due to low specificity and detail resolution.
FDG-PET (CT)	Fludeoxyglucose-18 (FDG) positron emission tomography is mainly used for oronasopharyngeal and paranasal malignant tumors (carcinomas); it is usually not useful due to the often ambiguous avidity patterns of rare odontogenic tumors; provides acute osteomyelitis diagnostics, if MRI is not possible.

▶ **Table 3** Comparison of common imaging modalities when assessing jaw tumors.

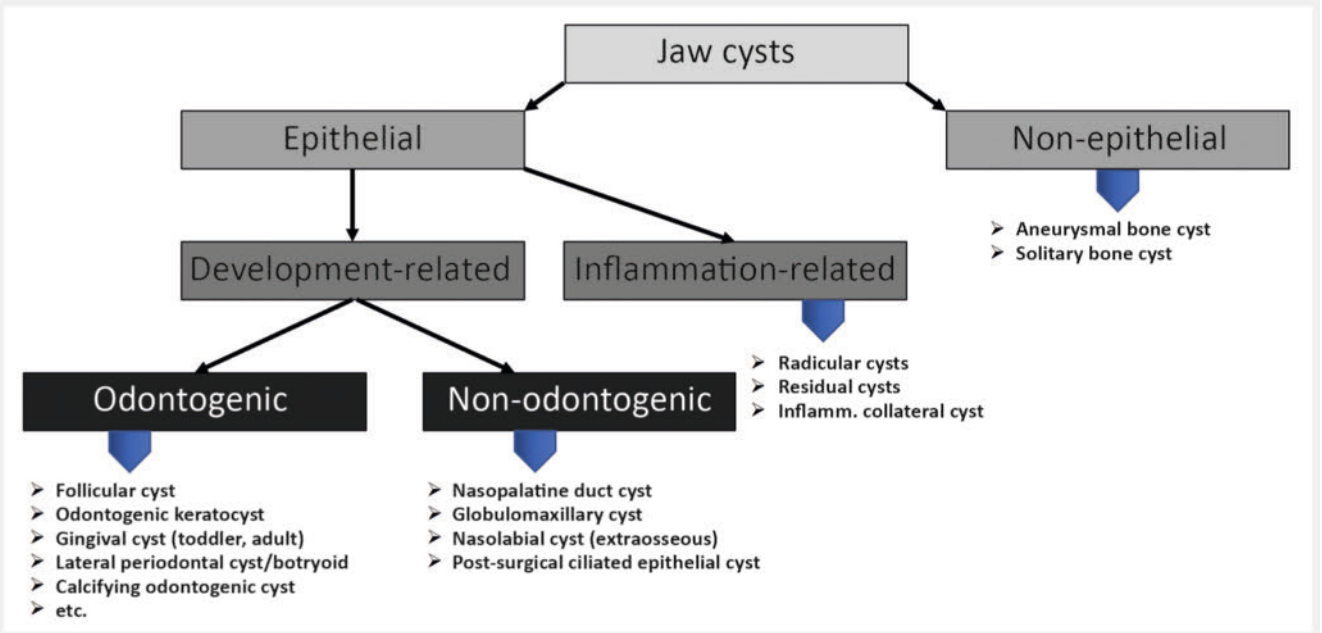
	Projection radiography (X-ray, OPG)	Radiation-based cross-sectional imaging (DVT, CT)	MRI/nuclear medicine
Pros	Overview: the lesion can be easily identified topographically	Freedom from overlay, multiplanar display; if necessary VRT, SSD, MIP, etc.	MRI: high soft tissue contrast: exact tumor demarcation (Bone marrow/surrounding area infiltration)
	Possibly even enables comparison with previous scans	high spatial resolution with great detail accuracy (allows for subtle matrix analysis)	MRI: Soft tissue characterization is possible: T1: Keratin, Methemoglobin; T2: Fluid, fluid-fluid level; fibrosis, siderosis, sclerosis; DWI: Abscess vs. tumor vs. keratocyst; contrast enhancement: necrosis vs. cyst; STIR/fatsat: Evidence of edema, etc.
	Lesion can be adequately characterized (radiolucent/radiopaque)	Density measurements possible (differentiation between fat – liquid – solid tissue)	Scinti/SPECT: robust and artifact-free Illustration of bone remodeling (benign or malignant)
	Tumor matrix analysis possible (fibrous, hard substance diff., matrix-free lysis)	exact definition of tumor location, destruction pattern and periosteal reaction	PET: artifact-free imaging of avid tumor foci in the jaw
	Assessment of tumor margins/periosteum (determination of biological growth behavior)	CT only: good soft tissue contrast and vitality assessment (contrast enhancement)	
	less susceptible to artifacts (e. g. dental filling materials)	DVT only: relative artifact robustness	
Cons	Upper jaw usually difficult to assess due to superposition	Radiation exposure (especially children)	MRI: Susceptibility to artifacts from metallic implants and air-containing spaces (e. g. maxillary sinuses)
	exact syntopy of the lesion in relation to teeth cannot be assessed	Diffuse tumor infiltration is difficult to determine (especially bone marrow space)	MRI: no analysis of the mineralized matrix (including teeth) is possible
	non-mineralized content of the lesion undetermined (cyst vs. solid osteolysis)	CT only: Artifact susceptibility to metallic materials	MRI: Tooth root reference is often inadequately displayed
	Soft tissue expansion cannot be assessed	DVT only: limited soft tissue contrast, not possible to administer contrast agent	MRI: little knowledge about MR pathomorphology of jaw tumors
	Motion and adjustment artifacts (OPG)		

- **Symptomatic bone lesion?**
  less reliable than the rest of the skeleton due to possible and frequent "toothaches," but it can mask serious bone lesions!
- **Patient age**
  odontogenic lesions and cysts in primary or mixed dentition; older patient age with an increase in potentially malignant lesions (carcinomas, metastases)
- **Anamnesis**
  known genetic abnormalities, underlying systemic disease with associated risks for teeth and jaw bone, previous surgical interventions
- **Lesion related to location in the jaw**
  Where is the lesion located? Upper jaw anterior/posterior? Mandible: Symphysis, corpus, retromolar, angulus, ramus, condylus? Central or peripheral?
- **Lesion related to the tooth**
  Is there a direct connection to the tooth or the tooth root? Retained tooth? Resorbed tooth bud? Is the tooth carious or otherwise infected?
- **Lesion in terms of shape and size**
  Form (single-chambered, lobulated, septate, multifocal); size (focal without bone destruction, extensive with ballooning, resorption, destruction of the local bone)
- **Lesion boundaries** (based on the Lodwick classification)
  Sharp, regular borders ("lesion can be traced with a pencil"); sharp, but irregular borders (tight transition); blurred borders, but geographical; still geographical, but completely blurred borders (moth-eaten); permeative bone destruction pattern
- **Lesion behavior in relation to neighboring structures**
  Displacing (spreading of the tooth roots and teeth; expansive neocortical formation); locally destructive (root destruction, bone resorption); infiltrating (per continuitatem from the bone into the soft tissue or vice versa); compartment crossing
- **Lesion density**
  Osteolysis (CAVE: Cyst already refers to an entity and is no longer a description); sclerosis (CAVE: there are several opacities in the jaw (bone, cement, dentin, enamel)); mixed sclerotic-lytic lesions
- **Lesion structure**
  Air/gas containing lesion; fatty lesion (density measurement!); soft tissue (solid lesion) or fluid (density measurement); contrast enhancement (avid lesion); differentiation of the hard substance: fibrous matrix (ground glass), spongiosa, compacta (> 1,000 HE), cement < dentin < enamel (with increasing density); dental filling materials including ceramics (CAVE: radiolucent plastics!), metallic foreign material present?

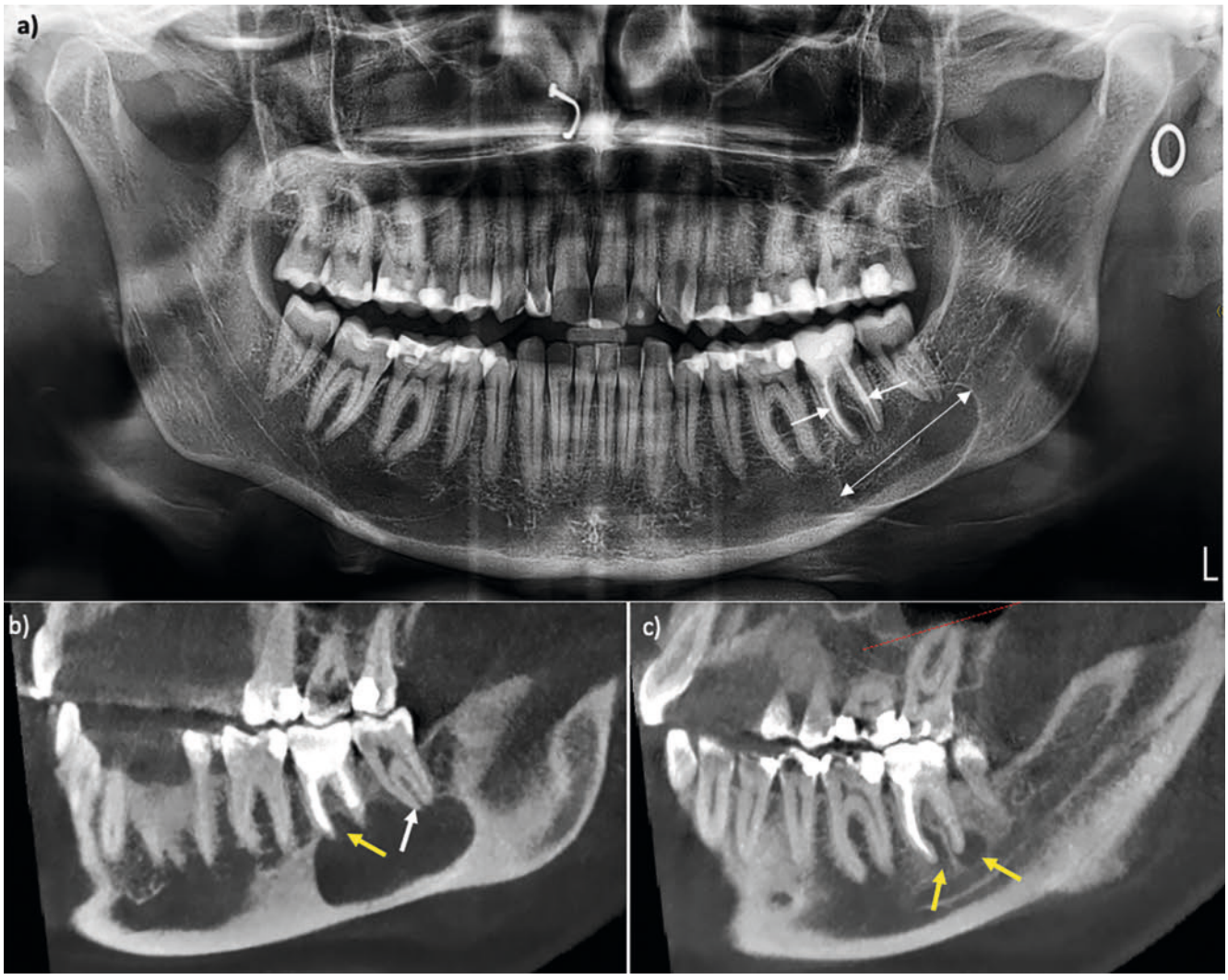
Jaw cysts

Jaw cysts represent a special feature of the gnathic bony system that must be discussed separately and specifically (▶ **Fig. 2**). Unlike the rest of the human skeleton, these are by no means just the well-known juvenile or aneurysmal bone cysts, but a whole series of cystic lesions, most of which are very specifically linked to the teeth or the periodontium (odontogenic cysts).

Non-odontogenic jaw cysts include fissural cysts (lateral and globulomaxillary cysts; medial or nasopalatal or median palatal cysts; median mandibular cyst), which have their embryological



▶ **Fig. 2** Overview of jaw cysts. This illustration is not a complete list of all odontogenic cysts. (Based on a lecture by PD Monika Probst, TU Munich, 2018, which was kindly made available.)



▶ **Fig. 3** Radicular cyst. 27-year-old woman. **a** OPG: large, narrowly marginal sclerosed cyst (double arrow) in the posterior mandibular region on the left with contact to the roots of the crowned and root canal treated tooth 37 (arrows), to a lesser extent also to 38. **b–c** DVT: Illustration of the relation of the root tips of 37 (yellow arrow) and 38 (white arrow) to the radicular cyst (**b**); a wide lateral section shows the actual exit of the radicular cyst from the root tips of 37 (yellow arrows in (**c**)).

origin from remnants of the epithelial crest, are mostly located in the anterior maxilla and affect 75 % of women [8]. They can usually be suspected or identified based on their characteristic localization.

The radicular cysts (apical or radicular cysts; ▶ **Fig. 3**) are basically of an inflammatory origin, as are the inflammatory collateral cysts (lateral periodontal cysts). Radicular cysts account for about 50 % of all jaw cysts [9]. They develop as a result of an inflammatory stimulus (e. g. propagated pulpitis due to deep caries) at the root tip from the so-called Malassez epithelial cell remnants. What is known as the root granuloma, on the other hand, represents a histological differential diagnosis, consisting of a chronic inflammatory conglomerate as a result of apical periodontitis without any epithelial lining.

Radiologically, the radicular cyst is a round, usually smooth-edged osteolysis that surrounds the root tip and has a more or less clearly recognizable marginal sclerosis. Depending on the duration and intensity of the inflammatory effect, reactive sclerosis will also be seen in the bony environment. However, the prerequisite is always a damaged, usually non-vital tooth. In the rarer lateral inflammatory periodontal cysts, the development process usually starts from irregularly laterally branching pulp ducts or marginal periodontitis. Radiologically, these cysts have a fundamentally identical appearance to radicular cysts, but they are located marginally along the tooth roots, but often close to the root tip.

Two non-inflammatory odontogenic cysts of great practical relevance must be distinguished from these, since they can already be recognized or suspected radiologically: the follicular cyst (dentigerous cyst) and the odontogenic keratocyst [10].

The follicular cyst represents a typical dysontogenic cyst, which always forms due to fluid accumulation between the reduced enamel epithelium and the non-erupted tooth crown; typically from the 3rd molars (“wisdom teeth”), but can also come

from other molars and premolars, sometimes even from canines, if they are displaced and have not broken through. Follicular cysts occur almost exclusively on permanent teeth; therefore, they are just as rarely observed in children's milk teeth as they actually only occur in connection with retained, displaced teeth.

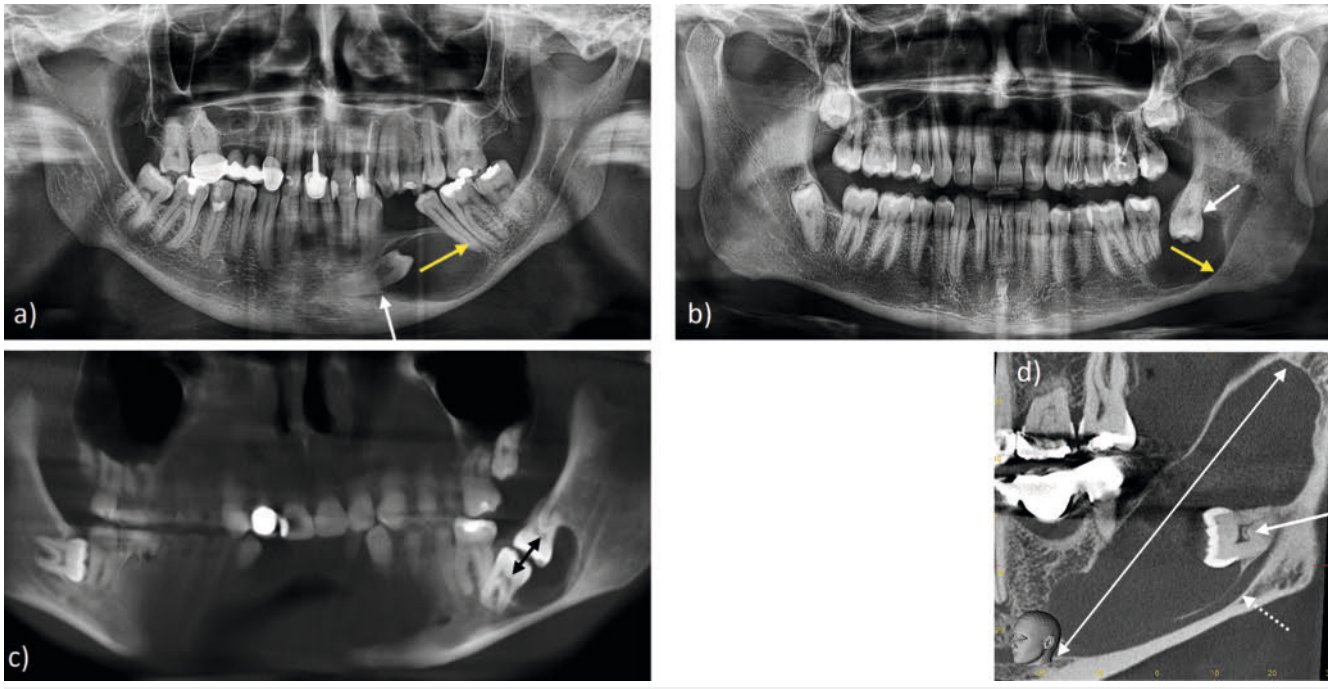
The follicular cyst is the second most common odontogenic cyst after the radicular cyst. In addition to its origin from an impacted tooth (▶ **Fig. 4**), these cysts either develop only narrowly around the impacted tooth crown (from a cyst size of 3–4 mm a follicular cyst is suspected) or the entire impacted tooth is enclosed in a large-volume cyst, whereby three morphological variants have been described depending on the inclusion of the crown and root of the impacted tooth [11]. However, the origin of the cyst can always be identified radiologically at the cervical/crown border, which facilitates identification as a follicular cyst. Although confusion with an ameloblastoma is possible due to its location in the posterior mandibular region, the detection of a displaced molar in the cyst suggests a follicular cyst (▶ **Fig. 5**). Odontogenic keratocysts as well as a number of systemic diseases (e. g. cherubism, mucopolysaccharidosis type IV, amelogenesis imperfecta, tuberous sclerosis and cleidocranial dysplasia) are part of the differential diagnostic considerations [11].

The odontogenic keratocyst typically occurs in the region of the 3rd molars, the angle of the mandible, and the ascending ramus of the mandible (65 %–85 %) (▶ **Fig. 6**). Histologically, the keratocyst is lined with a keratinized epithelial cell layer, can appear from cystic to solid and does not necessarily have to have a (retained) tooth crown, since they can also be derived from other odontogenic epithelial cell nests [12]. Radiologically, these are smooth-edged osteolyses of varying size with neocortical formation (scalloping) in large extensions. A multiple occurrence of keratocysts should raise suspicion of Gorlin-Goltz syndrome (basal cell nevus carcinoma syndrome) as well as the presence of hyperparathyroidism (osteitis fibrosa cystica). MRI offers specific identification options for the keratocyst:

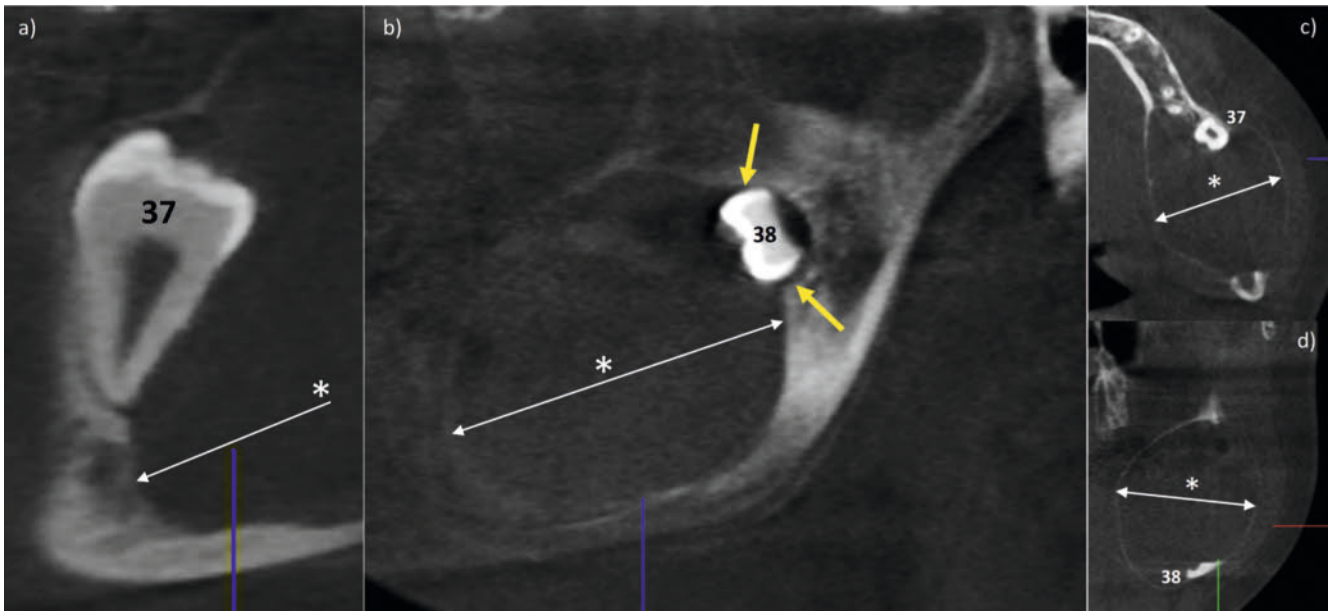
a) high native T1 signal due to keratin content;
b) diffusion restriction in DWI also due to keratin;
c) marginal contrast enhancement without nodular thickening (e. g. in ameloblastomas).

The extremely rare calcifying odontogenic cyst (so-called Gorlin cyst, not to be confused with Gorlin-Goltz syndrome) is only mentioned here, since they can imitate other, especially malignant tumors due to their irregular calcifications [13].

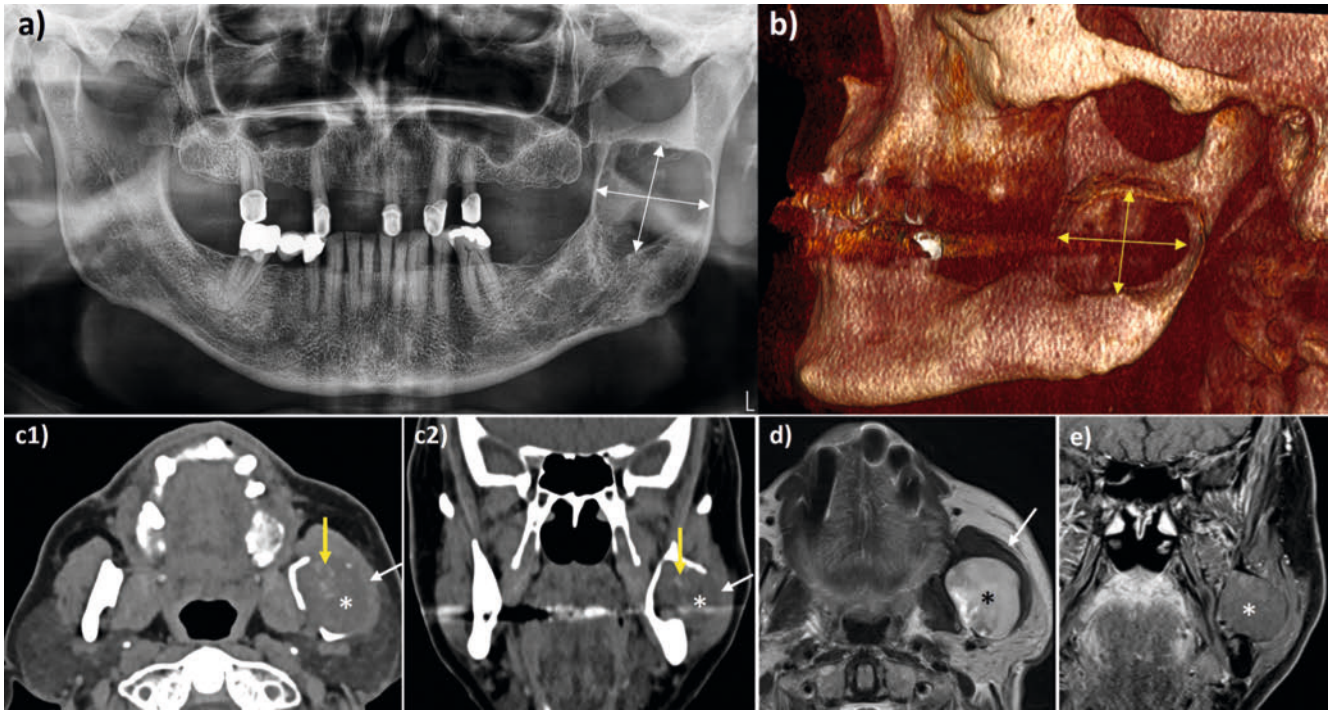
Other types of cysts include: residual, primordial, eruption, and gingival cysts, as well as lateral periodontal cysts. The globulomaxillary cyst has a typical configuration: it is drop-shaped and protrudes between the 2nd incisivus and caninus, displacing both and can be confused with a nasopalatine cyst [14]. However, Swiss oral surgeons point out that the globulomaxillary cyst is no longer an independent entity, but is only called that because of its anatomical location in the maxilla between the lateral incisor and the canine [15]. The so-called Stafne cavity is also not a cyst, but an anatomical variant of the norm in a typical location (retromolar in the mandibular angle on the lingula side below the N. aleveolaris inf.).



▶ **Fig. 4** A variety of follicular cysts. **a** OPG: 48-year-old patient with displaced supernumerary canine tooth, with a large cyst located at the cementoenamel junction (arrow) that is leading to displacement of the adjacent distal roots (yellow arrow); **b** OPG: 41-year-old patient: 38 rotated by 180° with cyst at the cementoenamel junction (arrow) with pressure on the mandibular canal (yellow arrow); **c** DVT: two opposing 37 and 38 (double arrow) that share a common cyst: 20-year-old man; **d** DVT: extensive cyst extending from region 36 into the mandibular ramus (double arrow), starting from the impacted tooth 38 (arrow), note the caudal displacement of the mandibular canal (dashed). arrow); DD keratocyst, ameloblastoma).



▶ **Fig. 5** Surprise finding of an ameloblastoma, which was initially thought to be a follicular cyst. 13-year-old boy with a strongly expansive space-occupying lesion in the posterior left mandible. CBCT sections. **a** mesial end of osteolysis (*) with displaced 37; **b** large osteolysis (double arrow *) that appears to originate from displaced 38 near the enamel border (yellow arrows); **c+d** huge expansive osteolysis (double arrow *) with eggshell-thin neocortex.



▶ **Fig. 6** Keratocyst. 72-year-old patient with a palpable tumor on the left ascending mandibular branch. **a** OPG: large, marginally sclerosed osteolysis in the left ramus mandibulae (double arrows); **b** shaded surface image from CT (VRT): oval hole defect (yellow double arrows); **c1** and **c2** each native CT image in the soft tissue window: expansive cystic bone lesion (*) with cortical resorption (white arrows); note the calcifications (yellow arrows); **d** T2 TSE axial: highly signal-intensity lesion (cyst, (*)) with displacement of the masseter muscle (arrow); **e** T1 Gd fs VIBE coronal: the cystic lesion (*) shows no enhancement.

▶ **Table 4** Overview of odontogenic and non-odontogenic cysts (selection); Note: Radicular, follicular and keratocysts >80 % of all jaw cysts.

Cyst type	Clinical-radiological characteristics
radicular cyst[1]	periapical osteolysis at the root tip (less frequently laterally along the root) with marginal sclerosis; always sets a **focalized** or dentally treated tooth or root canal
follicular cyst	pericoronal osteolysis always around a **retained/displaced tooth** (often wisdom tooth); the delicately marginally sclerotic cyst ends at the crown/neck transition of the tooth
Keratocyst	keratin-filled cyst, mostly in the posterior region of the mandible; important DD to ameloblastoma; lobulated osteolysis with marginal sclerosis; MRI offers differentiation option; CAVE! Frequent recurrences
Primordial cyst	**Degeneration state of a dental follicle**, therefore the tooth to the cyst is missing! Cyst itself with delicate marginal sclerosis; usually located in the dorsal mandible
Residual cysts	arise from the remains of pre-existing follicular or radicular cysts **after tooth extraction** and can continue to grow; interestingly, they are more common in the upper jaw!
Eruption cyst	known as a dentition cyst in a child: **Tooth bag** above the tooth that has not yet erupted; relevant only in case of inflammation or infection of the cyst
Globulomaxillary cyst[2]	today only as an expression of an anatomical cyst location between the 2nd incisivus and caninus in the upper jaw; according to current opinion, **it no longer counts as an independent entity**
Nasopalatine cyst (incisive duct cyst)	most common non-odontogenic cyst: arises from proliferating **epithelial remnants of the ductus nasopalatine** and is therefore located exactly median in the anterior hard palate; smooth bordered, symmetrical. Osteolysis
postoperative ciliated epithelial cyst	was newly introduced into the classification in 2022: arises from **artificial displacement of ciliated epithelium** from the nasal sinuses into the maxillary bone: usually asymptomatic. Osteolysis
Solitary bone cyst	**unicameral cyst** in the corpus mandibulae **without direct tooth reference**; radiologically and histologically identical to juvenile bone cysts of long tubular bones; traumatic genesis possible
aneurysmal bone cyst (ABC)	eccentric, lobulated osteolysis with sometimes extremely thin neocortical bone: MRI thanks to intralesional **level detection (fluid-fluid levels) diagnostic**; CAVE: secondary ABC in primary tumors
calcific. odontogenic cyst	Shadow cell-containing tumor whose ghost cells calcify (irregular calcifications): very rare and actually **not** diagnosable radiologically

1: This also includes lateral periodontal cysts and inflammatory collateral cysts; 2: The authors are familiar with the scientific debate about the existence or non-existence of the globulomaxillary cyst as an independent entity and choose explicitly to disregard it.

Note

1. **Jaw cysts are common: radicular cysts require an infected (avital) tooth; follicular cysts are associated with impacted teeth.**
2. **It is possible to confuse kerato- and follicular cysts with ameloblastomas, as well as with malignant tumors, when using projection radiographs.**
3. **Focal sclerosis, irregular borders, and the detection of solid parts in the MRI require histological confirmation.**

▶ **Table 4** and ▶ **Fig. 7** provide a compendium of typical jaw cysts.

Odontogenic tumors

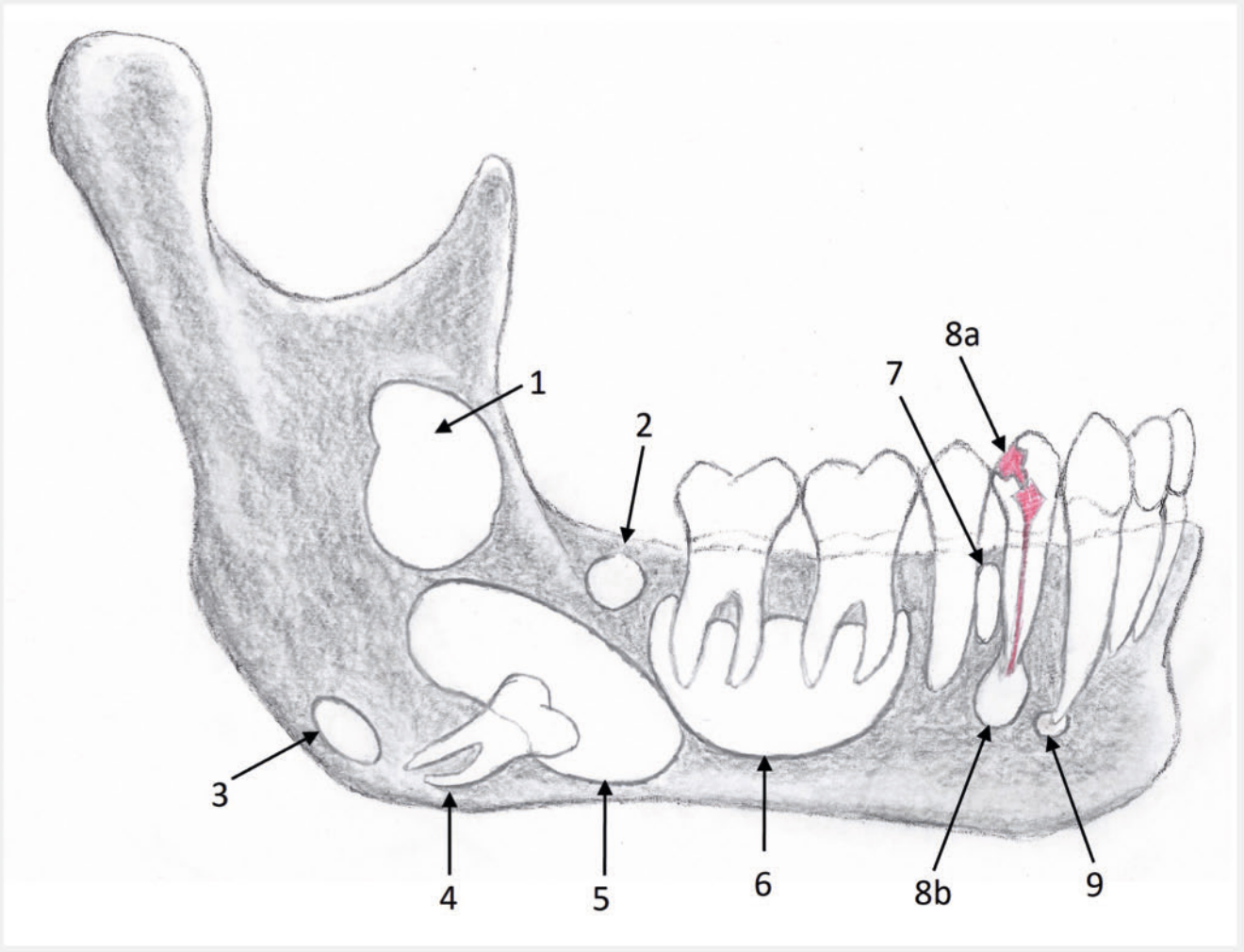
Benign epithelial odontogenic tumors

This group includes, among others, the adenomatoid odontogenic tumor, the squamous odontogenic tumor, and the calcifying epithelial odontogenic tumor (Pindborg tumor), which we will not discuss because they are rare; however, more important – also for the radiologist – is the ameloblastoma, which is listed in five subgroups: conventional, unicystic, extraosseous, adenoid, and – metastatic.

The ameloblastoma is the most common tumor of epithelial odontogenic origin (▶ **Fig. 8**). It is formed from remnants of the dental lamina or enamel organ. The very rare extraosseous ameloblastomas arise from the so-called Serres remnants, i. e. remnants of the dental lamina remaining in the gingiva (approx. 1 %) [16].

The radiologically characteristic feature is the multicystic, lobulated appearance (or soap-bubble appearance) of conventional ameloblastoma, preferably in the mandible (80 %). The tumor may appear very expansive, which may lead to extensive neocortical formation (somewhat inaccurately referred to as “bone swelling”). Tooth root resorptions are typical for ameloblastoma, which in turn also suggests a malignancy. MRI provides a good opportunity to identify solid tumor parts and thus differentiate a conventional ameloblastoma from a cyst. The unicystic type of ameloblastoma, on the other hand, represents a differential diagnosis to the unicameral cyst; with presence simultaneously of an impacted tooth, but also with the follicular cyst; there is a positive coincidence to it [16, 17] (▶ **Fig. 5**). Long-standing, large ameloblastomas can transform into malignant lesions, although this cannot be diagnosed radiologically based on the local findings themselves, but rather on the appearance of metastases [18].

The treatment of ameloblastoma is problematic, as it recurs in 60–80 % of cases after simple curettage, which is why marginal or



▶ **Fig. 7** Typical cysts of the mandible. **1** – keratocyst, primordial cyst; **2** – residual cyst (e.g. after tooth extraction); **3** – Stafne cavity; **4** – impacted and displaced tooth; **5** – follicular cyst (dentigerous cyst); **6** – simple bone cyst, DD eosinophilic granuloma, keratocyst, ameloblastoma, etc.); **7** – lateral periodontal cyst (DD inflammatory periodontal cyst); **8a** – caries profunda with pulpitis; **8b** – radicular cyst; **9** – root granuloma.

segmental resection is recommended. Unicystic ameloblastomas can be enucleated, if they are so-called luminal variants. In the mural type, extensive (post)resection is necessary due to local wall infiltration (personal communication with Prof. Baumhoer, Basel). There are late recurrences and these are described in the literature as difficult cases to treat [19, 20].

Note

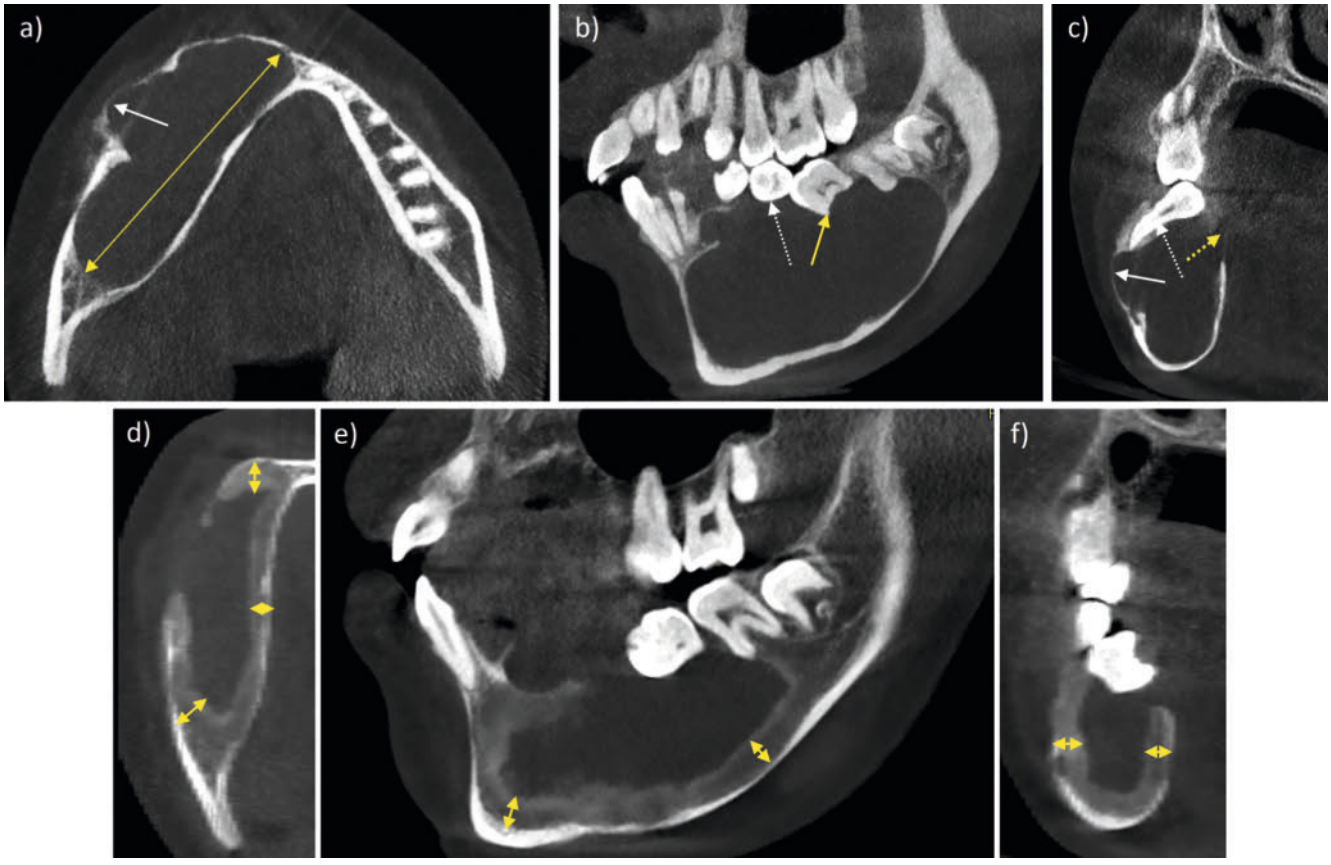
1. **Ameloblastomas are diverse, cystic, but mostly solid osteolyses.**
2. **There are no clear projection radiological imaging characteristics that would prove an ameloblastoma (remember this!). However, MRI can help to identify the solid parts of the tumor.**

Benign, mixed epithelial-mesenchymal odontogenic tumors

According to the current classification, these include, in addition to the odontoma, the primordial odontogenic tumor, the ameloblastic fibroma, and the dentinogenic ghost cell tumor [19]. However, only the odontoma will be discussed here.

The odontoma is the most common odontogenic tumor besides ameloblastoma, possibly even the most common, since many odontomas remain undetected or unmentioned. Odontomas are hamartomas that consist of hard tooth substance and a soft tissue portion and are usually a few millimeters to 2 cm in size, but can also grow up to 6 cm in size. A distinction was made between so-called compound odontomas and complex odontomas (nomenclature from 2017); nowadays only the compound odontoma is discussed (▶ **Fig. 9**). While the former occur in the anterior maxilla, the latter are predominantly found in the posterior mandible. Their clinical significance lies mainly in the fact that they block the eruption path of teeth that have not yet erupted, which leads to tooth misalignment and additional related gnathic problems [21].

Radiologically, mature, large odontomas form easily recognizable tooth-like structures, which are usually located between the roots of already erupted teeth or in the vicinity of a tooth that is



▶ **Fig. 8** Ameloblastoma. 15-year-old boy. **a–c** extensive, cystic osteolysis in the entire right mandibular corpus with enlargement to the symphysis (double arrow). Eggshell-like prominent neocortex on the vestibular side (white arrows). Root resorption of a molar (yellow arrow) and tooth displacement (dashed arrows); partial cortical resorption visible (dashed yellow arrow). Ameloblastoma, 3 months after curettage: **d–f** reduced expansion of osteolysis with significant circular remineralization of the lesion (yellow double arrows).

about to erupt. They have the same radiographic density as normal teeth and can be surrounded by a varying width, but often only narrow, osteolysis margin. However, in early stages and with only a small amount of calcified matrix, odontomas can cause differential diagnostic problems with regard to differentiation from calcifying odontogenic cysts and ameloblastic fibro-odontoma. The extremely rare case of an ameloblastic fibrodentinoma in a child, which also led to tooth eruption obstruction, was recently published [22]. Further differential diagnoses are osteoma and supernumerary teeth.

When multiple odontomas occur, the general radiologist should be reminded of the multiple occurrence of osteomas: here too, an association with Gardner syndrome (familial colorectal polyposis) has been described, as well as for otodental syndrome (abnormal dental crowns, megalodontia and sensorineural hearing loss) [23].

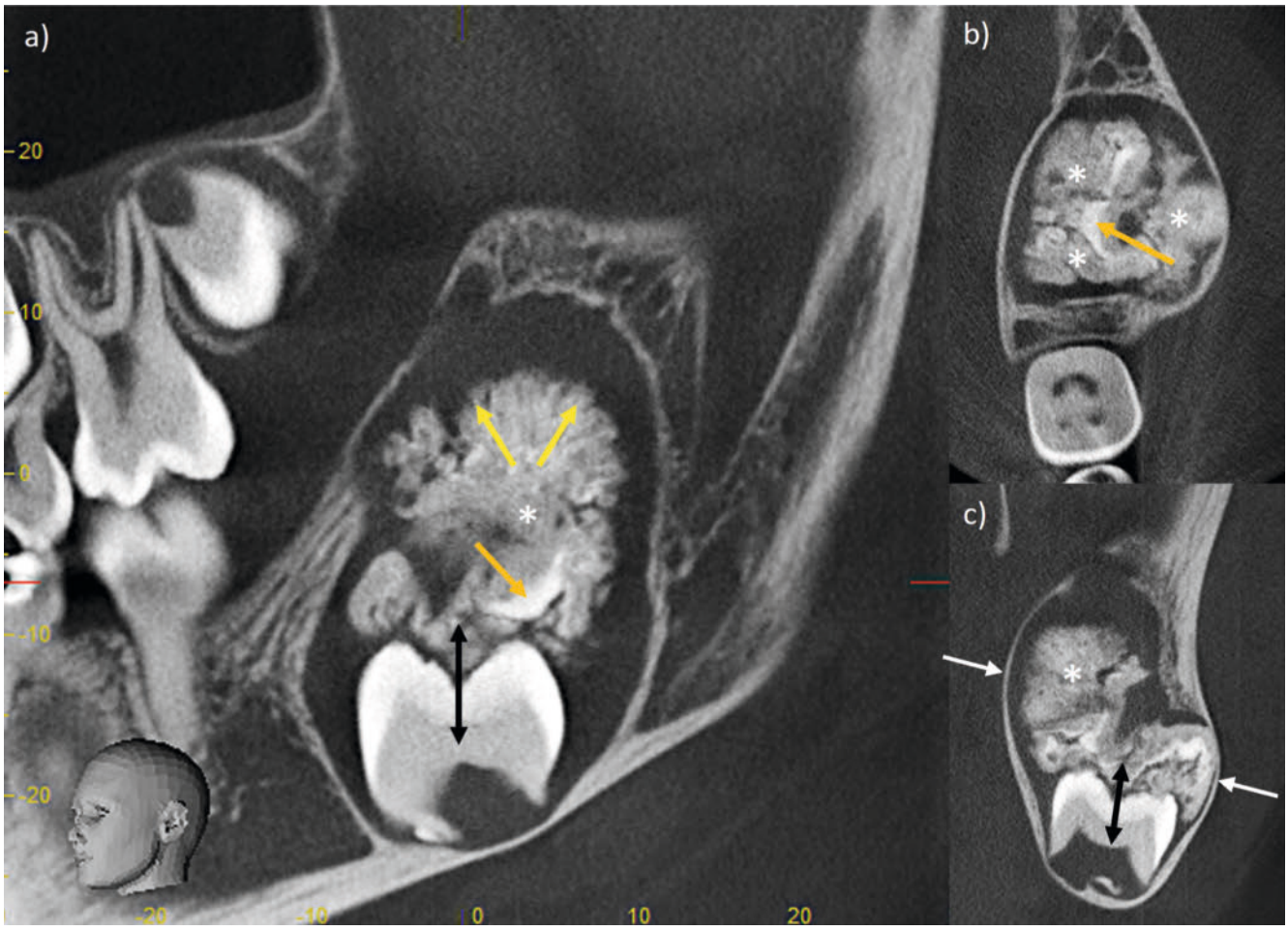
Benign mesenchymal odontogenic tumors

This group includes cemento-ossifying and odontogenic fibroma as well as cementoblastoma and odontogenic myxoma.

The cemento-ossifying fibroma (or simply ossifying fibroma) has now been defined as a completely independent entity. Women are affected significantly more often than men (ratio approx. 5:1). In the most common sporadic form, the neoplasia originates from progenitor cells of the periodontal membrane, which can differentiate to varying degrees into fibroblasts, osteoblasts, and cementoblasts, creating a “colorful” picture both histologically and radiologically. They are solitary, mostly large lesions in the mandible (90 %), much less frequently in the maxilla, which grow expansively and become increasingly radiopaque depending on age or stage of maturation as a result of mineralization (▶ **Fig. 10**) [24]. Supragnathic forms of ossifying bone fibroma can also affect the upper facial skull. Due to their slow but steady growth, ossifying fibromas should be resected [25].

The odontogenic myxoma is the third most common odontogenic tumor (after ameloblastoma and odontoma) and is found in two thirds of the mandible. It has a myxoid extracellular matrix and is rich in collagen fibers, therefore it appears as a mineralization-free osteolysis, which “swells” the mandibular bone in a multilobular manner, which radiologically appears as a typical soap-bubble or honeycomb pattern (soap-bubble, honeycomb appearance) [26].

The cementoblastoma is a rare benign tumor (about 0.7–8 % of all odontogenic tumors), which typically occurs in the root region of the 1st molars of the lower jaw [27]. It arises from the cementum or cement-like layer of the molar root sheath, thus it consists of a radiopaque hard substance, which has a narrow osteolytic



▶ **Fig. 9** Complex or compound odontoma. DVT in multiplanar playback. Above tooth 37 there is a large hard substance formation (* in **a–c**) consisting of different hard substance components (dentin, enamel) and appearing lobulated to gyrated (yellow arrows in a) with a surrounding, soft tissue-dense osteolytic margin and cortical ballooning (neocortical formation; white arrows in **c**). It prevents 37 from breaking through (black double arrows in **a**, **c**). Note the visible additional enamel evidence (orange arrows in **a**, **b**). A radiological differentiation between complex and compound odontoma is not possible; the former has also been omitted in the new nomenclature (2022).

margin at its periphery (▶ **Fig. 11**). The tumor surrounds the root tip; the root itself can then no longer be distinguished. In this respect, there are difficulties in differential diagnosis from periapical cemental dysplasia and hypercementosis, and less frequently from odontoma or chronic periapical osteitis [28].

The odontogenic fibroma is special in that the peripheral type, i. e. the extraosseous manifestation in the gingiva, is more common than the central form of odontogenic fibroma located in the jaw bone itself [29].

Note

1. **Tumors that form hard tissue or matrix can be better identified radiologically; this applies equally to odontomas and ossifying fibromas.**
2. **The decisive factor is the radiological identification of benign hard tissue lesions; their final subclassification is of secondary importance.**

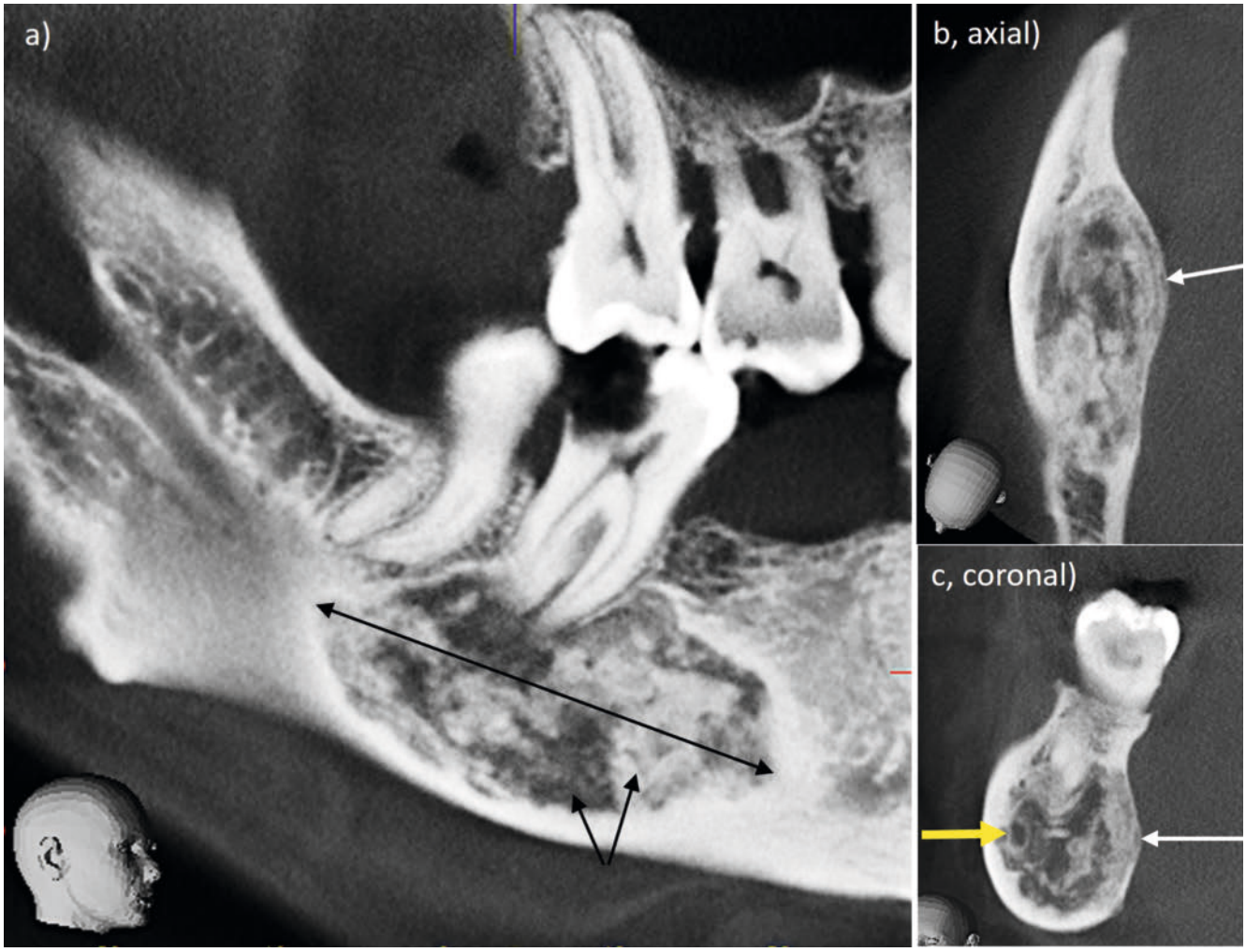
A summary of typical mandibular bone lesions is shown in ▶ **Table 5**, ▶ **Table 6** and ▶ **Fig. 12**.

Giant cell lesions and non-odontogenic bone cysts

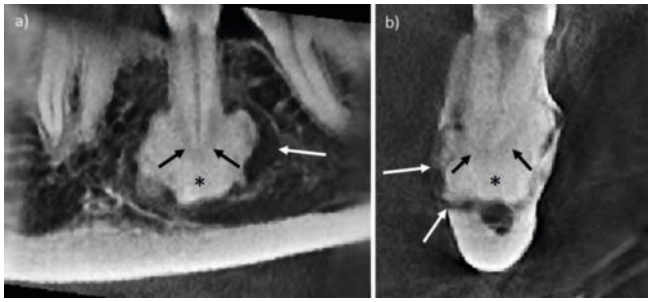
6.1 Central and peripheral giant cell granuloma

The distinction between central and peripheral giant cell granulomas refers – as always in the jaw – only to their location: the central giant cell granulomas are primarily located intraosseously in the upper or lower jaw, while the peripheral giant cell granulomas represent reactive gingival or alveolar lesions that originate from the periodontium and only secondarily erode the jaw bone or displace tooth roots (known as giant cell granulomas) [4].

First, an explanation of the term: the synonymous term reparative giant cell granuloma included a causal explanation in that these lesions often occur in connection with trauma (and consecutive bleeding), rarely inflammation, or as a result of foreign body inoculation, even after dental manipulation. They are not that rare, accounting for 1–7 % of all benign jaw lesions, and occur primarily in childhood and early adulthood [31].



▶ **Fig. 10** Ossifying fibroma. DVT. **a** Large subapical, marginally sclerotic osteolysis in region 45–47 (double arrow) with inhomogeneous new bone formation (black arrows) in a fibrous matrix (unmineralized portion). **b–c** mild expansivity of the lesion lingually (arrows) with neocortical formation, but without destruction. Buccal displacement of the mandibular canal (yellow arrow).



▶ **Fig. 11** Cementoblastoma. **a+b** DVT: periapical dental hard tissue of tooth 35 with preserved demarcation of the apical cement layer (black arrows); narrow perilesional osteolysis (white arrows). Note: The process is homogeneously cement- or dentin-tight (*) and emerges over a large area from the pericemental tooth root surface without a demarcated periodontal gap.

Giant cell granulomas are unique to the jaw and occur in a similar form only on the phalanges. In principle, they are benign, but both their radiological and histopathological appearance require in-depth knowledge of this type of lesion in order to avoid misinterpretation – possibly even a malignant interpretation of the findings (▶ **Fig. 13**).

The defining histological feature, the osteoclastic giant cell component of the tumor, leads to bone resorption, which typically appears as chambered osteolysis, but can also cause cortical destruction, thus manifesting radiologically as an aggressive lesion. There are case reports showing extensive destruction of the anterior maxilla (most common site of manifestation) by giant cell granulomas [32]. The lesions can undergo sclerosis from their edges through osteoblastic activation.

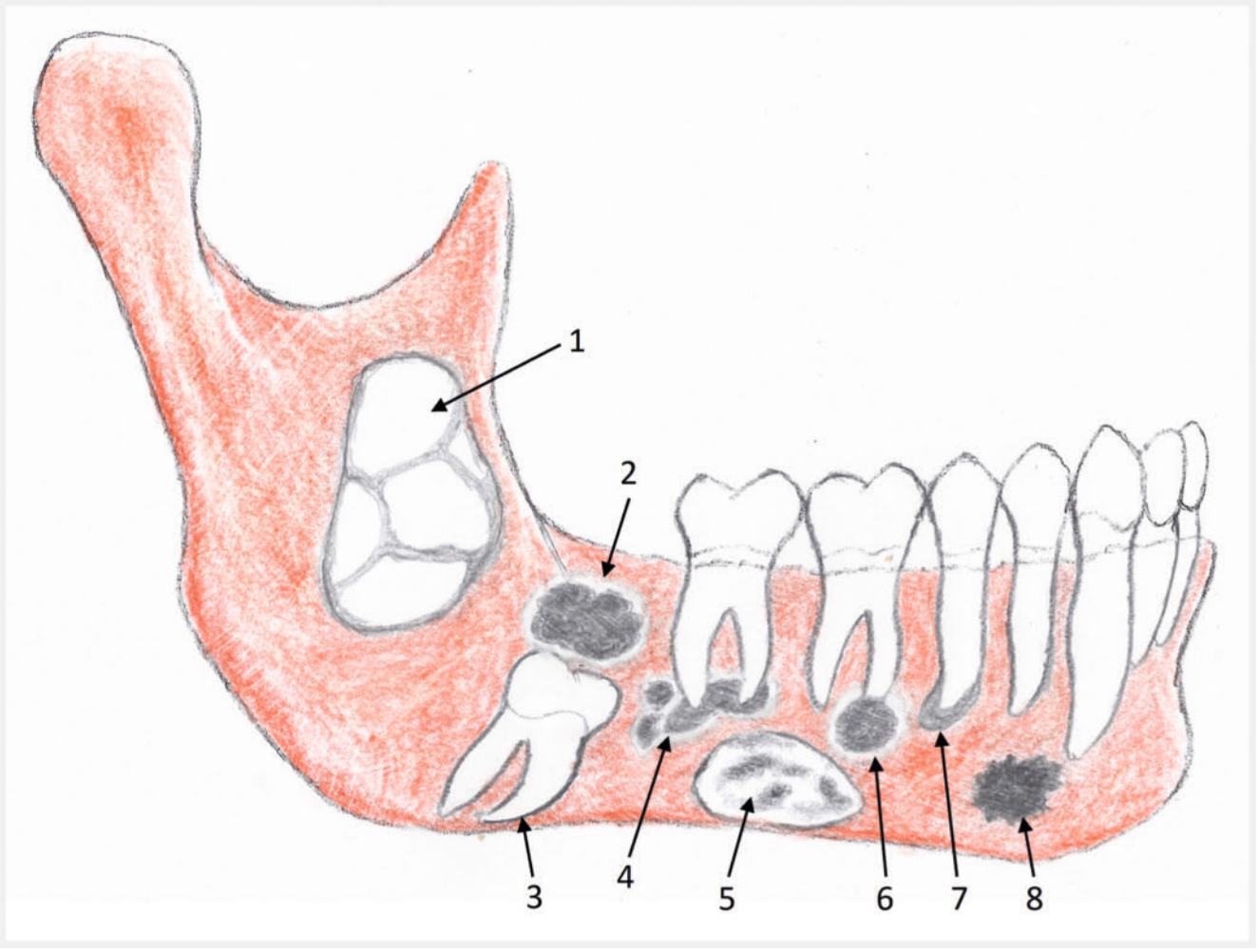
Due to the coincident encounter of intralesional blood or its degradation products and the osteoclastic giant cells, there is a differential diagnostic pitfall with regard to the differentiation from aneurysmal bone cysts, brown tumors (osteoclastomas) in hyperparathyroidism and cherubism when examining the lesion histopathologically alone [33, 34].

▶ **Table 5** Overview of location and frequency of bony lesions of the mandible (selection). Based on: Dunfee BL, Sakai O, Pistey R, Gohel A: Radiologic and pathologic characteristics of benign and malignant lesions of the mandible. RadioGraphics 2006; 26: 1751–1768 (DOI: 10.1148/rg.266055189) [30].

Classification acc. to …	Division by …	Entities
Localization	Anterior mandible	cemento-osseous dysplasia, giant cell granuloma (central), odontoma, less common: ademantoid odontogenic tumor
	posterior mandible	follicular cyst, odontogenic keratocyst, solitary bone cyst, ameloblastoma, amelofibroma, ossifying fibroma, cementoblastoma, odontogenic myxoma, Pindborg tumor
	non-specific	radicular cyst; metabolic diseases (e. g. hyperparathyroidism, renal osteodystrophy)
Frequency: Cysts	very common	Radicular cysts, follicular cysts
	quite common	odontogenic keratocyst, solitary bone cyst (traumatic, hemorrhagic, simple); Stafne cavity (not an actual cyst)
	rare	calcifying odontogenic cyst (also contains solid parts), aneurysmal bone cyst (primary/secondary)
Frequency: benign tumors	very common	Odontoma
	quite common	ameloblastoma, cemento-osseous dysplasia, ossifying fibroma
	less common	calcifying epithelial odontogenic tumor (Pindborg tumor), ameloblastic fibroma, odontogenic myxoma, cementoblastoma
	rare	clear cell, squamous and ademateid odontogenic tumor, calcifying odontogenic tumor (Pindborg tumor)
Frequency: malignant tumors	very common	squamous cell carcinoma from the adjacent mucosa
	quite common	metastases, plasmacytoma/multiple myeloma, lymphoma, leukemia; adenoid-cystic and mucoepidermoid carcinomas from the surrounding area
	rare	odontogenic carcinomas, odontogenic sarcomas, odontogenic carcinosarcomas; non-odontogenic sarcomas (e. g. osteosarcoma)

▶ **Table 6** Overview of location and frequency of tumors, cysts, and lesions in the mandible. It is a compilation of the most important, typical, and common lesions in the lower jaw.

Entity	Topography	Occurrence
Follicular cyst (dentigerous cyst)	most frequently: 3rd mandibular molar	up to 75 % in the lower jaw
Keratocyst (keratocystic odontogenic tumor)	most frequently in the corpus and ramus of mandible	up to 70 % in the lower jaw
solitary bone cyst	typically in the corpus between canine and the 3rd molars, less frequently at the symphysis (chin), ramus and condyle	> 90 % in the lower jaw
Stafne cavity	Proximity to the angle of the mandible under the mandibular canal	only in the lower jaw
Ameloblastoma	retromolar in the angulus/ramus of the mandible (association with follicular cyst and impacted tooth possible)	up to 80 % in the lower jaw
ossifying fibroma	tooth-bearing part of the lower jaw	up to 90 % in the lower jaw
Pindborg tumor (calcific. epithelial odontogenic tumor)	in the pre- and molar region of the lower jaw	> than 2/3 in the lower jaw
Osteoma (bone islands, idiopathic osteosclerosis, periapical osteopetrosis)	mostly near the 1st molars: periapical or distant to the tooth root	up to 90 % in the lower jaw



▶ **Fig. 12** Typical matrix-forming tumors or tumor-like lesions of the mandible. **1** – ameloblastoma; **2** – odontoma, here as a barrier to eruption (note lysis margin); **3** – impacted tooth; **4** – cemento-osseous dysplasia; **5** – ossifying fibroma; **6** – cementoblastoma (note lysis margin); **7** – periapical hypercementosis; **8** – osteoma (note pseudopodia; no lysis margin).

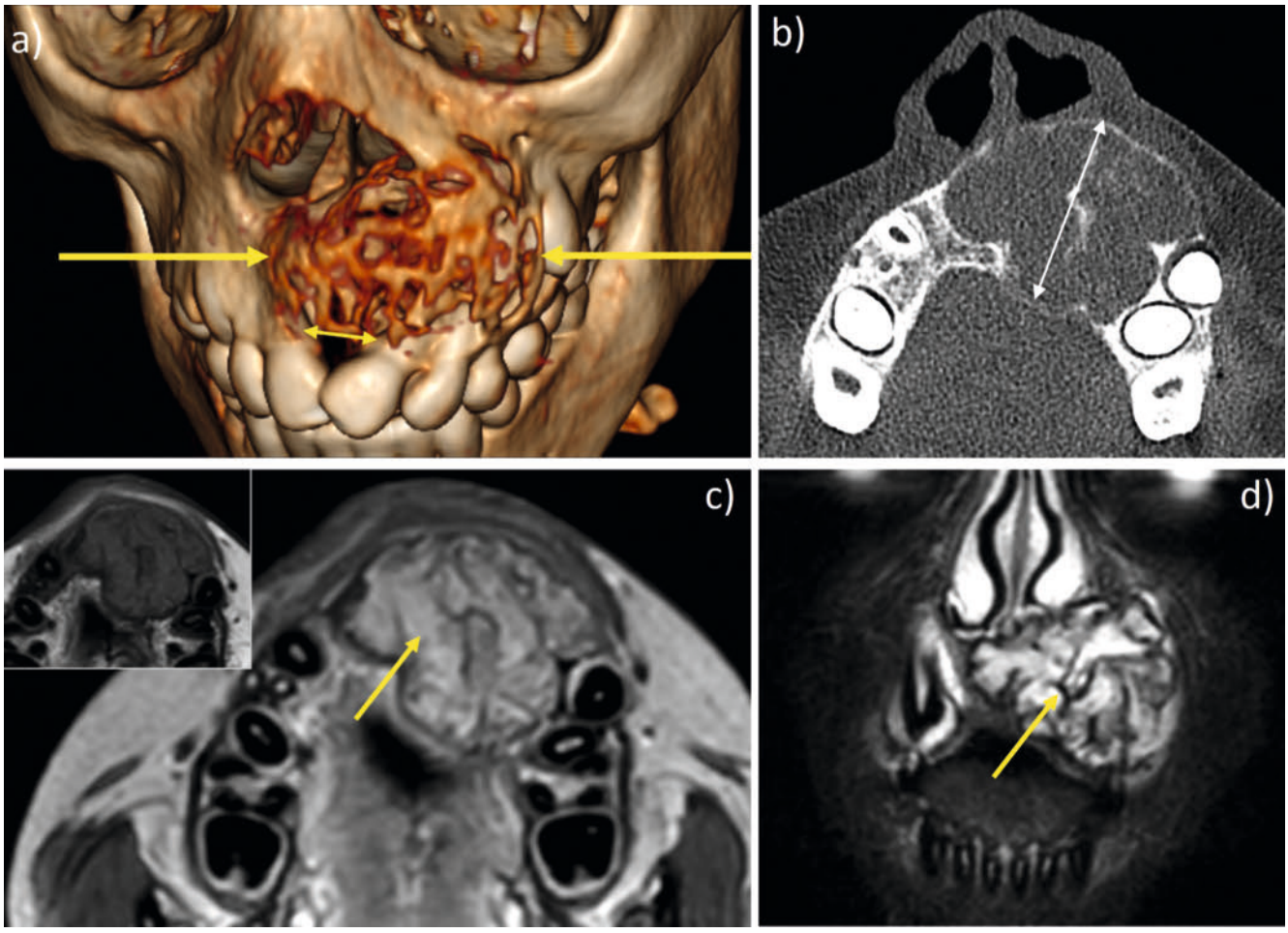
Non-odontogenic bone cysts

These are the aneurysmal and the simple bone cyst of the jaw, which have no fissural or odontogenic relationship. These are the same non-epithelial bone cysts that are found in other locations of the human skeleton.

The aneurysmal bone cyst (ABC) of the jaw also consists of giant cells like the central giant cell granuloma, which, in contrast to these, line large, multi-chambered, blood-filled sinusoidal cavities. In contrast to the previously discussed jaw pathologies and their X-ray or CT morphological appearances, MRI is now gaining in importance because it can detect the characteristic fluid-fluid levels within the blood-filled cavities of the multiple septate bone cysts in the mostly swollen jaw bones [35]. If these MR tomographic signs can be demonstrated, the diagnosis is considered to be largely confirmed by imaging alone, especially in young patients. However, it must be noted that – as in other parts of the human skeleton – this is not a secondary ABC, especially in connection with giant cell tumors, osteo- and chondroblastomas, but also osteosarcoma of the jaw. It is therefore imperative to search the ABC for possible solid tumor components in contrast-enhanced MRI and – in case of doubt – to biopsy it. Molecular genetic detection of the USP6 rearrangement is helpful here, as it proves a primary ABC; however, the lack of detection does not automatically indicate a secondary ABC [36].

At this point, we should add a brief comment about what are known as solid ABCs: Freyschmidt already said in 2009 that “the term reparative giant cell granuloma of the extremity bones is used synonymously with that of solid giant cell granuloma” and goes on to say that this also applies, by analogy, to reparative giant cell granuloma of the jaw [37]. It is important to understand that these giant cell-containing lesions are non-neoplastic in nature and histologically cannot be distinguished from what are known as brown tumors in hyperparathyroidism. However – and Freyschmidt also points this out – the osteoclast-rich form of osteosarcoma, for example, must be carefully excluded [37].

The solitary bone cyst of the jaw represents, in a sense, the gnathic counterpart to the juvenile bone cyst of the long tubular bones. Here, too, young patients are affected, often with previous jaw trauma. They are solitary, sometimes large, single-chambered

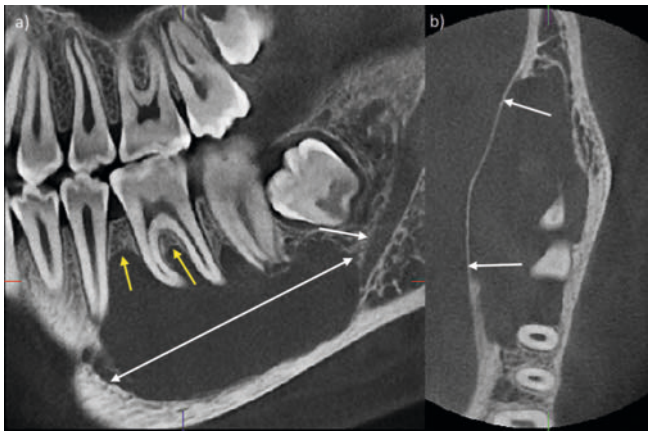


▶ **Fig. 13** Reparative giant cell granuloma. 10-year-old boy with asymmetric swelling of the left maxilla. **a** shaded surface image from VRT-CT: extensive protrusion and destruction of the infranasal alveolar process of the maxilla (arrows) with tooth deviation (double arrow); **b** axial native CT: massive bone expansion (double arrow) with neocortical formation and matrix calcification; **c** MRI: T1 after contrast administration: the tumor with avid contrast enhancement (yellow arrow) compared to the native T1 image (small insert image); **d** T2 fatsat coronar: expansive tumor with septal-like structure (yellow arrow).

cysts in the chin or corpus area of the lower jaw (▶ **Fig. 14**). The greatest challenge for the radiologist is to differentiate these benign bone cysts from all the other, already mentioned and very numerous cysts or cyst-like tumors of the jaw, but especially from ameloblastomas and keratocysts, which are the two most common cyst-like osteolytic tumors of the jaw [38].

Note

1. **Although non-odontogenic cysts of the jaw cannot be distinguished in principle from their identical counterparts in the rest of the skeleton, they represent a differential diagnostic challenge due to the abundance of odontogenic and fissural cysts in the jaw.**
2. **Reparative giant cell granulomas are a jaw-specific characteristic that must be differentiated from malignant tumors due to their radiological pattern of destruction.**



▶ **Fig. 14** Solitary (juvenile) bone cyst. Biplanar DVT: Adolescent patient with an extensive, well-demarcated, but barely marginally sclerotic osteolysis in the left mandibular corpus (double arrow in **a**), displacing the mandibular canal (white arrow in **a**). The root tips of teeth 35–37 appear to be in the cyst; note the finger-shaped bulges of the cyst interdentally and interradicularly (yellow arrows in **a**). The axial slice impressively shows the pressure-induced neocortical formation on the lingual side (arrows in **b**) without perforation. Differential diagnosis: Langerhans cell histiocytosis ("floating teeth").

Conflict of Interest

The authors declare that they have no conflict of interest.

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