ORIGINAL ARTICLE OPEN ACCESS

A Retrospective Radiologic Analysis of the Treatment Outcomes of Ameloblastomas

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Received: 24 July 2024 | **Accepted:** 14 November 2024

Funding: The authors received no specific funding for this work.

Keywords: ameloblastoma | bone regeneration | radiology | recurrence | treatment

ABSTRACT

Introduction: The current study reviewed the postoperative radiologic findings of 156 cases of ameloblastoma diagnosed at a tertiary institution in South Africa.

Methods: Histologically diagnosed cases of ameloblastomas between 2012 and 2022 were retrospectively reviewed. Only cases with both pre- and postoperative radiographs of diagnostic quality were included in the study. The demographics, treatment and follow-up radiologic findings, including recurrences, were assessed. This clinical data was collected from all available patient records and histopathologic reports.

Results: Seventy-nine cases of ameloblastoma (50.97%) diagnosed at the institution had post-treatment radiographs available and were included in the study for further analysis. Conservative treatment, including marsupialisation and/or enucleation, was performed in 11 cases (13.92%). The recurrence rate for conservatively treated cases was 44.4% after a mean follow-up of 31.4 months. Tumour resection was performed in 72 cases (91.1%), including 4 recurrent cases previously treated conservatively. Tumour recurrence was only noted in 4 cases (7.5%) treated via surgical resection after a mean follow-up of 25 months. Spontaneous bone regeneration was seen in 19 cases (35.8%) of ameloblastomas treated via surgical resection.

Conclusion: Ameloblastomas are benign neoplasms with high recurrence rates, emphasising the need for appropriate treatment and extended follow-up periods. The high recurrence rate reported in cases of ameloblastoma managed conservatively highlighted its inappropriate use in treating conventional subtypes. The presence of bony regeneration in this study was higher than the reported literature, correlating with the overall younger age of the current sample.

1 | Introduction

Ameloblastoma (AB) is a benign odontogenic neoplasm with localised destructive behaviour and high reported recurrence rates [1, 2]. This results from neoplastic tumour islands infiltrating beyond the macroscopic or radiologic margins [3]. Treatment for AB varies by subtype, ranging from conservative methods like enucleation or curettage to more radical approaches such as surgical resection [3–5]. In most instances, they are treated by radical surgical resection, which may involve segmental resection or hemimandibulectomy/hemimaxillectomy, with 1.5–2 cm bony margins extending beyond radiologic boundaries.

Ameloblastomas are neoplastic; hence, tumour recurrence is only possible if neoplastic cells remain after treatment. Therefore, the recurrence rate of ameloblastomas highly depends on the

treatment modality [3, 4]. The recurrence rate for conventional ABs is 8% for radical surgery versus 41% for conservative surgery [5], highlighting the limitations of conservative treatment for conventional ABs. In comparison, the recurrence rate for unicystic ABs has been reported at 3% for radical treatment and 21% for conservative surgery [5]. The reported high recurrence rates for ABs treated conservatively have resulted in some authors, advocating for the inclusion of a bony margin for all cases of AB, regardless of the subtype [6]. However, in general, the literature still advocates that the luminal and intraluminal variants of unicystic ABs may be treated conservatively by simple cystectomy. This reflects the biological behaviour of these unicystic variants, whereby a fibrous connective tissue wall confines the neoplastic epithelial cells of the tumour [2]. Unfortunately, areas of extension beyond this boundary (mural proliferations) may be underestimated in unicystic ABs and may only be confirmed after the entire cystectomy specimen is evaluated. If mural proliferations are present, secondary resective surgery is indicated to remove the remaining neoplastic islands. Tumour recurrences usually occur within 5 years after treatment [3]. Other reports indicate that 47% of recurrences are detected after 5 years, advocating an extended follow-up period [7]. In a 15-year review of recurrent ameloblastomas, the authors found that a small number of cases can recur in the previously affected soft tissue site following jaw resection [8].

Due to approximately 46%–82% of ABs harbouring *BRAF* mutations, novel targeted therapies have gained interest over the past decade [9, 10]. *BRAF* inhibitors have been approved for treating melanoma, non-small-cell lung cancer [11, 12] and other solid tumours with *BRAF* mutations, including ameloblastomas [10]. Reported cases in the literature of ABs receiving *BRAF* inhibitors have rendered significant improvements and responses; however, considerable side effects and response variations have been reported [9, 11]. In some cases, these targeted therapies were used to reduce the size of the tumour for ultimate resection, reducing patient morbidity, especially in cases involving children [10, 11].

The current study retrospectively reviews the postoperative radiologic findings of a large cohort of ABs treated at a tertiary institution in South Africa.

2 | Materials And Methods

Histologically confirmed cases of ameloblastomas diagnosed within the Department of Oral and Maxillofacial Pathology, University of Pretoria, between 2012 and 2022, were collected. Only cases with a confirmed histopathologic diagnosis with both pre- and postoperative radiographs of diagnostic quality were included in the study. First, the haematoxylin- and eosin-stained slides of included cases were collected, where the diagnosis of ameloblastoma and histopathologic subtype (conventional vs. unicystic) was confirmed using clinicopathological correlation. Only cases with sufficient tissue to confirm the subtype were included. The patient demographics, initial radiologic presentation and treatment performed were collected from all available patient records. Resection margins were reviewed from the respective histopathologic reports. The available radiographs were collected from the Departmental database, including panoramic radiographs and/or cone-beam computed tomography scans. The follow-up radiologic imaging was assessed for recurrences and other treatment outcomes.

3 | Results

One hundred and fifty-six (156) confirmed ABs with preoperative radiographs were collected during the study period. Only 79 (50.6%) cases had post-treatment radiographs available and were included in the study. The mean age of included cases was 30.2 years, with a 1.03:1 male-to-female ratio.

Only 3 cases (3.8%) were diagnosed as unicystic, with the remaining classified as conventional ABs. Most cases were located in the mandible ($n = 77$, 97.5%). The two maxillary cases involved both the anterior (central incisor to canine) and posterior regions of the jaws. Cases affecting the mandible primarily involved the posterior regions, including the ramus ($n = 47$, 59.5%), followed by both regions ($n = 47$, 36.7%), with a single case limited to the anterior region only. Radiologically, most cases showed focal areas of loss of demarcation ($n = 45$, 57%), with the rest remaining well-demarcated. Multilocular lesions were noted in 57 cases (72%). High frequencies of cortical destruction ($n = 69$, 87.3%) were noted.

Definitive treatment was performed at a mean period of 20.7 months after the initial radiographic examination (median 9.17). Conservative treatment, including marsupialisation and/or enucleation, was performed in 11 cases (13.92%) (Table 1). Four cases of conventional AB (5.1%) were treated via marsupialisation, with these cases having a mean age of 14.8 years, and 3 cases presenting with a unilocular appearance. These four cases recurred at 7, 16, 31 and 60 months, respectively. Enucleation was performed in 7 cases (8.9%), with a mean age of 37.5 years. Five of these cases had a unilocular radiologic appearance, with 2 cases diagnosed as unicystic AB. Two cases were lost to follow-up, and no recurrences were seen in the 5 cases that presented for follow-up radiologic assessment (3, 5, 17, 54 and 90 months, respectively).

Resections were performed in 72 cases (91.1%), including the 4 marsupialisation cases that recurred after initial conservative treatment. One unicystic case with extensive ramus involvement was resected. Only 53/72 (73.6%) of the included resection cases had radiologic follow-up imaging available after treatment. The mean follow-up period was 25.8 months (median 17, range 1–112 months). Tumour recurrence was only noted in 4 cases (7.5%) treated via surgical resection. Histology reports of the resections were available in 3 of these cases with one case resected at another institution. Two cases had reports of clear margins, with one having involved margins. All resection cases were reconstructed with a prefabricated reconstruction plate (Figure 1), and 22 cases (30.6%) had a silastic spacer placed as part of the surgical reconstruction (Figure 2). Only 6 cases (8.3%) received bone augmentation or fibula-free flap placement at the initial resection and reconstruction surgery.

During the study period, radiologic evidence of bone fill in the resected area was seen in 11 cases (20.8%) (6 via silastic spacer,

5 fibular bone graft). No evidence of bone fill was seen in cases treated with a reconstruction plate only, one case treated via a fibular flap and 16 cases (72.7%) treated with silastic spacers. The prefabricated reconstruction plate was rejected in 5 cases (2 with silastic spacers).

Spontaneous bone regeneration (Figure 3) in a region outside an area of bone augmentation was seen in 19 cases (35.8%) treated via surgical resection. The average age of patients presenting with bone regeneration was 28 years and included 10 females and 9 males. In these cases, the histopathologic resection report was available in 17 cases and was reported as tumour-free in 14 of the 17 cases (82.4%). In the other 3 cases, the tumour was present at the resection margins, mainly at the buccal and lingual aspects. In one patient, the piece of reactive bone was excised as it was suspected to be a sign of tumour recurrence. Following histopathologic evaluation, no recurrent or residual tumour cells were observed in the bony fragment, confirming its regenerative nature (Figure 4).

TABLE 1 | Outcomes of ABs treated conservatively versus resection.

Treatment	*n* (%)	Cases with follow-up	Mean follow-up period (months)	Treatment outcomes			
				Bone fill	Plate rejected	Bone regeneration	Recurrence
Conservative	11 (13.9)	9 (81.8)	31.4	4 (44.4)	n/a	—	4 (44.4)
Marsupialisation	4 (36.4)	4 (100)	28.5	n/a	n/a	—	4 (100)
Enucleation	7 (63.6)	5 (71.4)	33.8	4 (80)	n/a	—	—
Resection	72 (91.1)	53 (73.6)	25.8	11 (20.8)	5 (9.4%)	19 (35.8)	4 (7.5)
Reconstruction plate only	44 (61.1)	25 (56.8)	25.4	—	3 (12%)	8 (32)	2 (8)
Silastic spacer	22 (30.6)	22 (100)	24.3	6 (27.2)	2 (9.1%)	11 (50)	1 (4.5)
Fibula flap	6 (8.3)	6 (100)	26.3	5 (83.3)	—	—	1 (16.7)

4 | Discussion

Ameloblastoma is the most common odontogenic neoplasm and is especially prevalent in Africa [2, 13]. The mean age of presentation in the current study is earlier than that reported in other studies [14]. This finding is supported by the literature reporting that patients in developing countries, in particular from Africa, present with ABs at an earlier age [7, 15]. The predilection for the mandible and, specifically, the posterior region is well known in ABs [16–19], with frequent extension into the ramus complex [20]. The high rate of multilocular lesions corresponds to the literature [21], with higher rates of cortical destruction reported in the current study (87% vs. 29%), explaining the higher rates of loss of border demarcation [21].

Unicystic ABs are common variants of ABs, representing approximately 21% of all cases [20]. The low numbers of unicystic AB in the current study are likely due to numerous cases being excluded due to limited tissue or cases being enucleated without follow-up radiographs. Only following histopathologic assessment of the entire cystic lesion can a diagnosis of unicystic AB be confirmed [6, 22].

Due to the high prevalence of AB, paired with its ultimate treatment and reconstruction, it poses a significant burden on the healthcare system. The first observation from this study is that only 51% of patients who presented to the institution with ABs had records of surgical treatment for the lesion at the same institution. This may be due to patients being treated at other institutions or defaulting due to fear or other patient-related constraints. This study also reported a long duration between initial examination and definitive treatment. This could be due to limited theatre time or limited availability of reconstruction equipment. Delayed access to healthcare in developing countries is well known and leads to challenges in managing ABs [23]. These delays in treatment are also often caused by external factors, such as difficulty in travelling to healthcare facilities from remote areas, finances or other constraints.

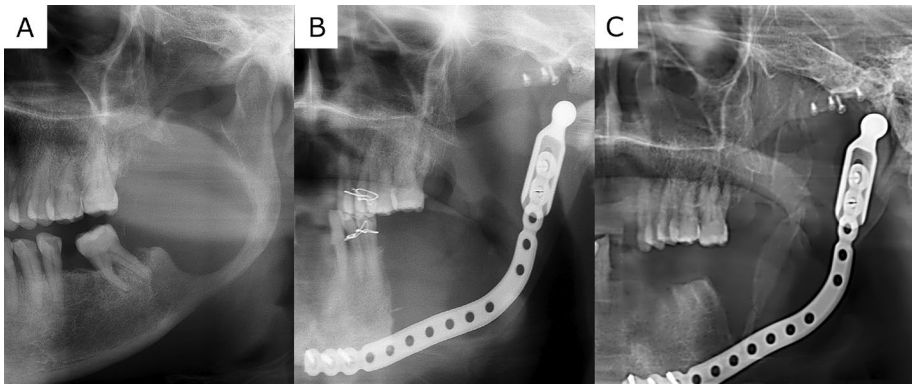

FIGURE 1 | (A) Preoperative radiograph of a unilocular conventional AB. (B) Immediate postoperative radiograph showing reconstruction of the tumour with a prefabricated plate only. (C) 45-month postoperative radiograph showing bone formation in the ramus region.

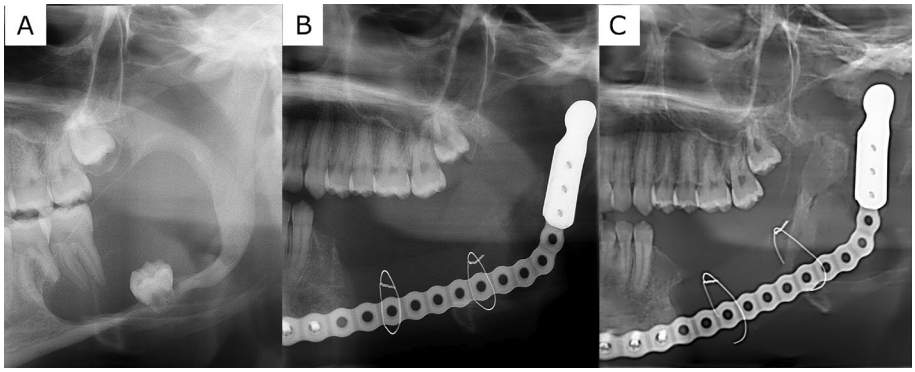

FIGURE 2 | (A) Pre-operative radiograph of a unilocular conventional AB. (B) Immediate postoperative radiograph showing resection with reconstruction using a prefabricated plate and silastic spacer. (C) 15-month postoperative radiograph showing bone formation in the ramus region.

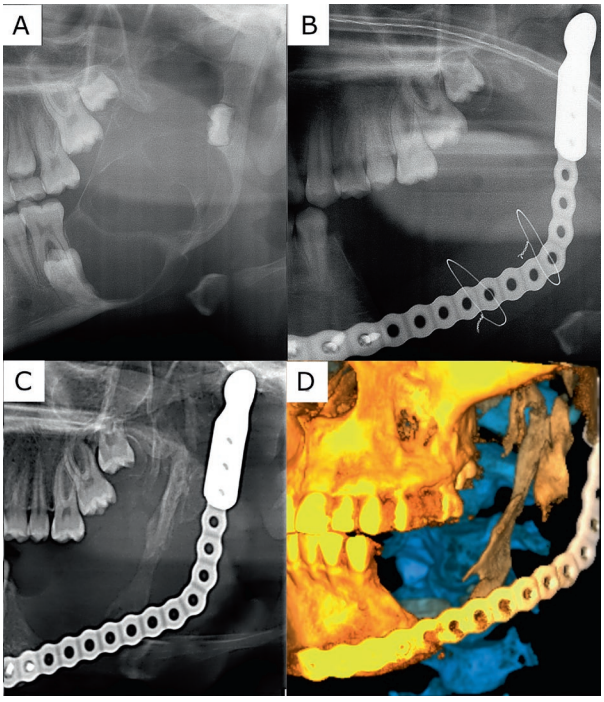

FIGURE 3 | (A) Preoperative radiograph of a multilocular conventional AB. (B) Immediate postoperative radiograph showing resection with reconstruction using a prefabricated plate and silastic spacer. (C) 22-month postoperative panoramic radiograph showing bone formation in the ramus region and on (D) CBCT imaging.

The risk of recurrence for ABs following conservative treatment is more than three-fold higher than radical surgery [5, 14, 24–26]. These figures have resulted in authors advocating radical treatment for both unicystic and conventional ABs. The treatment of recurrent ABs has also been investigated, showing that even after three rounds of conservative surgery, ABs may still recur, with radical surgery resolving the recurrence [26]. This high reported recurrence rate for ABs treated conservatively revolves around the surgery leaving residual neoplastic cells, allowing for continuous growth. However, no significant differences in recurrence are noted between marginal and segmental resection [14]. In the current study, 44% of recurrences was noted for conservative treatment versus 7.5% for cases treated via resection. Although resection and reconstruction are the mainstay of treatment, functional limitations may occur, such as chronic pain, change in appearance and difficulty in chewing and speech, resulting in psychological discomfort [29]. In a systematic review of the literature, only 26% of AB cases underwent oral rehabilitation after surgery, significantly impacting patient's quality of life [29]. Marsupialisation of conventional ABs was performed in young patients, likely due to the high morbidity of resections. However, all cases recurred and had eventual resection. The follow-up period only surpassed the 5-year mark in 11.4% of cases treated at the institution, showing a significant lapse in follow-up, likely due to constraints previously discussed.

Postoperative complications of radical surgery include infection at the reconstruction site, plate exposure, fracture or

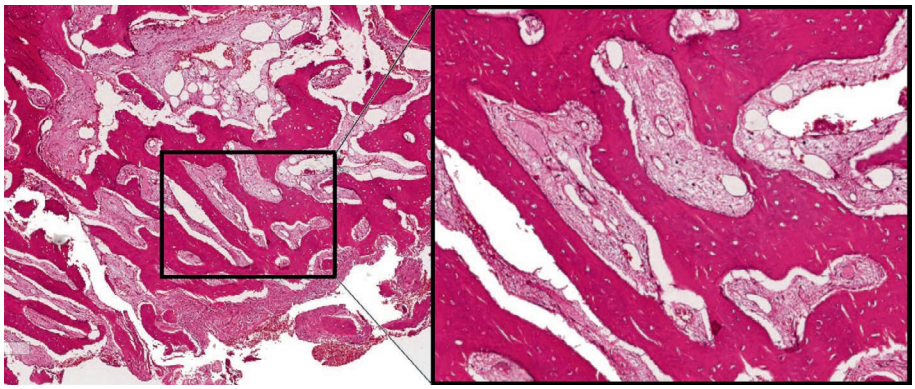

FIGURE 4 | H&E-stained histopathologic image of the regenerated bone removed due to suspected tumour recurrence. The sections show vital cancellous bone with fibro-fatty connective tissue and no signs of neoplastic cells.

loss and graft failure [29]. A 2012 study by Ferretti et al. [27] recommended an intermediate step in mandibular reconstructions to provide structural support for the healing of soft tissues and to maintain space for final bony grafts. The silastic spacer is a space maintainer consisting of a rigid ramus unit and a flexible silicone body unit that is secured to the reconstruction plate using screws and wires. The spacer is left in situ for 6–8 weeks to allow mucosal healing, then removed and replaced by a bony graft. The advantage of this procedure was the better contour of bony grafts, compared to free flaps, and the more predictable results along with soft tissue healing. A follow-up study found that if this procedure is performed correctly, a successful bone fill to restore the height and morphology of the mandible is achieved in 88% of patients [28]. However, the disadvantage is that a two-step procedure and prolonged spacer retention may result in extraoral extrusion [27]. In the current study, silastic spacers were commonly used; however, it was noted that not all patients returned for the second bone augmentation procedure. Ultimately, bone fill was only noted in 27% of cases, with plate rejection noted in 9% of cases.

Radiologic investigation plays a significant role in managing AB cases, including initial assessment and determination of resection margins. Furthermore, post-treatment clinical and radiologic follow-up of at least 10 years postsurgery is recommended [23, 26]. A systematic review analysing the radiologic features of recurrent ameloblastomas found that most cases presented with a multilocular appearance [3, 7, 30, 31]. The authors identified, amongst other factors, that tumour size (> 6 cm), cortical destruction and encroachment of anatomical structures were important features in predicting tumour recurrence [30]. Furthermore, Li et al. [32] reported that lesions with poorly defined radiologic margins typically show higher recurrence rates. This further highlights the importance of detailed radiologic analysis for cases of ABs. Compounding these factors, Merbold et al. [33] also reported that delayed treatment may result in lesion progression over time, complicating its management.

Bone regeneration is a well-known phenomenon after the enucleation of jaw cysts without bone grafting procedures [34]. However, in such cases, significant bone remains behind at the lesion periphery, and the basal bone remains intact. The unusual occurrence of bone regeneration after segmental jaw resection has also been reported in the literature [35–37]. The first reported case was described in 1946, [37] after which at least 32 cases have been reported [38]. The theories explaining this occurrence revolve around the presence of an intact periosteum, local infection or stresses on the remaining bone. Overall, bone regeneration is a rare occurrence (2%), with an equal sex distribution and a mean age of 26.6 years, with a statistically significant higher occurrence in younger patients [38]. In the current study, the incidence of radiologic bony regeneration was higher (35.8%); however, the younger age correlated with the literature. The size of defects reached up to 15 cm and signs of bony regeneration occurred as soon as 2 weeks postsurgery with a mean period of 4 months [38]. The regenerated bone resembled cortical bone stumps but did not span the entire width of the defect and lacked thickness. In a significant number of cases (30%), the periosteum was excised completely, and a bone fracture theory was employed. This new bony growth was theorised to be caused by the release of growth factors stimulating undifferentiated mesenchymal cells to produce new bone [38].

In the current study, 3 cases exhibiting radiologic evidence of bony regrowth had positive resection margins on histopathologic analysis. Additionally, 2 out of 4 cases with clinical signs of tumour recurrence also demonstrated bony growth. This raises the question of whether this bony reaction could indicate tumour recurrence from residual tumour tissue. However, 17 cases with radiologic signs of bony regrowth showed no recurrence to date, and histopathologic analysis confirmed clear resection margins in 14/17 cases with available reports. This bony growth was excised in one case, and no evidence of neoplastic cells was found. A report by Mesgarzadeh et al. [36] also noted bony regeneration in a case not associated with tumour recurrence after a 7-year follow-up period. Only long-term follow-up will resolve this question.

The limitations of the current study include a lack of extensive follow-up, a common issue in resource-limited countries. Despite this, the study underscores significant postoperative radiologic findings of treated ABs, providing valuable insights into the outcomes and challenges faced in such settings.

Author Contributions

Chané Smit: conceptualisation, data curation, formal analysis, investigation, methodology, writing – original draft, writing – review and editing. Liam Robinson: data curation, investigation, methodology, writing – review and editing. Felipe P. Fonseca investigation, project administration, supervision, writing – review and editing. Willie F.P. van Heerden: investigation, project administration, supervision, writing – review and editing. André Uys: investigation, project administration, supervision, writing – review and editing.

Ethics Statement

This study was approved by the University of Pretoria, Faculty of Health Sciences Research Ethics Committee (Reference no.: 723/2022). All procedures followed the ethical standards of the Helsinki Declaration of 1975, as revised in 2008.

Conflicts of Interest

The authors declare no conflicts of interest.

Data Availability Statement

The data of the current study is summarised in the figures and tables. Access to raw data is subject to approval by the University of Pretoria, Faculty of Health Sciences Research Ethics Committee.

References

1. C. Smit, L. Robinson, J. Ker-Fox, F. P. Fonseca, W. F. P. van Heerden, and A. Uys, "Clinicoradiologic Features of Ameloblastomas: A Single-Centre Study of 155 Cases," *Journal of Oral Pathology & Medicine* 53, no. 2 (2024): 133–141.

2. E. W. Odell, "Odontogenic and Maxillofacial Bone Tumours," in *World Health Organization Classification of Tumours Editorial Board. Head and Neck Tumours*, 5th ed. (Lyon (France): International Agency for Research on Cancer, 2024).

3. S. Ueno, K. Mushimoto, and R. Shirasu, "Prognostic Evaluation of Ameloblastoma Based on Histologic and Radiographic Typing," *Journal of Oral and Maxillofacial Surgery* 47, no. 1 (1989): 11–15.

4. A. Laborde, R. Nicot, T. Wojcik, J. Ferri, and G. Raoul, "Ameloblastoma of the Jaws: Management and Recurrence Rate," *European Annals of Otorhinolaryngology, Head and Neck Diseases* 134, no. 1 (2017): 7–11.

5. F. N. Hendra, D. S. Natsir Kalla, E. M. Van Cann, H. C. W. de Vet, M. N. Helder, and T. Forouzanfar, "Radical vs Conservative Treatment of Intraosseous Ameloblastoma: Systematic Review and Meta-Analysis," *Oral Diseases* 25, no. 7 (2019): 1683–1696.

6. S. P. Ngwenya, E. J. Raubenheimer, and C. E. E. Noffke, "Internal Morphology of Ameloblastomas: A Study of 24 Resected Specimens," *Oral Surgery, Oral Medicine, Oral Pathology, Oral Radiology, and Endodontology* 108, no. 5 (2009): 754–762.

7. P. A. Reichart, H. P. Philipsen, and S. Sonner, "Ameloblastoma: Biological Profile of 3677 Cases," *European Journal of Cancer. Part B, Oral Oncology* 31, no. 2 (1995): 86–99.

8. Z. Lin, G. Sun, T. Wang, Q. Hu, F. Chen, and S. Wen, "Soft Tissue Recurrent Ameloblastomas Also Show Some Malignant Features: A Clincopathologcial Study of a 15-Year Database," *Medicina Oral, Patologia Oral y Cirugia Bucal* 20, no. 3 (2015): 365–371.

9. Z. You, S. Liu, J. Du, Y. Wu, and S. Zhang, "Advancements in MAPK Signaling Pathways and MAPK -Targeted Therapies for Ameloblastoma: A Review," *Journal of Oral Pathology & Medicine* 48, no. 3 (2019): 201–205.

10. S. Grynberg, M. Vered, R. Shapira-Frommer, et al., "Neoadjuvant BRAF-Targeted Therapy for Ameloblastoma of the Mandible: An Organ Preservation Approach," *JNCI Journal of the National Cancer Institute* 116, no. 4 (2024): 539–546.

11. M. Ebeling, M. Scheurer, A. Sakkas, S. Pietzka, A. Schramm, and F. Wilde, "BRAF Inhibitors in BRAF V600E-Mutated Ameloblastoma: Systematic Review of Rare Cases in the Literature," *Medical Oncology* 40, no. 6 (2023): 163.

12. A. Mullard, "BRAF Plus MEK Inhibitor Combo Secures Tumour-Agnostic FDA Approval," *Nature Reviews. Drug Discovery* 21, no. 8 (2022): 548.

13. F. O. Oginni, P. J. W. Stoelinga, S. A. Ajike, et al., "A Prospective Epidemiological Study on Odontogenic Tumours in a Black African Population, With Emphasis on the Relative Frequency of Ameloblastoma," *International Journal of Oral and Maxillofacial Surgery* 44, no. 9 (2015): 1099–1105.

14. R. d A. Almeida, E. S. Andrade, J. C. Barbalho, A. Vajgel, and B. C. Vasconcelos, "Recurrence Rate Following Treatment for Primary Multicystic Ameloblastoma: Systematic Review and Meta-Analysis," *International Journal of Oral and Maxillofacial Surgery* 45, no. 3 (2016): 359–367.

15. F. N. Hendra, E. M. Van Cann, M. N. Helder, et al., "Global Incidence and Profile of Ameloblastoma: A Systematic Review and Meta-Analysis," *Oral Diseases* 26, no. 1 (2020): 12–21.

16. M. Vered, S. Muller, and K. Heikinheimo, "Ameloblastoma," in *WHO Classification of Head and Neck Tumours*, 4th ed., eds. A. K. El-Naggar, J. K. C. Chan, J. R. Grandis, T. Takata, and P. J. Slootweg (International Agency for Research on Cancer (IARC): Lyon, 2017), 215–218.

17. C. A. Waldron and S. K. El-Mofty, "A Histopathologic Study of 116 Ameloblastomas With Special Reference to the Desmoplastic Variant," *Oral Surgery, Oral Medicine, and Oral Pathology* 63, no. 4 (1987): 441–451.

18. S.-G. Kim and H.-S. Jang, "Ameloblastoma: A Clinical, Radiographic, and Histopathologic Analysis of 71 Cases," *Oral Surgery, Oral Medicine, Oral Pathology, Oral Radiology, and Endodontology* 91, no. 6 (2001): 649–653.

19. A. Filizzola, T. Bartholomeu-dos-Santos, and F. Pires, "Ameloblastomas: Clinicopathological Features From 70 Cases Diagnosed in a Single Oral Pathology Service in an 8-Year Period," *Medicina Oral, Patologia Oral y Cirugia Bucal* 19, no. 6 (2014): 556–561.

20. K. Dhanuthai, S. Chantarangsu, S. Rojanawatsirivej, et al., "Ameloblastoma: A Multicentric Study," *Oral Surgery, Oral Medicine, Oral Pathology, Oral Radiology* 113, no. 6 (2012): 782–788.

21. D. MacDonald-Jankowski, R. Yeung, K. Lee, and T. Li, "Ameloblastoma in the Hong Kong Chinese. Part 2: Systematic Review and Radiological Presentation," *Dento Maxillo Facial Radiology* 33, no. 3 (2004): 141–151.

22. L. Robinson, F. P. Fonseca, J. C. T. Lacerda, and W. F. P. van Heerden, "Unicystic Ameloblastoma With Stromal Giant Cells: A Case Series of a Rare Entity," *Oral Surgery, Oral Medicine, Oral Pathology, Oral Radiology* 133, no. 1 (2022): e20–e25.

23. O. Effiom, O. Ogundana, A. Akinshipo, and S. Akintoye, "Ameloblastoma: Current Etiopathological Concepts and Management," *Oral Diseases* 24, no. 3 (2018): 307–316.

24. T. Milman, G.-S. Ying, W. Pan, and V. LiVolsi, "Ameloblastoma: 25 Year Experience at a Single Institution," *Head and Neck Pathology* 10, no. 4 (2016): 513–520, https://doi.org/10.1007/s12105-016-0734-5.

25. G. N. Antonoglou and G. K. Sándor, "Recurrence Rates of Intraosseous Ameloblastomas of the Jaws: A Systematic Review of Conservative Versus Aggressive Treatment Approaches and Meta-Analysis of Non-randomized Studies," *Journal of Cranio-Maxillo-Facial Surgery: Official*

Publication of the European Association for Cranio-Maxillo-Facial Surgery 43, no. 1 (2015): 149–157.

26. O. Hammarfjord, J. Roslund, P. Abrahamsson, et al., "Surgical Treatment of Recurring Ameloblastoma, Are There Options?," *British Journal of Oral & Maxillofacial Surgery* 51, no. 8 (2013): 762–766.

27. C. Ferretti, E. Rikhotso, E. Muthray, and J. Reyneke, "Interim Reconstruction and Space Maintenance of Mandibular Continuity Defects Preceding Definitive Osseous Reconstruction," *British Journal of Oral & Maxillofacial Surgery* 51, no. 4 (2013): 319–325.

28. C. Ferretti, E. Muthray, E. Rikhotso, J. Reyneke, and U. Ripamonti, "Reconstruction of 56 Mandibular Defects With Autologous Compressed Particulate Corticocancellous Bone Grafts," *British Journal of Oral & Maxillofacial Surgery* 54, no. 3 (2016): 322–326.

29. W. G. de Campos, G. L. Alkmin Paiva, C. V. Esteves, A. C. Rocha, P. Gomes, and C. A. Lemos Júnior, "Surgical Treatment of Ameloblastoma: How Does It Impact the Oral Health-Related Quality of Life? A Systematic Review," *Journal of Oral and Maxillofacial Surgery* 80, no. 6 (2022): 1103–1114.

30. V. Ajila and S. Hegde, "Ameloblastomas vs Recurrent Ameloblastomas: A Systematic Review," *Journal of Oral Medicine and Oral Surgery* 28, no. 1 (2022): 11.

31. E. R. Fregnani, D. E. da Cruz Perez, O. P. de Almeida, L. P. Kowalski, F. A. Soares, and A. F. de Abreu, "Clinicopathological Study and Treatment Outcomes of 121 Cases of Ameloblastomas," *International Journal of Oral and Maxillofacial Surgery* 39, no. 2 (2010): 145–149.

32. Y. Li, B. Han, and L.-J. Li, "Prognostic and Proliferative Evaluation of Ameloblastoma Based on Radiographic Boundary," *International Journal of Oral Science* 4, no. 1 (2012): 30–33.

33. L. Merbold, C. Smit, J. Ker-Fox, and A. Uys, "The Radiologic Progression of Ameloblastomas," *South African Journal of Radiology* 27, no. 1 (2023): 1–8.

34. M. Chiapasco, A. Rossi, J. J. Motta, and M. Crescentini, "Spontaneous Bone Regeneration After Enucleation of Large Mandibular Cysts: A Radiographic Computed Analysis of 27 Consecutive Cases," *Journal of Oral and Maxillofacial Surgery* 58, no. 9 (2000): 942–948.

35. C. E. Anyanechi, B. D. Saheeb, and G. O. Bassey, "Spontaneous Bone Regeneration After Segmental Mandibular Resection: A Retrospective Study of 13 Cases," *International Journal of Oral and Maxillofacial Surgery* 45, no. 10 (2016): 1268–1272.

36. A. H. Mesgarzadeh, A. H. B. S. Abadi, and F. Keshani, "Seven-Year Follow-Up of Spontaneous Bone Regeneration Following Segmental Mandibulectomy: Alternative Option for Mandibular Reconstruction," *Dental Research Journal* 16, no. 6 (2019): 435–440.

37. V. Kazanjian, "Spontaneous Regeneration of Bone Following Excision of Section of the Mandible," *American Journal of Orthodontics and Oral Surgery* 32, no. 4 (1946): A242–A248.

38. O. Ahmad and G. Omami, "Self-Regeneration of the Mandible Following Hemimandibulectomy for Ameloblastoma: A Case Report and Review of Literature," *Journal of Maxillofacial and Oral Surgery* 14, no. S1 (2015): 245–250, https://doi.org/10.1007/s12663-012-0462-7.