Odontogenic tumours and lesions from 1992-2016 in a single specialist Oral and Maxillofacial Pathology Unit in the United Kingdom

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Abstract

Objectives: Odontogenic tumours (ODTs) are a heterogeneous group of lesions derived from elements of the tooth-forming tissues. There are no published detailed data on the incidence of odontogenic tumours in the UK. **Aim:** to retrospectively describe the range and incidence of odontogenic tumours from 1992-2016 in a single specialist unit and to compare this with other populations. **Study Design:** Using the Oral and Maxillofacial Pathology database, Sheffield, both local and referred consultation cases were included. A proportion of diagnoses were re-classified in accordance with the 2017 WHO classification. **Results:** In total, 559 odontogenic tumours were diagnosed. Overall, the most common lesions were ameloblastoma (196; 33.8%), odontome (148; 25.5%) and odontogenic myxoma (37; 6.3%), but this varied between local and referral case populations, with odontomes most common in the local population (43%). The sites affected, gender and age of patients were similar to other western populations. Malignant ODTs comprised 33 cases (5.7%), of which nine (27.3%) were ameloblastic carcinoma. The majority of the malignant ODTs were referral cases. **Conclusions:** These are the first detailed data on odontogenic tumours within a UK population and the pattern of incidence from the local population is similar to other western populations. The exceptional rarity of malignant ODTs emphasises the need for specialist centres in order to gain diagnostic experience.

Keywords

Odontogenic tumours, Ameloblastoma, Odontome, Odontogenic carcinoma

Introduction

Odontogenic tumours (ODTs) are a group of heterogeneous lesions that derive from the tooth-forming tissues[1]. These tumours are histologically diverse and comprise a range of lesions from hamartomatous to benign and malignant neoplasms. Predominantly, they occur within the tooth bearing areas of the jaws, but rarely may present in an extraosseous location as a localized gingival swelling. Several surveys of ODTs have been published from different parts of the world and there is a variation in the distribution of ODTs worldwide[2]. Ameloblastoma is the most prevalent tumour in Africa and some Asian countries whilst in Europe and America, odontome is the most common tumour [3-5]. An extensive demographic study by Jones *et al* gave a breakdown of the number of different oral and maxillofacial pathologies in paediatric and adult populations in the UK[6, 7], but a detailed epidemiological study of odontogenic tumours has not been reported.

The classification of odontogenic tumours has evolved over many years, but since 1971 the WHO has published a unified classification with the intention of promoting a standard terminology[8]. In 2005, the 3rd edition of the WHO classification made a number of significant changes, including the exclusion of the odontogenic cysts and the designation of the odontogenic keratocyst and the calcifying odontogenic cyst as neoplasms[9]. After much debate[10], the latest 4th edition of the WHO classification revised the classification and restored these lesions to the category of benign cysts[11, 12]. In the intervening decade, studies of the incidence of odontogenic tumours have therefore been confused by uncertainty regarding the designation of some lesions as cysts or tumours. The aim of this study was to retrospectively determine the incidence of odontogenic tumours in a UK population, according to the 2017 WHO classification, using the Oral and Maxillofacial Pathology database, Sheffield, over a 24-year period and to compare this with the published epidemiological data from various geographical areas across the world.

Materials and Methods

The diagnostic database of the department of Oral and Maxillofacial Pathology, Charles Clifford Dental Hospital, Sheffield, was searched for all accessioned cases of ODTs over a 24-year period (1992-2016). All cases were from this period were included, and only those with incomplete data were later excluded on review. Local and referred cases were reviewed and some were re-classified histologically in accordance with the WHO classification of head and neck tumours 2017[11] by two

experienced oral and maxillofacial pathologists. Clinical information including age, gender and location of the tumour were recorded. Age data are presented as mean ± SD. In order to analyse the site distribution, the mandible was divided into anterior, premolar, molar, angle and ramus areas; the maxilla into anterior, premolar, molar, tuberosity and antrum. Site was determined according to the clinical records and by reference to the associated radiology where this was available. Cases received from the local population and referral cases were included in the study, but were also analysed separately in order to allow an estimate of prevalence in the local population. In cases with multiple biopsies or recurrences, only the index biopsy was considered. Descriptive statistical analysis of the data was performed using the frequencies of categorical variables. Continuous variables were expressed as mean, median and standard deviation. Categorical variables were expressed as absolute number of cases and percentage values.

Results

After excluding cases with incomplete data or inaccurate diagnostic coding, the final sample comprised 559 cases (Table 1). Overall, there were 526 benign (94.1%) and 33 malignant (5.9%) lesions and the most common benign tumours were ameloblastoma (including unicystic variant; 196, 37.2%) followed by odontomes (148, 28.1%). The centre is a tertiary referral centre for oral and maxillofacial pathology and 329 (59.3%) cases were referral ODTs and 230 (40.7%) were from our local region, which serves a population of approximately 575,000 (Table 2). When considering only local cases (n=230), odontomes predominated with 98 cases (42.6%) compared with 68 ameloblastomas (29.6%). Ameloblastoma made up the largest category among the referred cases (128/329; 38.9%). Malignant odontogenic tumours were rare with only 33 cases (5.9% of all ODTs). The results presented below will focus on the relative incidence of tumours from the local population, with additional comment on the referred cases.

Benign epithelial odontogenic tumours

The mean age of occurrence of ameloblastoma in the local population, was 46.8 ± 20 (range 11-86) years, similar to that for the referral cases (49.2 ± 19). Overall, the male to female ratio was 1.5:1 with a male preponderance (Fig 1a). The majority of ameloblastomas occurred in the mandible (76%) with 20% in maxilla. The site was not specified in the remaining cases. This is very similar that that seen in other large series of ameloblastoma[13].

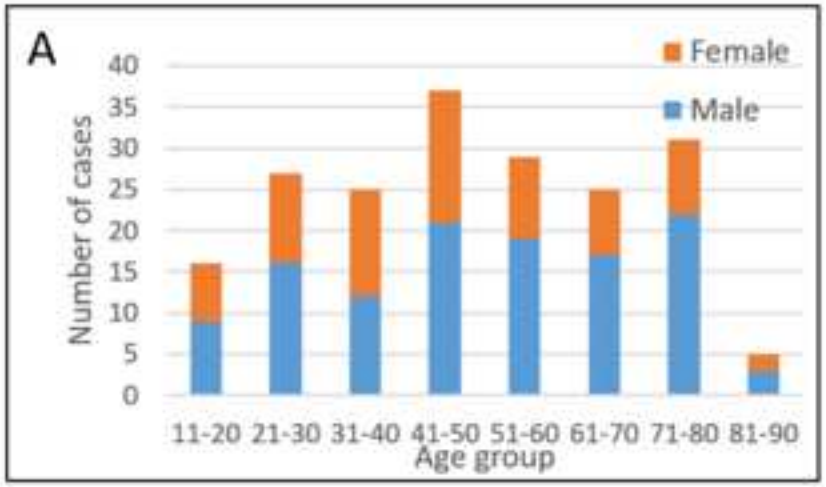
Table 1. Total number of odontogenic tumours received at the Oral and Maxillofacial Pathology diagnostic service between 1992 and 2016

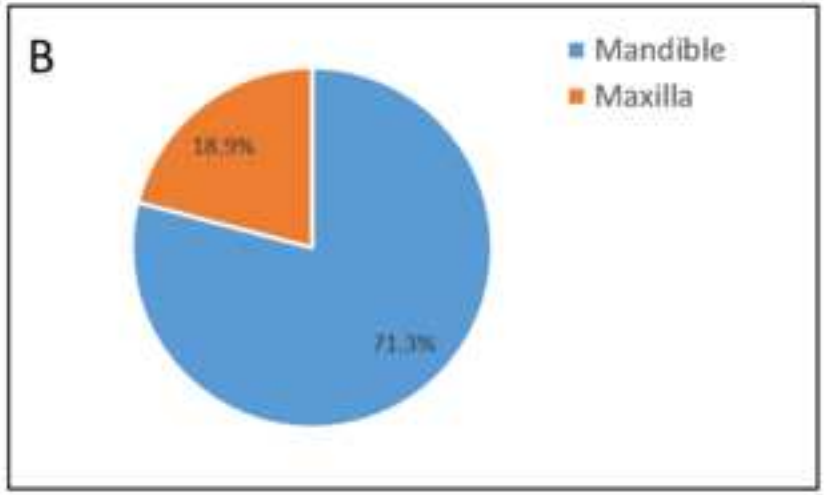
Diagnosis	Total Number	% of Total ODTs	Mean age (±SD)	Age range	M:F ratio
Benign epithelial odontogenic tumours					
Ameloblastoma	196	33.8	48.4 (±19.4)	11-86	1.5:1
Squamous Odontogenic Tumour (SOT)	2	-	45	6-83	1:1
Calcifying epithelial odontogenic tumour (CEOT)	28	4.8	45.8 (±15.9)	18-88	1.15:1
Adenomatoid odontogenic tumour (AOT)	35	6	19.5 (±12.3)	8-63	1:1.14
Benign mixed epithelial and mesenchymal odontogenic tumours					
Ameloblastic fibroma	8	1.4	15.1 (±3.04)	12-21	6:1
Odontome (total)	**148**	25.5	18 (±13.6)	3-71	1.2:1
Odontome Complex	86	14.8	17.25 (±12.8)	3-71	1.2:1
Odontome Compound	62	10.7	19.08 (±14.6)	4-66	1:1
Dentinogenic ghost cell tumour	9	1.5	46 (±26.5)	5-69	3.5:1
Benign mesenchymal odontogenic tumours					
Odontogenic Fibroma	24	4.1	39 (±15.9)	14-72	1.6:1
Odontogenic Myxoma	37	6.3	36.4 (±14.3)	1-79	1:1.8
Cementoblastoma	16	2.7	34 (±16.48)	16-83	1:1
Malignant odontogenic tumours					
Odontogenic carcinomas/sarcomas (**total**)	**33**	5.7	54.96 (±17.1)		
Ameloblastic carcinoma	9	1.5	61.7 (±15.9)	26-73	1:1.2
Primary intraosseous squamous cell carcinoma	9	-	69.5 (±28.9)	6-90	1.3:1
Sclerosing odontogenic carcinoma	5	-	45.2 (±8.6)	43-54	1:4
Clear Cell Odontogenic Carcinoma	7	1.2	55 (±13.7)	36-76	2.5:1
Ghost cell odontogenic carcinoma	1	-	57		male
Ameloblastic (odontogenic) carcino-sarcoma	2	-	70.5	64-77	1:1
Other odontogenic lesions/ tumours that are not listed in 4th edition of WHO[8]					
Odontogenic Gingival Epithelial Hamartoma	12	2	25.8	1-61	3:1
Ameloblastic fibro-odontome/dentinoma	11	1.9	10 (±2.06)	7-14	2.7:1
TOTAL	**559**				

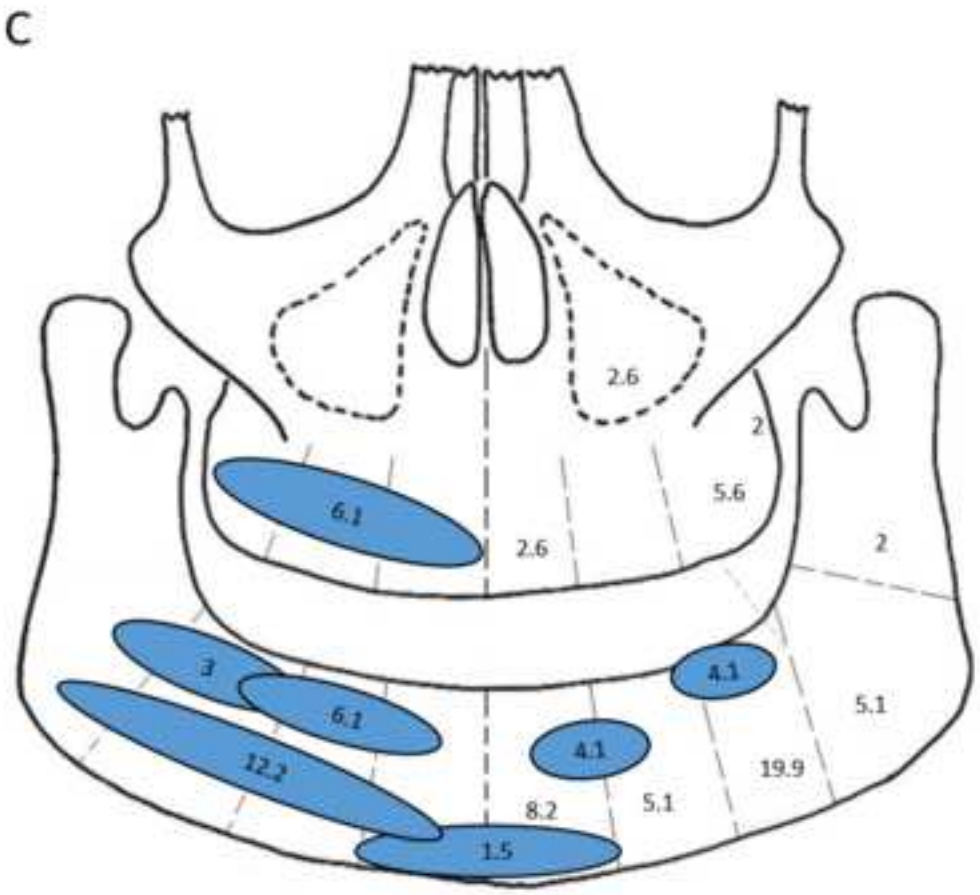
Table 2: Number of odontogenic tumours received from local region sources and external/tertiary referrals between 1992 and 2016.

Diagnosis	Local			Referral		
	total	M/F (number)	Mean age	total	M:F (number)	Mean age
Benign epithelial odontogenic tumours						
Ameloblastoma	68	47/21	46.8	128	71/57	49.2
Squamous Odontogenic Tumour (SOT)	2	1/1	45.0	-	-	-
Calcifying epithelial odontogenic tumour (CEOT)	8	4/4	40.8	20	11/9	44.4
Adenomatoid odontogenic tumour (AOT)	17	8/9	18.0	18	6/7	21.4
Benign mixed epithelial and mesenchymal odontogenic tumours						
Ameloblastic fibroma	-	-	-	8	6/1	15.1
Odontome (total)	98			50		
Odontome Complex	54	30/24	17.5	32	19/13	16.8
Odontome Compound	44	20/24	20.6	18	11/7	15.3
Dentinogenic ghost cell tumour	-	-	-	9	7/2	46
Benign mesenchymal odontogenic tumours						
Odontogenic Fibroma	11	7/4	34.7	13	8/5	43.4
Odontogenic Myxoma	11	4/7	36.5	26	9/17	36.4
Cementoblastoma	4	1/3	49.5	12	8/4	28.6
Malignant odontogenic tumours						
Ameloblastic carcinoma	1	1/0	72	8	3/5	60.0
Primary intraosseous squamous cell carcinoma	-	-	-	9	2/0	69.5
Sclerosing odontogenic carcinoma	1	0/1	54	4	1/3	43.0
Clear Cell Odontogenic Carcinoma	-	-	-	7	5/2	55.0
Ghost cell odontogenic carcinoma	-	-	-	1	1/0	57
Ameloblastic (odontogenic) carcino-sarcoma	-	-	-	2	1/1	70.5
Other odontogenic lesions/ tumours that are not listed in 4th edition of WHO[8]						
Odontogenic Gingival Epithelial Hamartoma	5	5/0	34.2	7	4/3	19.9
Ameloblastic fibro-odontome/ dentinoma	4	4/0	10	7	5/2	10.3
TOTAL	**230**			**329**		

Figure 1A: Age and gender distribution of Ameloblastoma Figure 1B: site of occurrence of Ameloblastoma. Figure 1C: Site distribution of Ameloblastoma by percentage, including those confined to a single site and those that extend over a region. Laterality is NOT implied by position on the schematic diagram. The body of the mandible and maxilla have been separated into anterior/incisor, premolar, molar regions with angle and ramus added for the mandible and tuberosity added for the maxilla. In addition, I case was identified in the hard palate, 9 peripheral tumours were identified (4.6%) and the site was not specified in 8 cases (4.1%).







Out of the total 149 ameloblastoma cases in the mandible (both local and referred), 73.2% were in the posterior segments and less than 20% were in the anterior mandible. (Fig 1b). Similarly, 75% of maxillary tumours were found in the posterior region and a small number were reported in the maxillary sinus (2.6%). The molar region was the commonest site affected in both mandible and maxilla. Exemplar cases are presented in Figures 2 and 3.

The second commonest tumour was adenomatoid odontogenic tumour (AOT: 7.4% of local cases) and the least common was squamous odontogenic tumour, of which only two cases were reported (both local cases; figure 4). Although AOT is primarily a paediatric tumour with the majority occurring between 10-20 years (mean age 19.5±12) there was an age range from 8-63 yrs. In contrast with ameloblastoma, AOT showed a slight female predominance (M:F 1:1.14) (Fig 5).

Calcifying epithelial odontogenic tumour (CEOT) accounted for 3.5% of the local OTs (6% of referred cases). Overall, there was a male predominance (1.15:1) and age range from 18-88 years (mean 43.3±15.9) (Fig 6a). The mandible was the most common site (61%; Fig 6b), with the majority of cases in the molar-premolar region followed by the anterior region. The next most common site was the maxillary premolar region. 30% of maxillary lesions were associated with the maxillary antrum (Fig 6c).

Odontogenic gingival epithelial hamartomas (OGEH) are believed to originate from remnants of dental lamina and considered to represent a transitional stage between a tumour like growth and a true benign neoplasm. Diagnostic criteria are not clear. All cases with this diagnosis in the archive were reviewed and this diagnosis was supported in only 12 (2%) cases over 24 years.

Benign mixed epithelial and mesenchymal odontogenic tumours

Odontome, which are hamartoma rather than true neoplasms, were the most common lesion in the cases from the local population (42.6%), but only comprised 28% of the full cohort. They accounted for 15% of referred cases. Overall, the mean age was 18±13.6 with a male predominance (M: F, 1.7:1). The age ranged from 3-71yrs. There was no significant difference between complex and compound types with respect to age and gender distribution, except for site where the complex type mostly occurred in the posterior mandible (63%) and the compound type in the anterior maxilla (81.8%). There was, however a large variation in site of occurrence and

Figure 2: A representative section of a resection specimen from a white female, aged 42 with a large multilocular radiolucency in left body of mandible. Much of the specimen shows conventional ameloblastoma but there is a central focus with marked crowing and cytological atypia. This case was signed out as ameloblastoma with a focus of 'in-situ' Ameloblastoma. A high-resolution version of the image is available as eSlide: VM05372

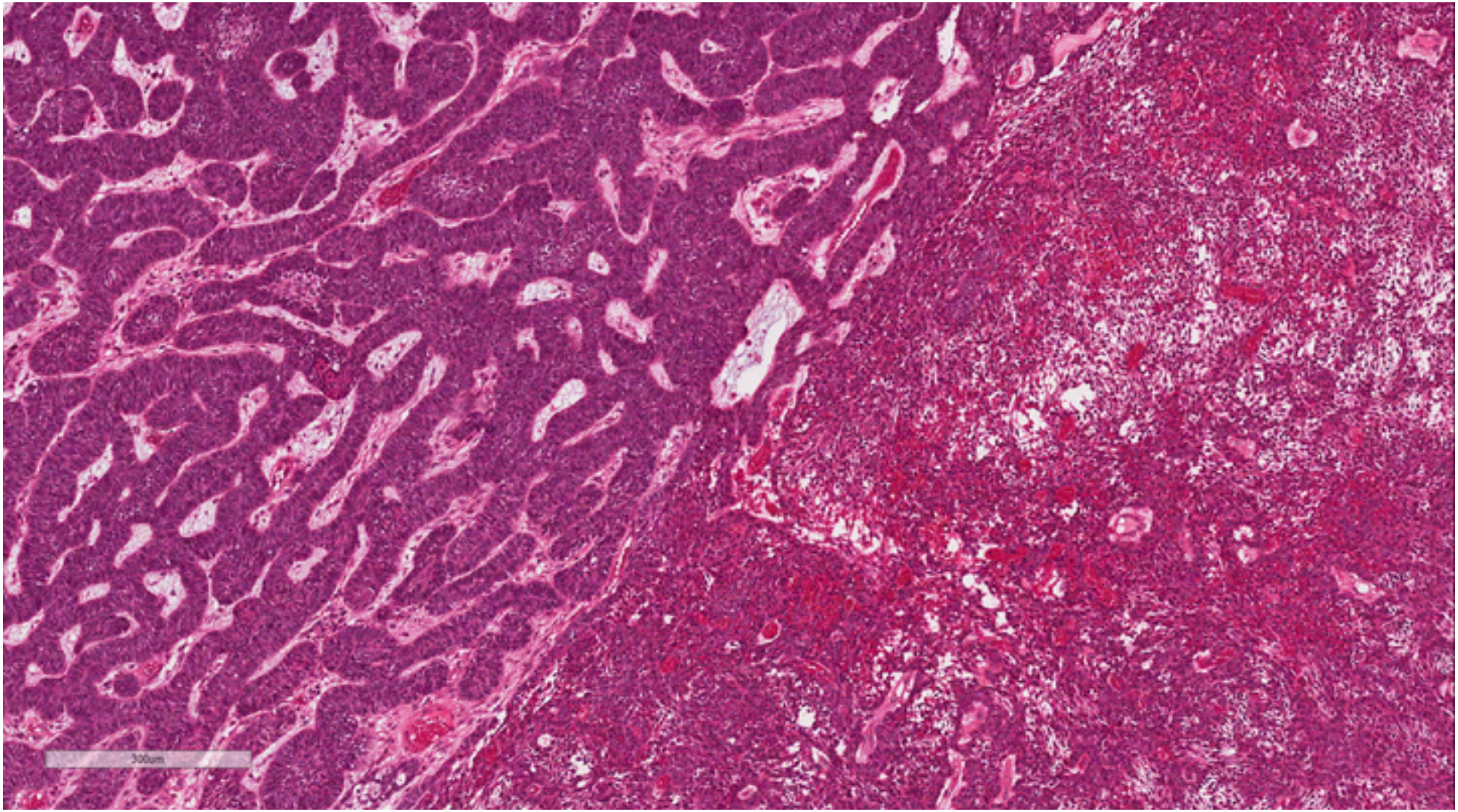


Figure 3: A representative section of and excisional biopsy from a white male, aged 76. There was an expansile lesion of left maxillary tuberosity with no intrabony lesion. A diagnosis of peripheral ameloblastoma was made. A high-resolution version of the image is available as eSlide: VM05373

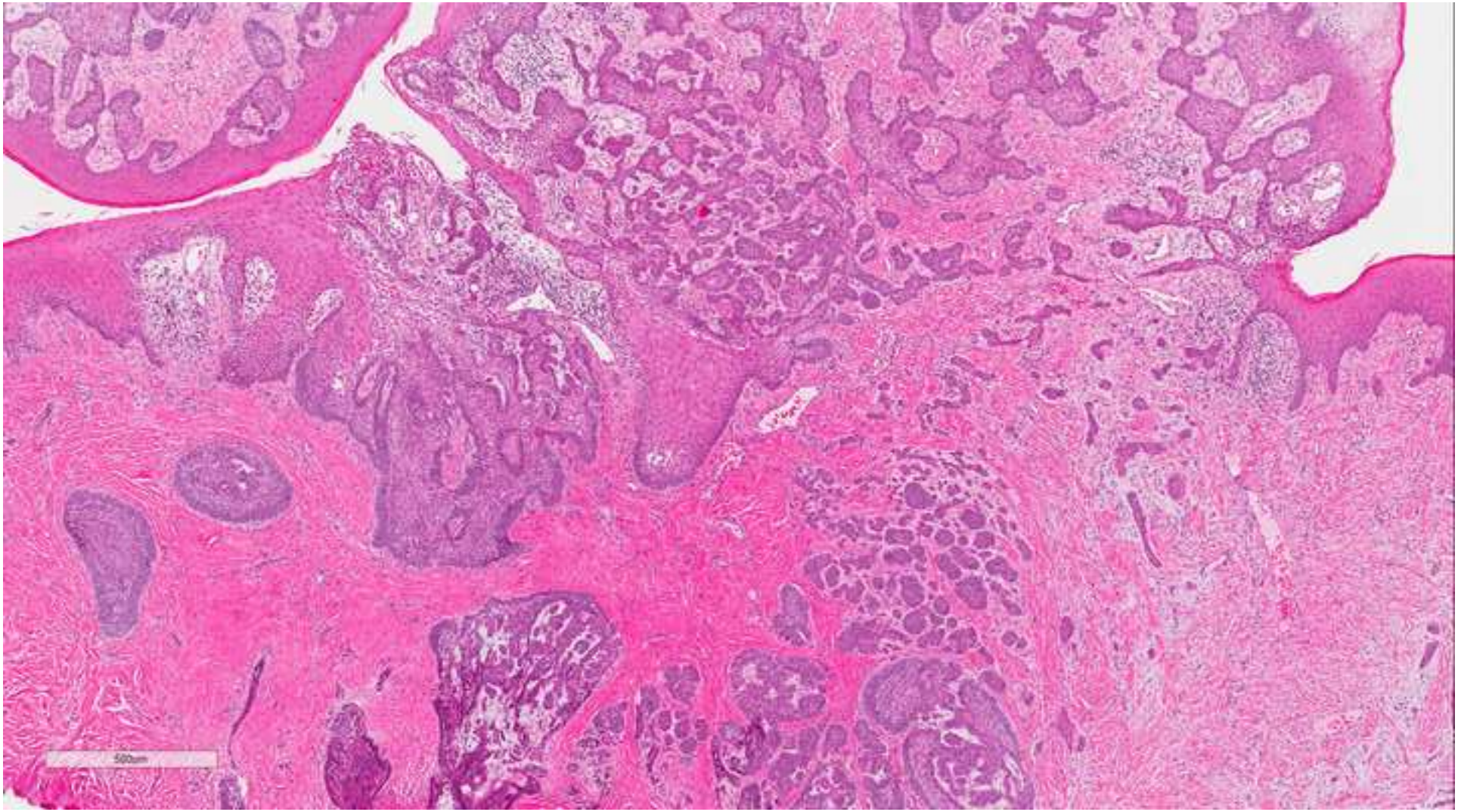
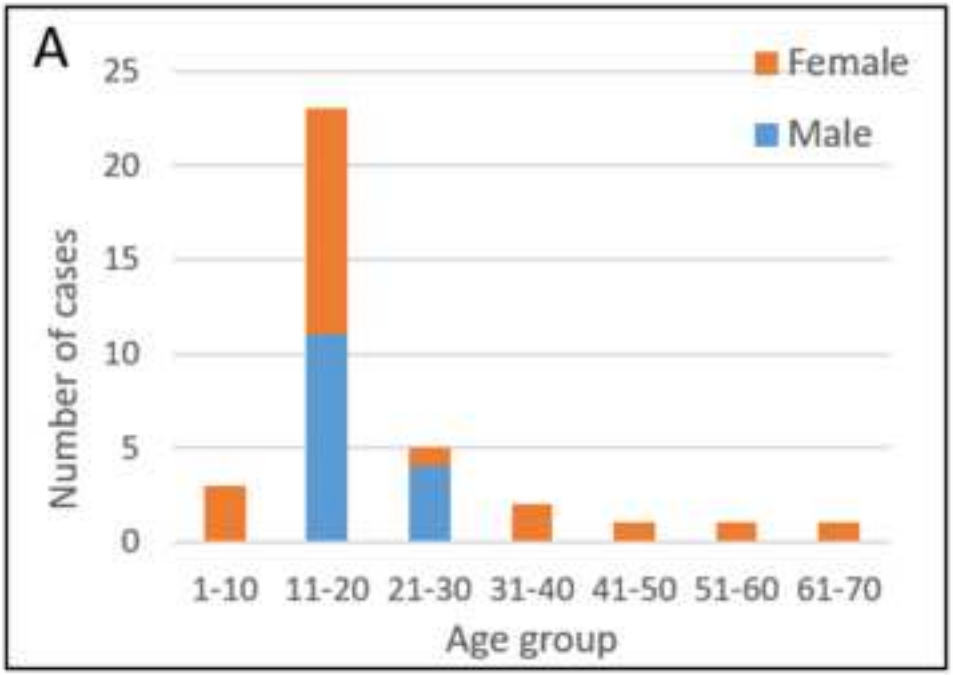
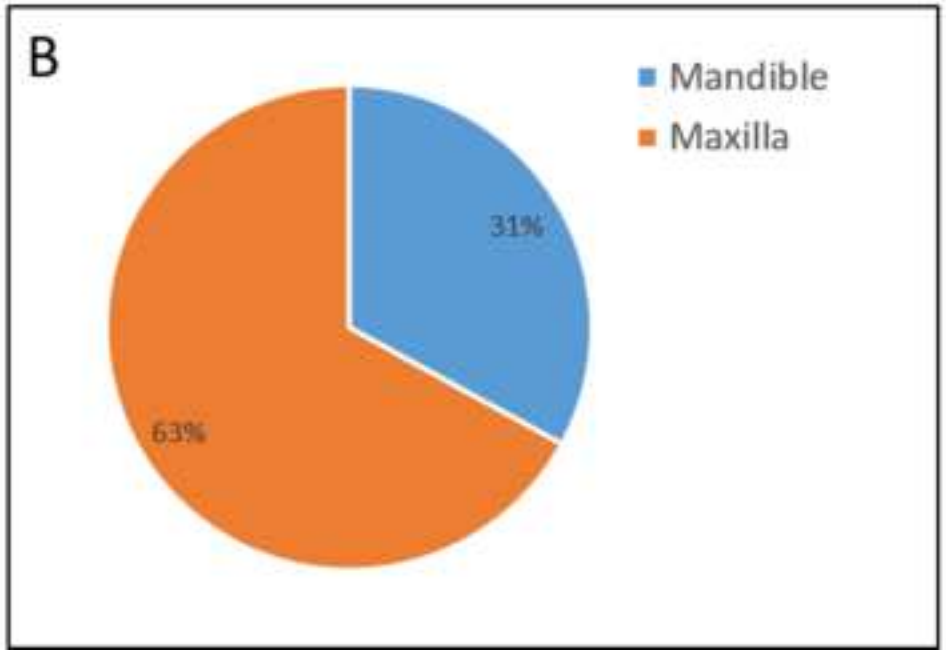


Figure 4: A representative section of an enucleation specimen from a white female, aged 61. The “cystic” lesion was adjacent to, but separate from the retained root of UR4A. A diagnosis of a squamous odontogenic tumour was made. A high-resolution version of the image is available as eSlide: VM05374

Figure 5A: Age and gender distribution of Adenomatoid odontogenic tumour. Figure 5B: Site of occurrence of Adenomatoid Odontogenic Tumor. Figure 5C: Site distribution of Adenomatoid Odontogenic Tumor by percentage. The body of the mandible and maxilla have been separated into anterior/incisor, premolar, molar regions with angle and ramus added for the mandible and tuberosity added for the maxilla. The site was not specified for 2 cases (5.7%)





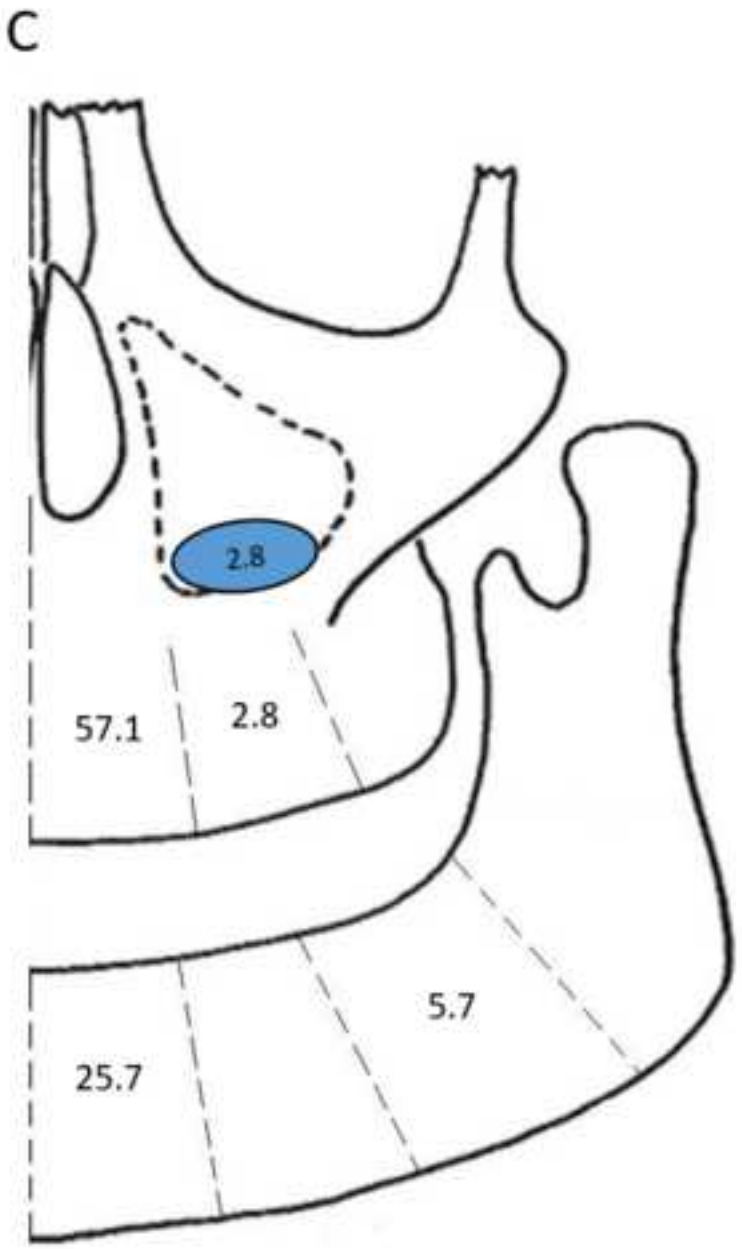
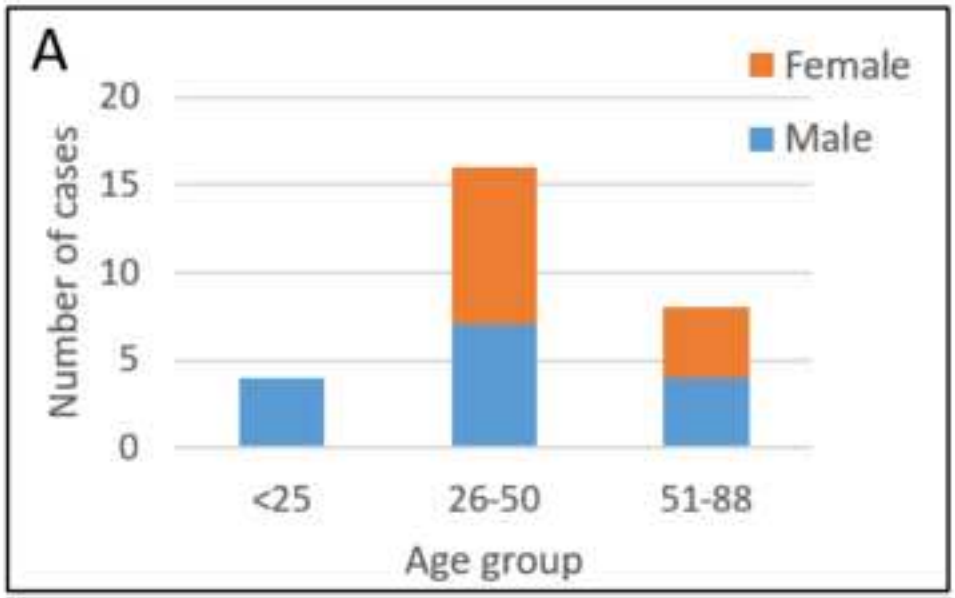
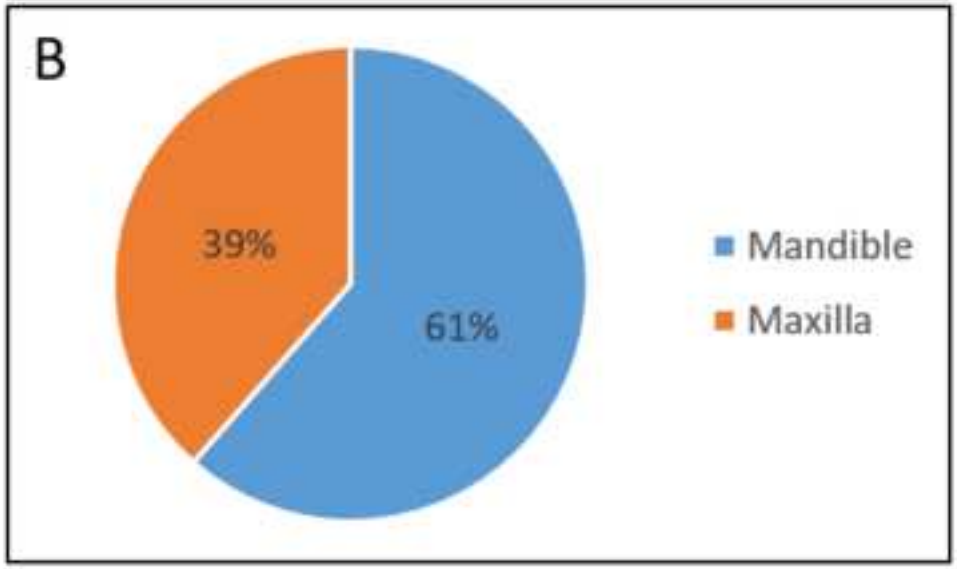
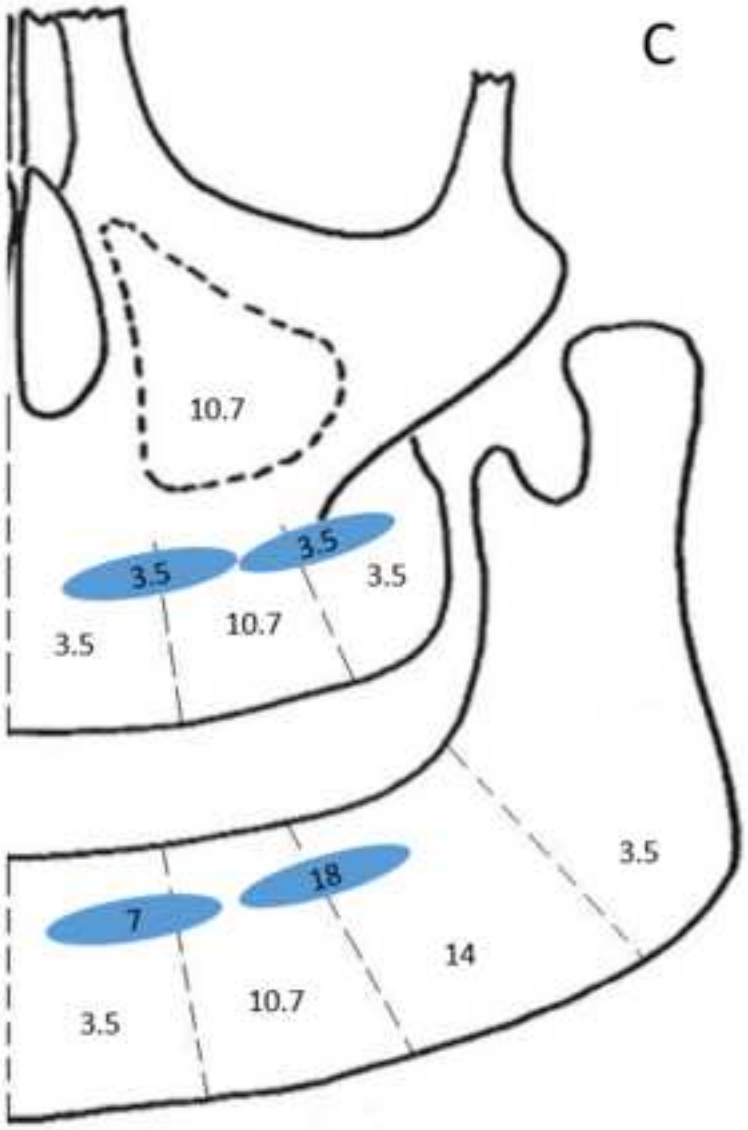


Figure 6A: Age and gender distribution of CEOT. Figure 6B: site of occurrence of CEOT. Figure 6C: Site distribution of CEOT by percentage, including those confined to a single site and those that extend over a region. The body of the mandible and maxilla have been separated into anterior/incisor, premolar, molar regions with angle and ramus added for the mandible. The site was not specified for two cases (7%).







odontomes were diagnosed in every segment of either jaw. A number of complex odontomes did occur in the anterior maxilla (16%), perhaps indicative of the variation in histological features and difficulties in precise classification of odontomes if they do not present as discrete denticles.

A total of 30 lesions which contained ghost cells as a significant/prominent histological feature were identified in the database and all were reviewed. Of these, only nine met the diagnostic criteria for dentinogenic ghost cell tumour (Table 1; figure 7), all of which were referred cases (Table 2). As calcifying odontogenic cysts have returned to the odontogenic cyst classification in the 4th edition of the WHO classification, these have not been included in our data. We did not identify any primordial odontogenic tumours on our review of the cases.

Although ameloblastic fibro-odontome/dentinoma have been removed from the 2017 OT classification, we identified 11 cases with a male predominance (M: F, 4:1). Age ranged from 7-14 years with a mean age of 10±2.1. The majority (7/11) of these cases were referrals. These two subtypes of odontogenic tumours were re-evaluated with additional clinical and radiographic information by PMS and KDH to exclude developing odontome and confirm the diagnosis. An exemplar case is shown in figure 8.

Benign mesenchymal odontogenic tumours

In the local population, the most common types were odontogenic myxoma and odontogenic fibroma (both 4.8%). Odontogenic myxoma occurred over a wide age range from 1-79yrs, with most patients between 31-40 years (mean age of 36.4±14.3; fig 9a). 68.8% were found in the mandible (fig 9b), and most occurred in premolar and molar area (40.6%). However, not all lesions were confined to a single sub-site as most tumours were large at presentation (fig 9c). A total of 16 cementoblastomas were diagnosed, all of which were in the mandible, with 13 (81%) attached to the first or second permanent molar.

Malignant odontogenic tumours

Malignant odontogenic tumours were rare with just 33 cases overall (5.7% of all OTs). Only two of these cases came from the local population (<1% of total population), one ameloblastic carcinoma, and one sclerosing odontogenic carcinoma. Overall, there were nine cases each of ameloblastic carcinoma and primary intraosseous carcinoma (Table 1 and 2). Seven of the nine intraosseous

Figure 7: A representative section of an excision biopsy for a clinical diagnosis of a fibrous epulis in a 49 year old white male. The lesions was a gingival swelling between LR4 and LR5. The features are those of a peripheral dentinogenic ghost cell tumour. There was no intrabony component. A high-resolution version of the image is available as eSlide: VM05375

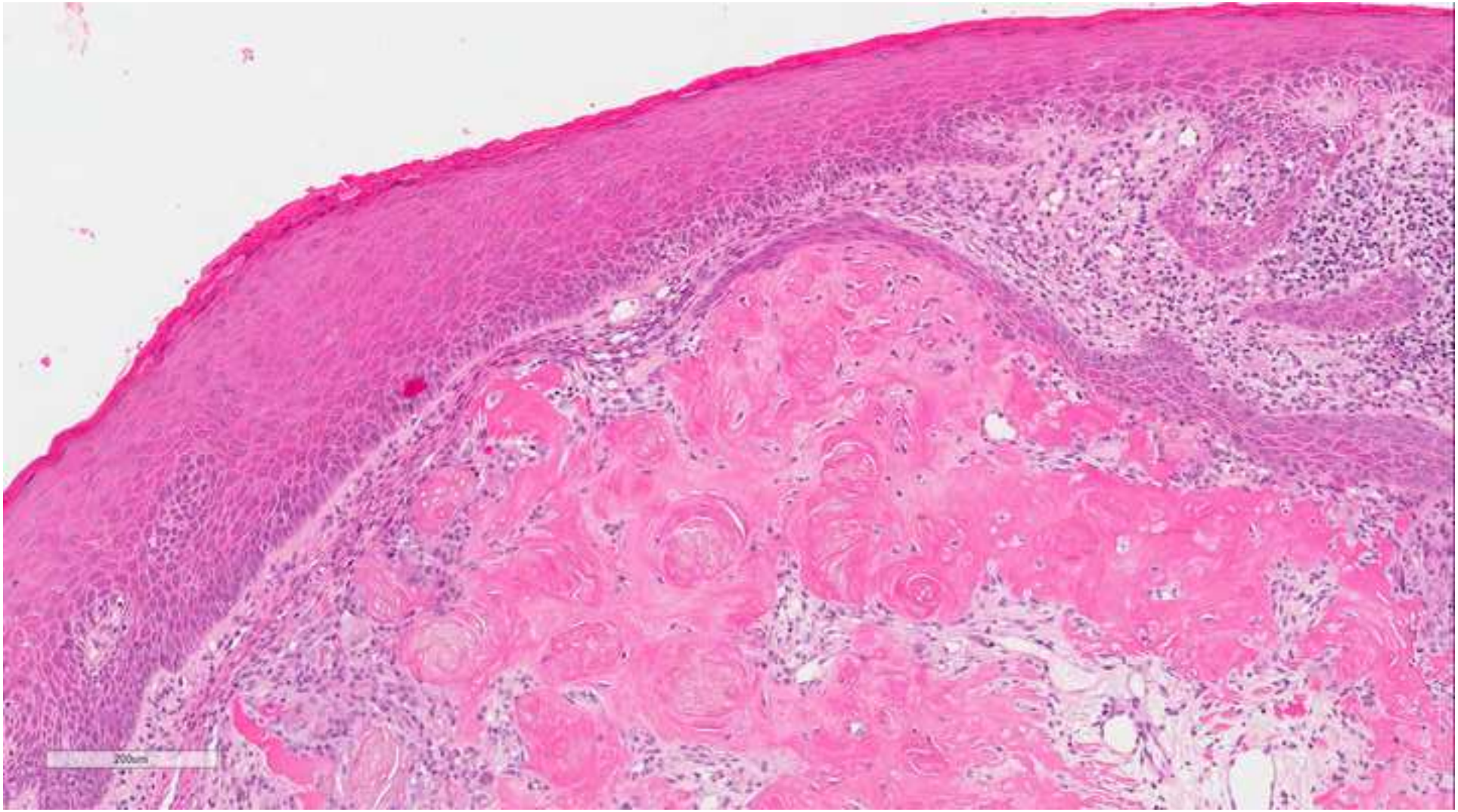


Figure 8: A radiological image (8A) and representative section of an enucleation specimen

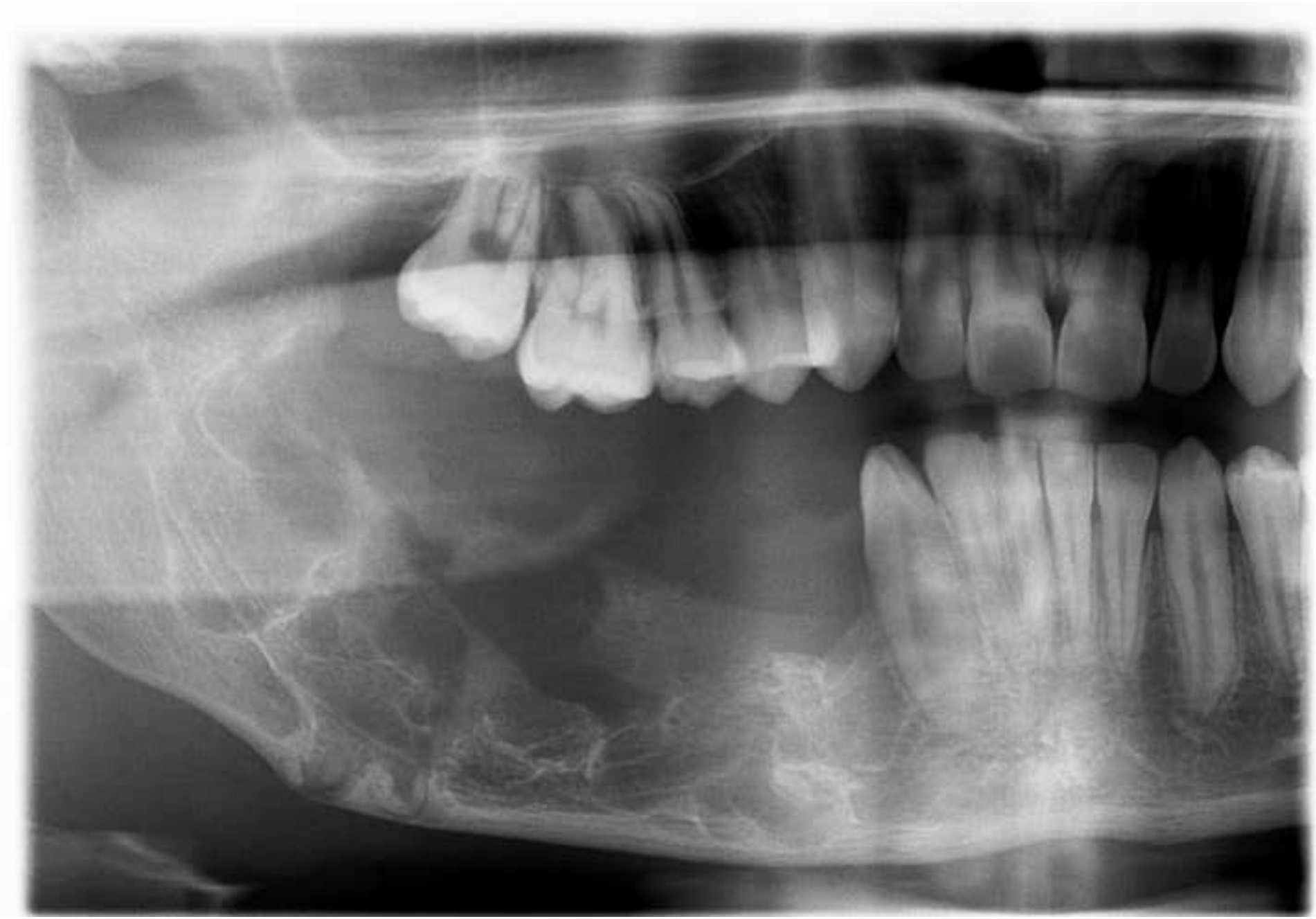


Figure 8: (8B) from a lesion in the mandible in a white male, aged 12 years. This was an extensive multilocular lesion of the right ramus with gross expansion and loss of cortication of the mandible in areas. The lesion enucleated intact. A diagnosis of ameloblastic fibro-odontome was made in this case and this diagnosis was upheld in the review process outlined in this paper. A high-resolution version of the image is available as eSlide: VM05376

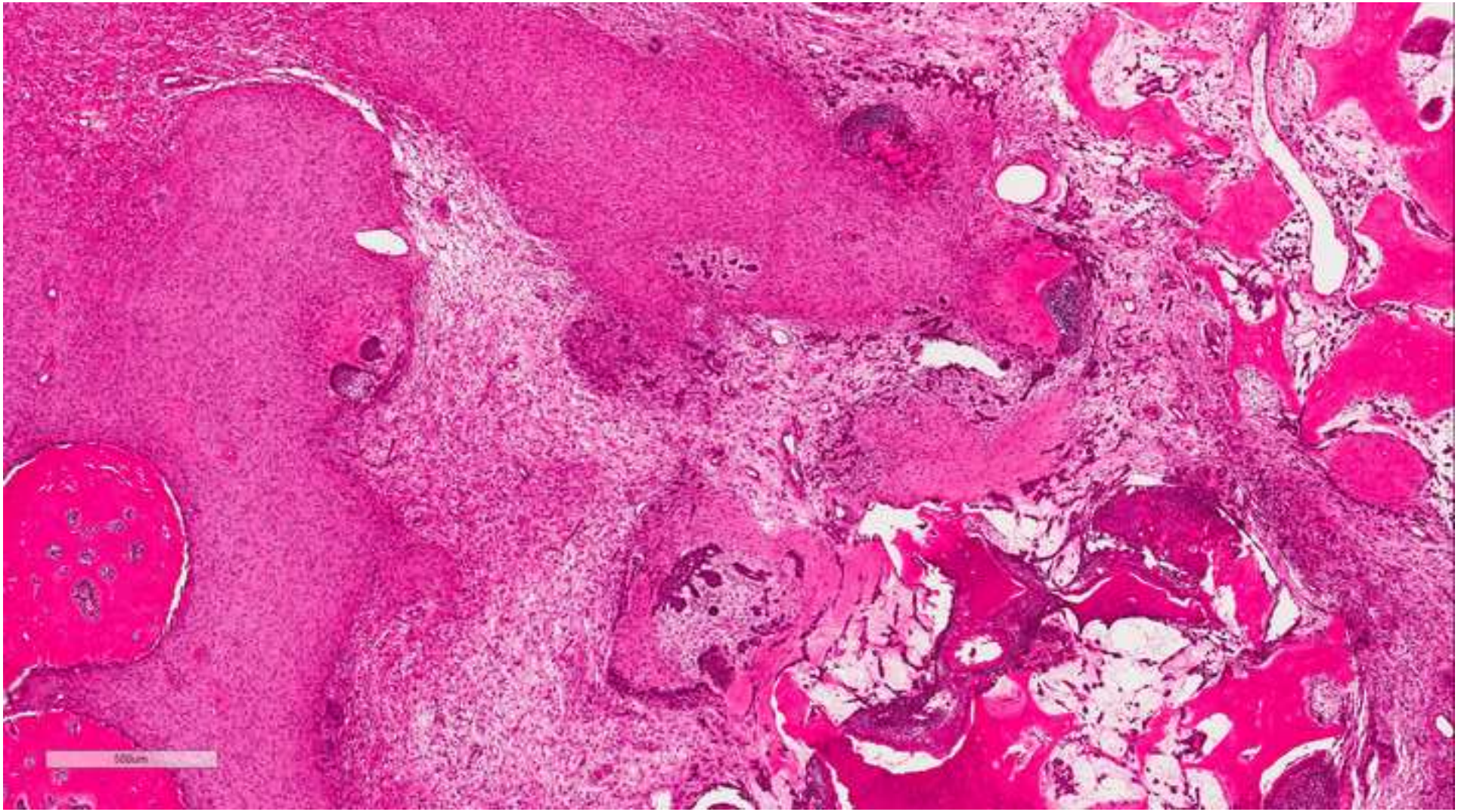
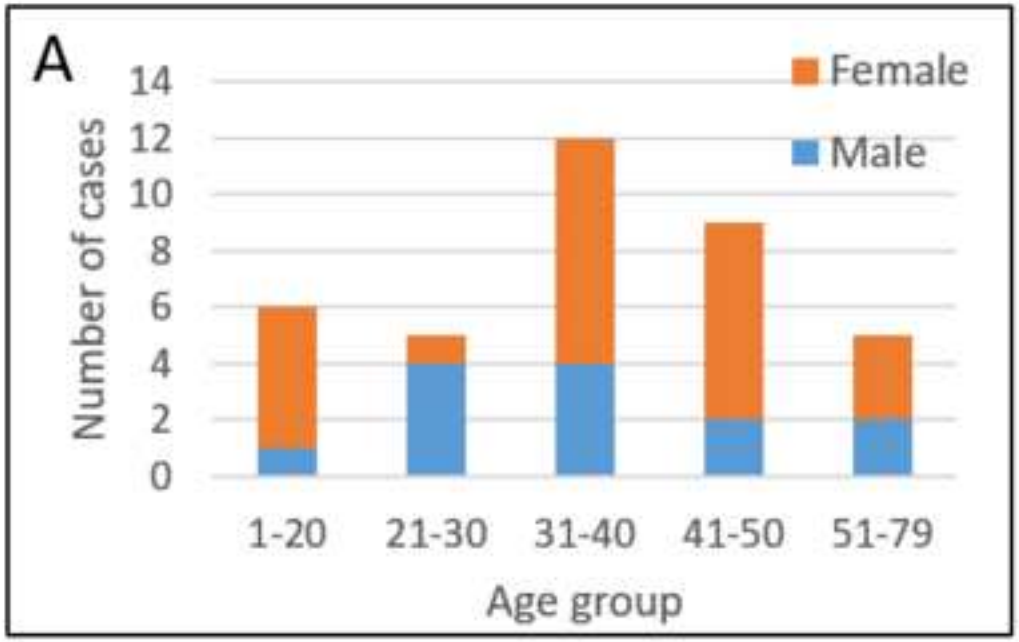
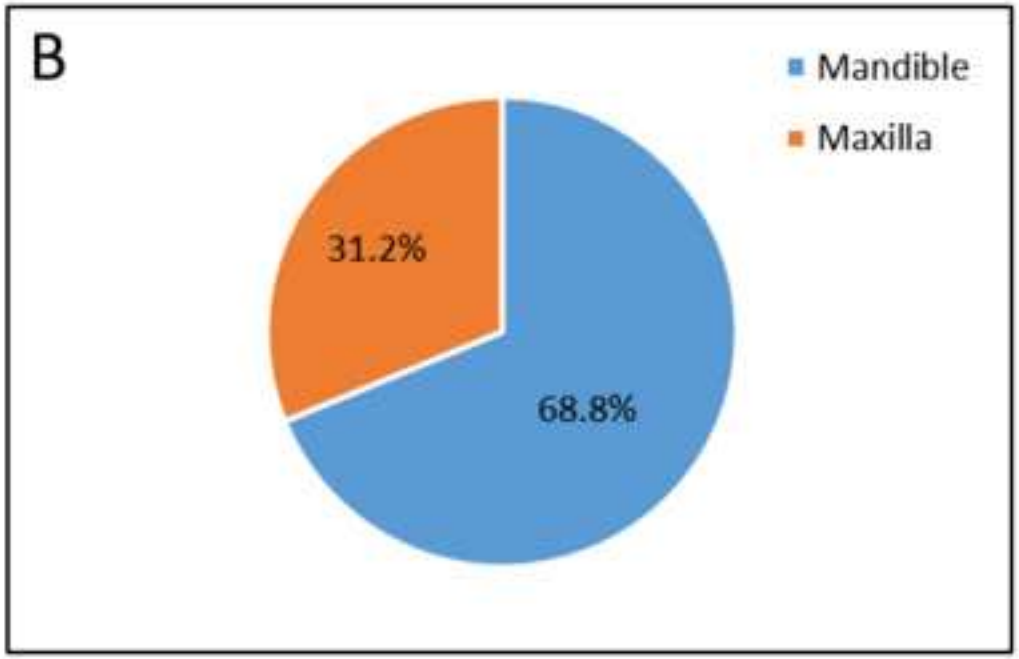


Figure 9A**:** Age and gender distribution of odontogenic myxoma (n=37). Figure 9B: site of occurrence of odontogenic myxoma. Figure 9C: Site distribution of odontogenic myxoma by percentage, including those confined to a single site and those that extend over a region. The body of the mandible and maxilla have been separated into anterior/incisor, premolar, molar regions with angle and ramus added for the mandible. The exact site was not specified in five cases (13.5%).





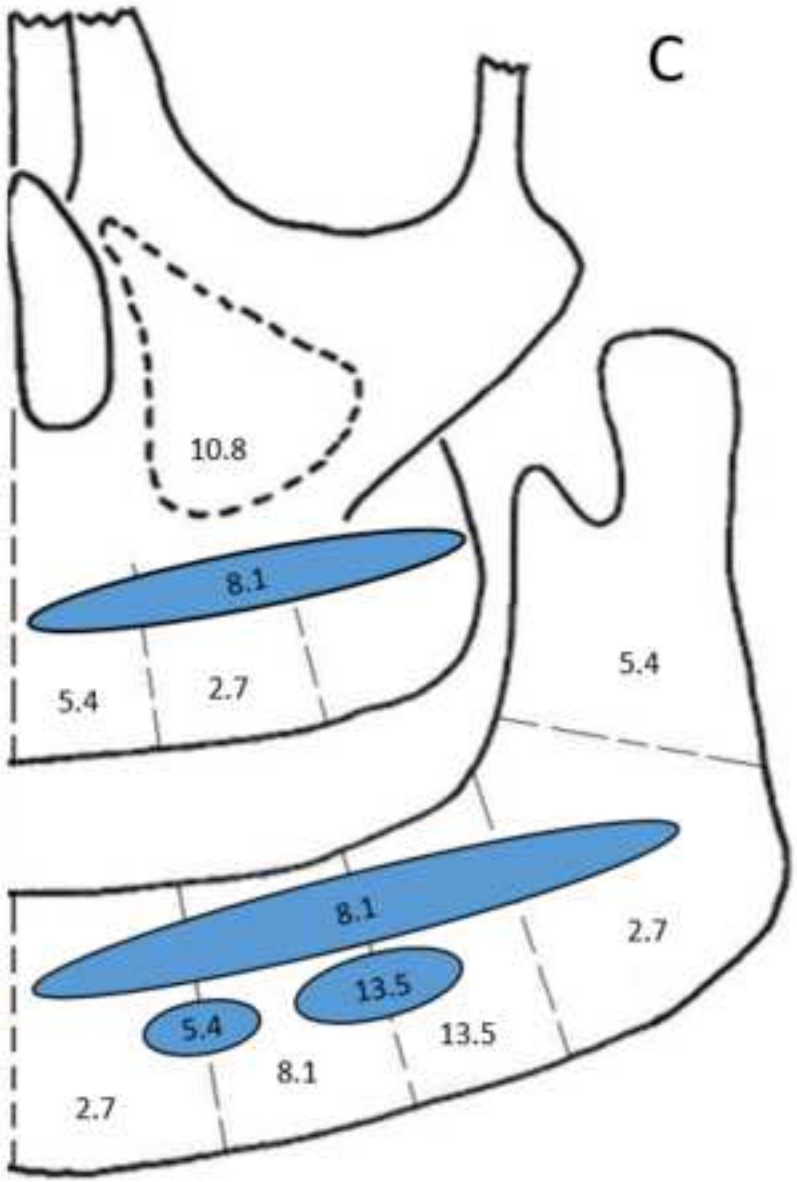
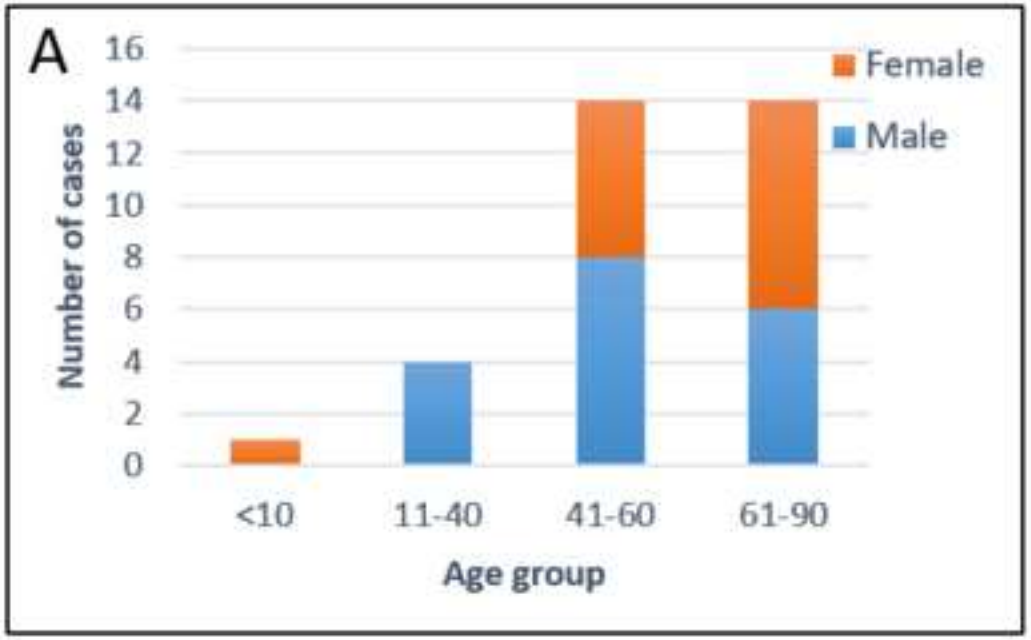
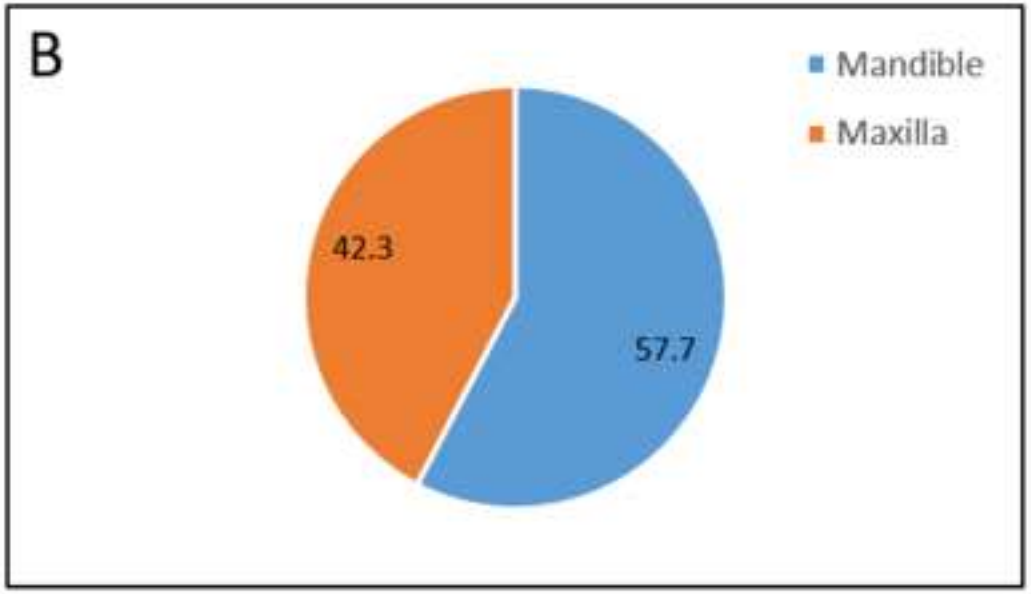


Figure 10A: Age and gender distribution of malignant Odontogenic Tumours. Figure 10B: site of occurrence of malignant ODTs. Figure 10C: Site distribution of malignant odontogenic tumours (n=33) by percentage, including those confined to a single site and those that extend over a region. The body of the mandible and maxilla have been separated into anterior/incisor, premolar, molar regions with angle and ramus added for the mandible. One case primarily involved the maxillary antrum. The site was not specified in six cases (18%) and one lesion was solely within maxillary gingiva (3%).





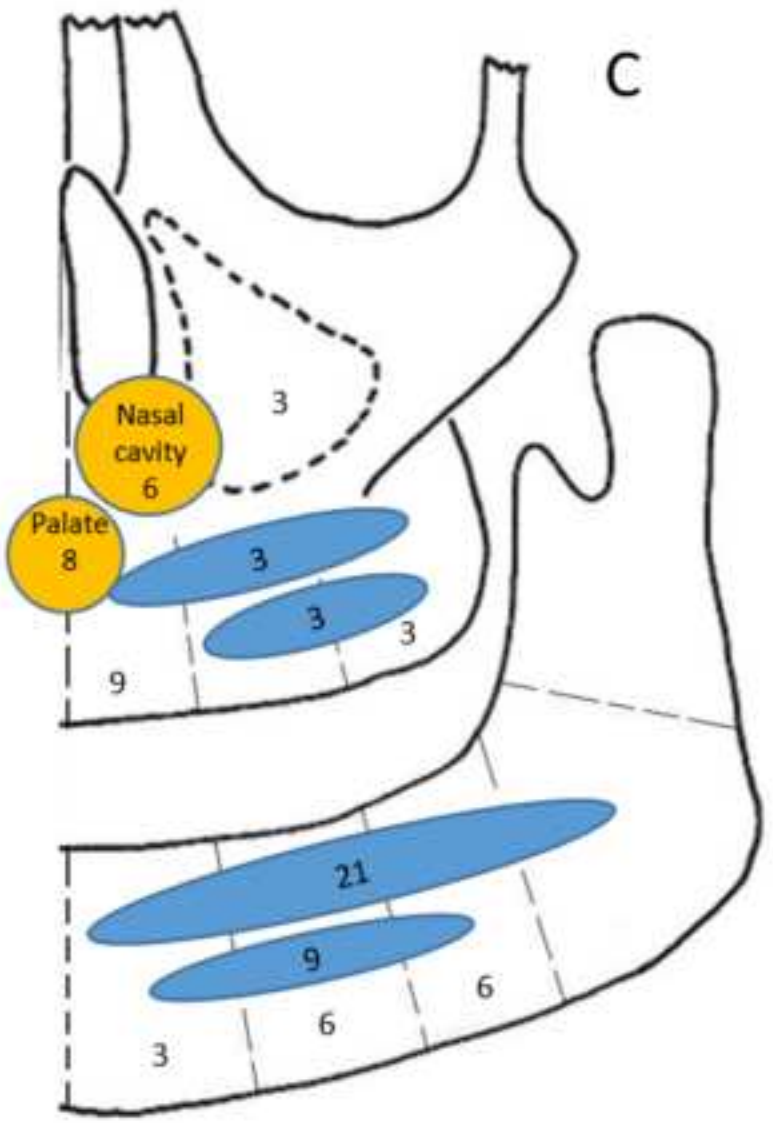


Figure 11: A representative section from an incisional biopsy from a 72 year old male. There was a large and destructive lesion in the left anterior/body of mandible. The diagnosis of ameloblastic carcinoma was made. A high-resolution version of the image is available as eSlide: VM05377

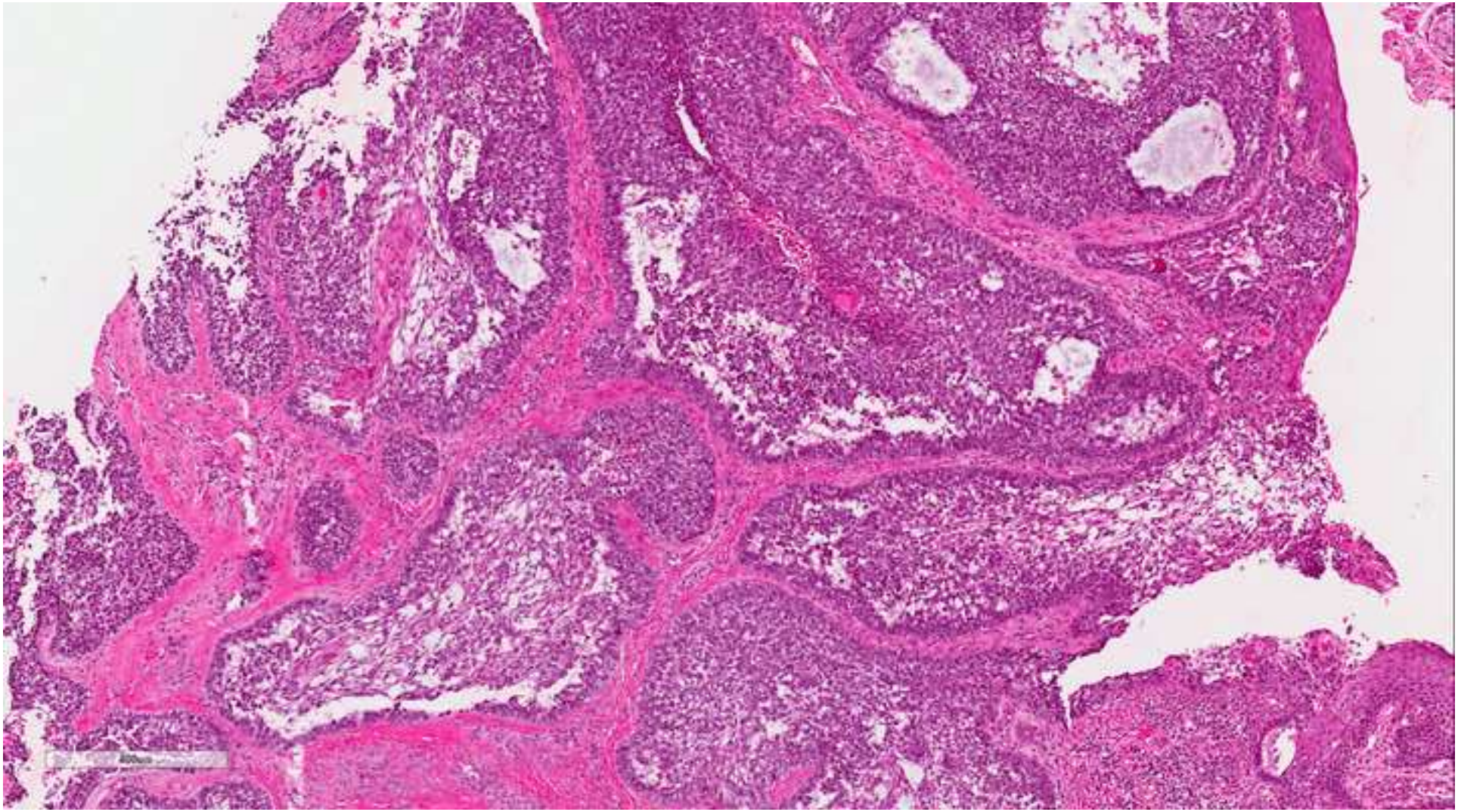
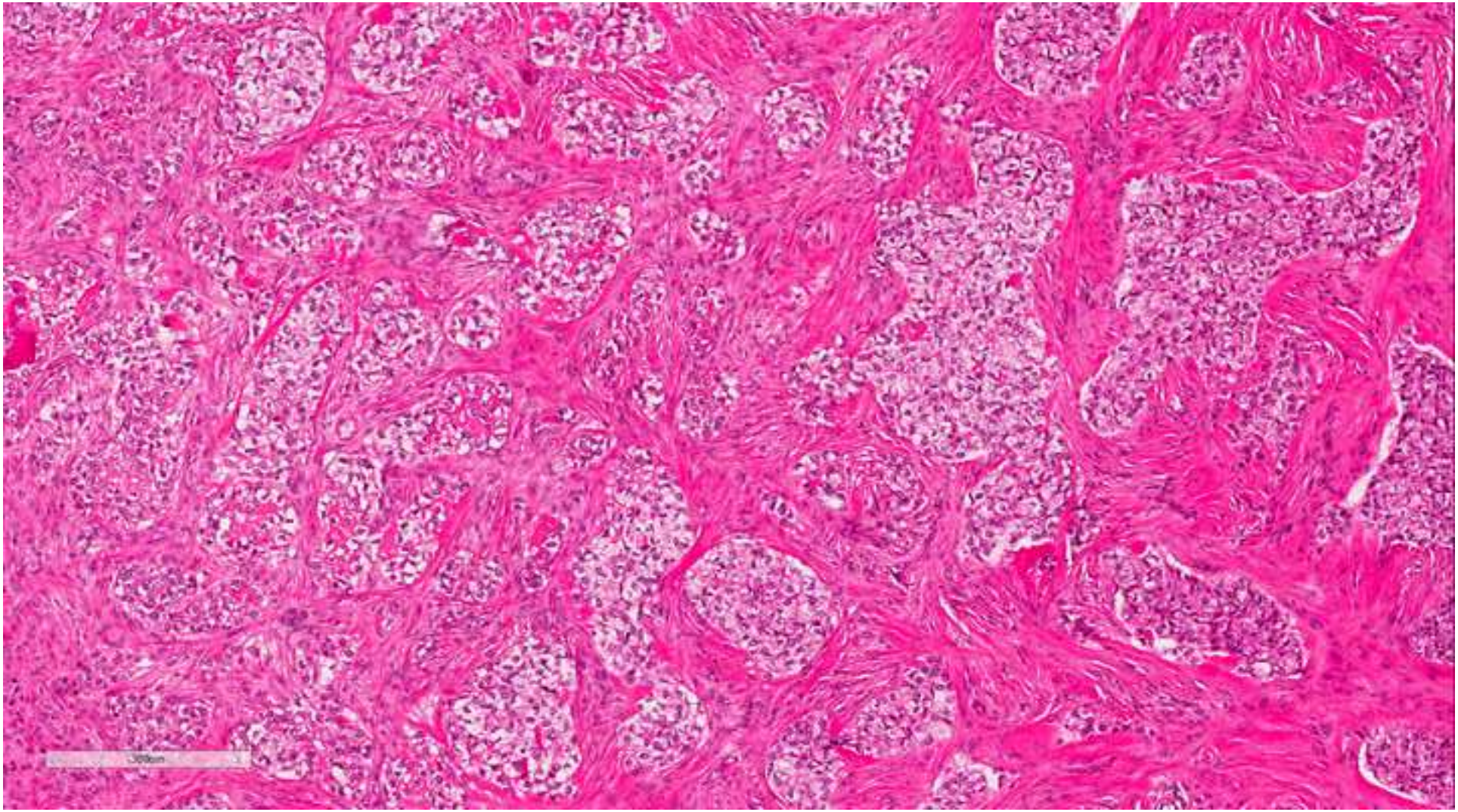


Figure 12: A representative section from an excision specimen from a female, aged 76. There was an extensive, destructive lesion of left anterior maxilla. Cytogenetic analysis revealed EWSR1 gene re-arrangements. The final diagnosis was of a clear cell odontogenic carcinoma. A high-resolution version of the image is available as eSlide: VM05378



carcinomas arose in association with an odontogenic cyst. The mean age of all the malignant tumours was 54.96 ± 17.1. The mandible was most commonly affected (Fig 10b), and the majority of cases involved the whole body of the mandible (28%, Fig 10c). Exemplar cases are shown in figures 11 and 12.

Referred cases

The relative proportions of lesions that were referred to the unit were different from the local population (Table 2). The proportion of odontomes is much lower in the referred population and consequently the proportion of ameloblastomas is much higher (Table 2). There is also bias towards the more rare tumours and those in which diagnostic difficulties are well described, including the malignant tumours, 94% of which were referrals.

Discussion

This study is the first to look in detail at the relative frequency of odontogenic tumours in a UK population. A previous demographic study of all odontogenic pathology from our department, reviewed specimens received over a 30-year period. Out of 44,007 specimens, only 331 were diagnosed as odontogenic tumours (0.75%)[6, 7]. A similar proportion was also seen in the United States, where odontogenic tumours accounted for 1.2% of all cases over a 20-year period [5]. The benefit of the present study is that it includes data from both local hospitals and referrals from other centres, with the referrals contributing to a greater proportion of the odontogenic tumour diagnoses (59.3%). Once the referred cases have been removed, it could cautiously be argued that the local data is reflective of the relative incidence of these lesions across the United Kingdom and indeed, the pattern of incidence is very similar to that described in other western populations.

The referral data was removed for much of the analysis as including it introduces bias to the population. This separation of the cohort into local cases served by the diagnostic service and those accessioned as referrals is informative for a number of reasons. The distribution of cases in the referred population is very different (table 2). This reflects the fact that the referred cases are biased towards the more rare and diagnostically difficult tumours, and they reflect the areas of difficulty in diagnosis that often prompt an onward speciality referral [14].

The commonest tumour overall is ameloblastoma, comprising 33.8% of the total number of odontogenic tumours, but this is not the case when only considering the local cases, where odontomes predominate (43%). The relative incidence of these lesions is also largely determined by the age of the patient, as Jones and Franklin showed ameloblastoma to be commonest in adults, comprising 30.8% [7], but <5% in children, where odontomes predominated (76%)[6]. Ameloblastoma has been reported as the most frequent odontogenic tumour in Turkey[2], Egypt[15] and in a study that reviewed the worldwide frequency of 8544 odontogenic tumours[16]. However, other studies, such as that carried out in California identified odontomes as the most frequently occurring odontogenic tumour [5]. The reasons for this variability are complex, and whilst there may be true differences in the incidence of odontogenic tumours in different populations, some element of the variation may be due to differences in submission of lesions for histological examination. In some circumstances, a diagnosis of odontome may be made on radiological appearances only and therefore the tissue may not be sent for histological examination: indeed, many of the case series come from populations in the developing world, where access to histopathology services may be limited.

Despite the removal of ameloblastic fibro-odontome (AFO) and ameloblastic fibro-dentinoma (AFD) from the 2017 WHO classification, we have separately reported these in Tables 1 and 2. The nature of the mixed odontogenic tumours, including ameloblastic fibroma (AF), has been a subject of debate and disagreement for some years [17]. It is widely accepted that AF is an entity in its own right as the mean age is higher than for AFO, which does not support the concept of an AF-AFO-Odontome continuum. The issue with the relationship of AFO and odontome is more problematic. AFO are often histologically indistinguishable from a developing odontome and the vast majority are best regarded as developing odontomes. However large, destructive AFO have been reported [18, 19], which may indicate that there is a spectrum of biological potential: while most are probably hamartoma, some may be truly neoplastic.

Table 3 shows a summary of published case series from around the world. Direct comparisons between the present study and previous studies are difficult to make. Multiple reasons for this exist, and whilst this is the first study that has looked at frequency of odontogenic tumours in line with the 2017 WHO classification [11], we have attempted to make the data as comparable as possible; for example, by removal of keratocystic odontogenic tumour (KCOT) and Calcifying cystic odontogenic tumour (CCOT) from the data. We identified three similar studies published in 2017,

Table 3. A summary of studies that have reported incidence of odontogenic tumours. The data for the present series is the local data only, to allow for comparisons. In some cases*, the individual cohorts have been combined if they come from the same country, and the mean values are stated. Other than for the current cohort, all of the assessment of the tumours was completed using WHO Classification 3rd edition (2005). KCOT (odontogenic keratocyst) and CCOT (calcifying odontogenic cyst) have been removed from the published totals, where appropriate

	Present study	*Saudi Arabia*[1]	**Iran*[2, 3]	**Turkey*[4, 5]	**India*[6-13]	*Pakistan*[14]	*Sri Lanka*[15]	**China*[16, 17]	*Thailand*[18]	*Ethiopia*[19]	*Rural Africa*[20]	*Africa*[21]	*Egypt*[22]	**Libya*[23, 24]	**Nigeria*[25-27]	**Brazil*[28-30]	*Mexico*[31]	*Chile*[32]	*Argentina*[33]	*USA*[34]	*Estonia*[35]	*UK (adult)*[36]	*UK (children)*[37]
Benign epithelial odontogenic tumours																							
Ameloblastoma	30%	43%	53%	32%	62%	79%	68%	63%	59%	54%	59%	80%	52%	46%	70%	37%	25%	21%	20%	12%	25%	41%	5%
Squamous Odontogenic Tumour (SOT)	<1%	-	-	-	-	-	1%	-	-	-	-	-	-	-	1%	-	-	1%	-	-	-	-	-
Calcifying epithelial odontogenic tumour (CEOT)	3%	2%	1%	11%	2%	-	2%	1%	1%	-	2%	1%	5%	2%	1%	1%	1%	1%	1%	-	1%	5%	-
Adenomatoid odontogenic tumour (AOT)	7%	7%	6%	2%	8%	6%	6%	5%	5%	-	6%	4%	5%	3%	4%	6%	6%	7%	5%	2%	1%	2%	6%
Benign mixed epithelial and mesenchymal tumours																							
Ameloblastic fibroma	-	1%	2%	1%	2%	-	1%	1%	1%	6%	-	2%	3%	1%	3%	2%	-	1%	2%	2%	16%	-	5%
Odontome (total)	43%	26%	21%	31%	19%	6%	14%	10%	22%	4%	7%	3%	16%	28%	2%	39%	48%	48%	53%	78%	35%	32%	76%
(Ameloblastic fibro-dentinoma)	-	-	-	-	-	*2%*	-	*1%*	-	-	*3%*	-	-	*2%*	-	-	-	*1%*	-	*2%*	-	-	-
(Ameloblastic fibro-odontome)	*2%*	*3%*	*2%*	*1%*	-	-	*1%*	*1%*	*1%*	-	-	-	-	-	-	-	-	*2%*	*5%*	-	-	-	*3%*
Dentinogenic ghost cell tumour	-	-	-	1%	-	-	-	1%	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
Benign mesenchymal tumours																							
Odontogenic Fibroma	5%	1%	1%	3%	2%	2%	1%	2%	1%	7%	5%	2%	-	1%	3%	2%	5%	6%	3%	1%	-	2%	2%
Odontogenic Myxoma	5%	11%	10%	6%	2%	4%	5%	6%	5%	10%	10%	6%	10%	8%	12%	9%	14%	10%	8%	2%	12%	1%	3%
Cementoblastoma	2%	3%	2%	2%	1%	-	-	3%	2%	-	3%	-	5%	2%	-	3%	-	2%	2%	1%	8%	1%	1%
Malignant odontogenic tumours																							
Odontogenic carcinomas/sarcomas (total)	<1%	2%	2%	8%	-	2%	2%	7%	1%	19%	4%	1%	3%	1%	3%	-	-	1%	-	-	1%	-	-
Malignant/metastasising ameloblastoma	-	-	-	-	-	-	-	-	-	-	-	-	2%	-	-	-	-	-	-	-	-	-	-
Other odontogenic lesions																							
Odontogenic Hamartoma	2%	-	-	-	-	-	-	-	-	-	-	-	-	5%	-	-	-	-	-	-	-	-	-
Odonto-ameloblastoma	-	-	1%	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
Total number of cases	**230**	**119**	**469**	**232**	**1027**	**142**	**1247**	**1854**	**445**	**140**	**572**	**3034**	**66**	**178**	**892**	**426**	**410**	**362**	**153**	**1087**	**75**	**262**	**175**

however these assessed the prevalence of odontogenic tumours in line with the 2005 WHO classification[20-22]. The 2017 WHO classification made some substantial changes to odontogenic tumours, including re-classification of the KCOT to the odontogenic keratocyst, removing it from the tumour category [11]. During the period of this study, 374 odontogenic keratocysts were diagnosed in Sheffield. This would have had a marked effect on the relative frequency of odontogenic tumours, as its original introduction in 2005 caused an increase in the overall frequency and prevalence of odontogenic tumours [23]. Studies in populations that are directly comparable to our cohort are very few but, in general, the patterns of OT incidence are very similar to that seen in our local population. In western populations, odontome are the most common odontogenic tumour, followed by ameloblastoma, although there is still marked variability in the relative proportions[5, 24].

Malignant tumours comprise a very small proportion of odontogenic tumours. Only 6% of all odontogenic tumours were malignant, most of them accessioned as referral cases (31/33). As these lesions are so rare, this emphasises the need for access to specialist expertise in order to gain experience in diagnosing such lesions. This has implications for the provision of training of oral and maxillofacial pathologists and in maintenance of expertise, given that the number of malignant odontogenic tumours diagnosed is so low. It is thus important that the centres which have experience of these tumours (either locally or referred), make these available for training and continuing education, so that the expertise in the diagnoses of these exceedingly rate tumours can be maintained.

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Table 1. Total number of odontogenic tumours received at the Oral and Maxillofacial Pathology diagnostic service between 1992 and 2016

Table 2: Number of odontogenic tumours received from local region sources and external/tertiary referrals between 1992 and 2016.

Table 3. A summary of studies that have reported incidence of odontogenic tumours. The data for the present series is the local data only, to allow for comparisons. In some cases*, the individual cohorts have been combined if they come from the same country, and the mean values are stated. Other than for the current cohort, all of the assessment of the tumours was completed using WHO Classification 3rd edition (2005). KCOT (odontogenic keratocyst) and CCOT (calcifying odontogenic cyst) have been removed from the published totals, where appropriate.

	Present study	*Saudi Arabia*[25]	**Iran*[26, 27]	**Turkey*[2, 28]	**India*[21, 29-35]	*Pakistan*[36]	*Sri Lanka*[4]	**China*[3, 37]	*Thailand*[38]	*Ethiopia*[22]	*Rural Africa*[39]	*Africa*[20]	*Egypt*[15]	**Libya*[40, 41]	**Nigeria*[42-44]	**Brazil*[45-47]	*Mexico*[23]	*Chile*[48]	*Argentina*[49]	*USA*[5]	*Estonia*[24]	*UK (adult)*[7]	*UK (children)*[6]
Benign epithelial odontogenic tumours																							
Ameloblastoma	30%	43%	53%	32%	62%	79%	68%	63%	59%	54%	59%	80%	52%	46%	70%	37%	25%	21%	20%	12%	25%	41%	5%
Squamous Odontogenic Tumour (SOT)	<1%	-	-	-	-	-	1%	-	-	-	-	-	-	-	1%	-	-	1%	-	-	-	-	-
Calcifying epithelial odontogenic tumour (CEOT)	3%	2%	1%	11%	2%	-	2%	1%	1%	-	2%	1%	5%	2%	1%	1%	1%	1%	1%	-	1%	5%	-
Adenomatoid odontogenic tumour (AOT)	7%	7%	6%	2%	8%	6%	6%	5%	5%	-	6%	4%	5%	3%	4%	6%	6%	7%	5%	2%	1%	2%	6%
Benign mixed epithelial and mesenchymal tumours																							
Ameloblastic fibroma	-	1%	2%	1%	2%	-	1%	1%	1%	6%	-	2%	3%	1%	3%	2%	-	1%	2%	2%	16%	-	5%
Odontome (total)	43%	26%	21%	31%	19%	6%	14%	10%	22%	4%	7%	3%	16%	28%	2%	39%	48%	48%	53%	78%	35%	32%	76%
(Ameloblastic fibro-dentinoma)	-	-	-	-	-	*2%*	-	*1%*	-	-	*3%*	-	-	*2%*	-	-	-	*1%*	-	*2%*	-	-	-
(Ameloblastic fibro-odontome)	*2%*	*3%*	*2%*	*1%*	-	-	*1%*	*1%*	*1%*	-	-	-	-	-	-	-	-	*2%*	*5%*	-	-	-	*3%*
Dentinogenic ghost cell tumour	-	-	-	1%	-	-	-	1%	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
Benign mesenchymal tumours																							
Odontogenic Fibroma	5%	1%	1%	3%	2%	2%	1%	2%	1%	7%	5%	2%	-	1%	3%	2%	5%	6%	3%	1%	-	2%	2%
Odontogenic Myxoma	5%	11%	10%	6%	2%	4%	5%	6%	5%	10%	10%	6%	10%	8%	12%	9%	14%	10%	8%	2%	12%	1%	3%
Cementoblastoma	2%	3%	2%	2%	1%	-	-	3%	2%	-	3%	-	5%	2%	-	3%	-	2%	2%	1%	8%	1%	1%
Malignant odontogenic tumours																							
Odontogenic carcinomas/sarcomas (total)	<1%	2%	2%	8%	-	2%	2%	7%	1%	19%	4%	1%	3%	1%	3%	-	-	1%	-	-	1%	-	-
Malignant/metastasising ameloblastoma	-	-	-	-	-	-	-	-	-	-	-	-	2%	-	-	-	-	-	-	-	-	-	-
Other odontogenic lesions																							
Odontogenic Hamartoma	2%	-	-	-	-	-	-	-	-	-	-	-	-	5%	-	-	-	-	-	-	-	-	-
Odonto-ameloblastoma	-	-	1%	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
Total number of cases	**230**	**119**	**469**	**232**	**1027**	**142**	**1247**	**1854**	**445**	**140**	**572**	**3034**	**66**	**178**	**892**	**426**	**410**	**362**	**153**	**1087**	**75**	**262**	**175**

References

1. Reichart P, Philipsen HP. *Odontogenic Tumors and Allied Lesions* Quintessence; 2004.
2. Sekerci AE, Nazlim S, Etoz M, Deniz K, Yasa Y. Odontogenic tumors: a collaborative study of 218 cases diagnosed over 12 years and comprehensive review of the literature. *Med Oral Patol Oral Cir Bucal.* 2015;20:e34-44.
3. Jing W, Xuan M, Lin Y, et al. Odontogenic tumours: a retrospective study of 1642 cases in a Chinese population. *Int J Oral Maxillofac Surg.* 2007;36:20-25.
4. Siriwardena BS, Tennakoon TM, Tilakaratne WM. Relative frequency of odontogenic tumors in Sri Lanka: Analysis of 1677 cases. *Pathol Res Pract.* 2012;208:225-230.
5. Buchner A, Merrell PW, Carpenter WM. Relative frequency of central odontogenic tumors: a study of 1,088 cases from Northern California and comparison to studies from other parts of the world. *J Oral Maxillofac Surg.* 2006;64:1343-1352.
6. Jones AV, Franklin CD. An analysis of oral and maxillofacial pathology found in children over a 30-year period. *International Journal of Paediatric Dentistry.* 2006;16:19-30.
7. Jones AV, Franklin CD. An analysis of oral and maxillofacial pathology found in adults over a 30-year period. *Journal of Oral Pathology & Medicine.* 2006;35:392-401.
8. Pindborg J, Kramer IRH. *Histological Typing of Odontogenic Tumours, Jaw Cysts, and Allied Lesions*. Geneva: World Health Organisation; 1971.
9. Barnes L, Eveson JW, Reichart P, Sidransky D. *Pathology and Genetics of Head and Neck Tumors.* Lyon: IARC Press; 2005.
10. Wright JM, Odell EW, Speight PM, Takata T. Odontogenic tumors, WHO 2005: where do we go from here? *Head Neck Pathol.* 2014;8:373-382.
11. El-Naggar AK, Chan JKC, Grandis JR, Takata T, Slootweg PJ. *WHO Classification of Head and Neck Tumours*. Lyon: WHO Press; 2017.
12. Speight PM, Takata T. New tumour entities in the 4th edition of the World Health Organization Classification of Head and Neck tumours: odontogenic and maxillofacial bone tumours. *Virchows Arch.* 2017.
13. Dhanuthai K, Chantarangsu S, Rojanawatsirivej S, et al. Ameloblastoma: a multicentric study. *Oral surgery, oral medicine, oral pathology and oral radiology.* 2012;113:782-788.
14. Mullin MH, Brierley DJ, Speight PM. Second opinion reporting in head and neck pathology: the pattern of referrals and impact on final diagnosis. *Or Surg or Med or Pa.* 2015;119:656-660.
15. Tawfik MA, Zyada MM. Odontogenic tumors in Dakahlia, Egypt: analysis of 82 cases. *Oral Surg Oral Med O.* 2010;109:E67-E73.
16. Avelar RL, Primo BT, Pinheiro-Nogueira CB, et al. Worldwide incidence of odontogenic tumors. *J Craniofac Surg.* 2011;22:2118-2123.
17. Nelson BL, Thompson LD. Ameloblastic fibro-odontoma. *Head Neck Pathol.* 2014;8:168-170.
18. Kirjavainen A, Tuovinen V, Sandor GK. Large ameloblastic fibro-odontoma in a 7-year-old girl with analysis of 108 cases. *Annals of maxillofacial surgery.* 2016;6:15-20.
19. Banihashem Rad SA, Mortazavi H, Eshghpour M, Salehinejad J, Shahakbari R. A Large Ameloblastic Fibro-odontoma of the Maxillary Sinus. *Iranian journal of otorhinolaryngology.* 2014;26:111-114.
20. Ogundana OM, Effiom OA, Odukoya O. Pattern of distribution of odontogenic tumours in sub-Saharan Africa. *Int Dent J.* 2017;67:308-317.
21. Nalabolu GRK, Mohiddin A, Hiremath SKS, Manyam R, Bharath TS, Raju PR. Epidemiological study of odontogenic tumours: An institutional experience. *Journal of infection and public health.* 2017;10:324-330.

22. Kebede B, Tare D, Bogale B, Alemseged F. Odontogenic tumors in Ethiopia: eight years retrospective study. *BMC oral health.* 2017;17:54.
23. Gaitan-Cepeda LA, Quezada-Rivera D, Tenorio-Rocha F, Leyva-Huerta ER. Reclassification of odontogenic keratocyst as tumour. Impact on the odontogenic tumours prevalence. *Oral Diseases.* 2010;16:185-187.
24. Tamme T, Soots M, Kulla A, et al. Odontogenic tumours, a collaborative retrospective study of 75 cases covering more than 25 years from Estonia. *J Cranio Maxill Surg.* 2004;32:161-165.
25. AlSheddi MA, AlSenani MA, AlDosari AW. Odontogenic tumors: analysis of 188 cases from Saudi Arabia. *Annals of Saudi medicine.* 2015;35:146-150.
26. Taghavi N, Rajabi M, Mehrdad L, Sajjadi S. A 10-year retrospective study on odontogenic tumors in Iran. *Indian J Dent Res.* 2013;24:220-224.
27. Saghravanian N, Jafarzadeh H, Bashardoost N, Pahlavan N, Shirinbak I. Odontogenic tumors in an Iranian population: a 30-year evaluation. *Journal of oral science.* 2010;52:391-396.
28. Cizmeci Senel F, Dayisoylu EH, Ersoz S, et al. The relative frequency of odontogenic tumors in the Black Sea region of Turkey: an analysis of 86 cases. *Turk J Med Sci.* 2012;42:1463-1470.
29. Sriram G, Shetty RP. Odontogenic tumors: a study of 250 cases in an Indian teaching hospital. *Oral Surg Oral Med Oral Pathol Oral Radiol Endod.* 2008;105:e14-21.
30. Ebenezer V, Ramalingam B. A cross-sectional survey of prevalence of odontogenic tumours. *Journal of maxillofacial and oral surgery.* 2010;9:369-374.
31. Varkhede A, Tupkari JV, Sardar M. Odontogenic tumors: A study of 120 cases in an Indian teaching hospital. *Med Oral Patol Oral.* 2011;16:C895-C899.
32. Bhagwat A, Barpande SR, Bhavthankar JD, Mandale MS, Humbe J, Singh P. Odontogenic tumors: Review of 127 cases in Marathwada region of Maharashtra. *Journal of oral and maxillofacial pathology : JOMFP.* 2017;21:457-458.
33. Deepthi PV, Beena VT, Padmakumar SK, Rajeev R, Sivakumar R. A study of 1177 odontogenic lesions in a South Kerala population. *J Oral Maxillofac Pathol.* 2016;20:202-207.
34. Kadashetti V, Chaudhary M, Patil S, Gawande M, Shivakumar KM, Badiyani BK. Odontogenic tumors; a retrospective study of 102 cases. *Int J Oral Care Res.* 2014;2:7-10.
35. S. G, J. C, D. J. Odontogenic tumors in Western India (Gujarat): Analysis of 209 cases. *J Clin Exp Dent.* 2011;3:e78-83.
36. Naz I, Mahmood MK, Akhtar F, Nagi AH. Clinicopathological Evaluation of Odontogenic Tumours in Pakistan - A Seven Years Retrospective Study. *Asian Pac J Cancer P.* 2014;15:3327-3330.
37. Luo HY, Li TJ. Odontogenic tumors: A study of 1309 cases in a Chinese population. *Oral Oncology.* 2009;45:706-711.
38. Worawongvasu R, Tiensuwan M. Odontogenic tumors in Thailand: A study of 590 Thai patients. *J Oral Maxillofac Su.* 2015;27:567-576.
39. Mamabolo M, Noffke C, Raubenheimer E. Odontogenic tumours manifesting in the first two decades of life in a rural African population sample: a 26 year retrospective analysis. *Dentomaxillofac Rad.* 2011;40:331-337.
40. El-Gehani R, Orafi M, Elarbi M, Subhashraj K. Benign tumours of orofacial region at Benghazi, Libya: A study of 405 cases. *J Cranio Maxill Surg.* 2009;37:370-375.
41. Goteti SH. Odontogenic Tumors: A Review of 675 Cases in Eastern Libya. *Nigerian journal of surgery : official publication of the Nigerian Surgical Research Society.* 2016;22:37-40.

42. Adebayo ET, Ajike SO, Adekeye EO. A review of 318 odontogenic tumors in Kaduna, Nigeria. *J Oral Maxil Surg.* 2005;63:811-819.
43. Lawal AO, Adisa AO, Olusanya AA. Odontogenic tumours: A review of 266 cases. *Journal of clinical and experimental dentistry.* 2013;5:e13-17.
44. Ladeinde AL, Ajayi OF, Ogunlewe MO, et al. Odontogenic tumors: a review of 319 cases in a Nigerian teaching hospital. *Oral Surg Oral Med Oral Pathol Oral Radiol Endod.* 2005;99:191-195.
45. Avelar RL, Antunes AA, Santos Tde S, Andrade ES, Dourado E. Odontogenic tumors: clinical and pathology study of 238 cases. *Braz J Otorhinolaryngol.* 2008;74:668-673.
46. Santos JN, Pinto LP, de Figueredo CR, de Souza LB. Odontogenic tumors: analysis of 127 cases. *Pesqui Odontol Bras.* 2001;15:308-313.
47. Osterne RL, Brito RG, Alves AP, Cavalcante RB, Sousa FB. Odontogenic tumors: a 5-year retrospective study in a Brazilian population and analysis of 3406 cases reported in the literature. *Oral Surg Oral Med Oral Pathol Oral Radiol Endod.* 2011;111:474-481.
48. Ochsenius G, Ortega A, Godoy L, Penafiel C, Escobar E. Odontogenic tumors in Chile: a study of 362 cases. *Journal of Oral Pathology & Medicine.* 2002;31:415-420.
49. Guerrisi M, Piloni MJ, Keszler A. Odontogenic tumors in children and adolescents. A 15-year retrospective study in Argentina. *Med Oral Patol Oral Cir Bucal.* 2007;12:E180-185.