# Oral and Maxillofacial Lesions in a Thai Pediatric Population: A Retrospective Review from Two Dental Schools

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**Objective:** To determine the prevalence of oral and maxillofacial lesions in a Thai pediatric population. **Material and Method:** Oral biopsy records from pediatric patients between the ages of 0 and 15 years in the files of Faculty of Dentistry, Mahidol University, and the files of Faculty of Dentistry, Khon Kaen University were reviewed. The patients were divided into three age groups, including 0 to 5, 6 to 10, and 11 to 15 years. Excluding the diagnosis of normal tissues, the oral and maxillofacial lesions were classified into nine categories.

**Results:** Of 13,050 biopsied oral and maxillofacial lesions, 1,389 cases (10.6%) came from pediatric patients. The largest number of lesions was odontogenic cysts and tumors, followed by inflammatory and reactive lesions, and salivary gland pathology. The top ten most prevalent lesions contributed 73% of all oral biopsies. The most common lesion was dentigerous cyst, followed by mucocele and pyogenic granuloma.

**Conclusion:** The vast majority of oral diseases in children were benign and related to either developmental or tissue reaction, while malignant lesions were found in a very small proportion of all oral biopsies.

Keywords: Pediatric, Oral lesions, Prevalence, Thai

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Oral and maxillofacial lesions found in children are distinct from those found in adults. This may be a result of physical development and growth that extensively take place in children. Several lesions predominantly found in children include melanotic neuroectodermal tumor of infancy, Langerhans cell histiocytosis, lymphangioma, and hemangioma<sup>(1)</sup>. Several studies on oral lesions in children were published in the literature. Those results were variable as most of them focused on particular pathology in children such as oral and maxillofacial tumors<sup>(2,3)</sup>, tumors and tumor-like lesions<sup>(4,5)</sup>, or odontogenic tumors<sup>(6,7)</sup>.

Regarding general oral and maxillofacial lesions in children, several studies have been reported from different regions of the world including the USA<sup>(8,9)</sup>, Argentina<sup>(10)</sup>, Brazil<sup>(11-13)</sup>, Nigeria<sup>(14)</sup>, Turkey<sup>(15)</sup>, and Chile<sup>(16)</sup>. However, the data from the countries in Asia is very limited<sup>(17-19)</sup> and only one study came from Thailand<sup>(19)</sup>.

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The purpose of the present study was to determine the prevalence of oral and maxillofacial pathology among a group of Thai pediatric patients, aged 0 to 15 years, from the tissue biopsies submitted for histopathological diagnosis in two dental schools of Thailand.

#### **Material and Method**

The authors obtained the approval of the Institutional Review Board, Mahidol University and the Khon Kaen University Ethics Committee in Human Research. Oral biopsies from pediatric patients up to 15 years old were retrieved from the Archives of the Department of Oral and Maxillofacial Pathology, Faculty of Dentistry, Mahidol University, over a period of 39 years (1973-2011) and the Archives of the Department of Oral Diagnosis, Faculty of Dentistry, Khon Kaen University, over a period of 20 years (1992-2011). The collected data included sex, age, and the histopathological diagnosis of the lesions. Multiple biopsies from the same patient and the same location were regarded as one lesion. The biopsies diagnosed as normal tissue were excluded from the study. The oral and maxillofacial pathology were subclassified into nine categories: 1) Dental and periapical pathology,

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2) Periodontal pathology, 3) Odontogenic cysts and tumors, 4) Inflammatory and reactive lesions, 5) Mucosal pathology, 6) Salivary gland pathology, 7) Bone pathology, 8) Neoplasms, and 9) Miscellaneous pathology. The pediatric patients were divided into three age groups: 1) 0 to 5 years, 2) 6 to 10 years, and 3) 11 to 15 years.

# Statistical analyses

The collected data were expressed as percent (%). Chi-square test (p < 0.05) was calculated to determine differences between sexes and among age groups.

# Results

Excluding eight normal tissues, 1,389 pediatric oral biopsies (10.6%) were obtained from the 13,050 oral biopsies received in the 39-year period of the Faculty of Dentistry, Mahidol University, and in the 20-year period of the Faculty of Dentistry, Khon Kaen University. Of the 1,389 biopsies, 110 various diseases were diagnosed in the present study. Table 1 showed the distribution of patients with respect to sex, age groups, and the frequency of oral lesions in each diagnostic group. Overall, no statistical difference was found in the prevalence between sexes (M:F =1.06:1). According to age group distribution, statistical differences (p < 0.05) was observed among three age groups. The predominant distribution of age came from children between 11 and 15 (61.3%), followed by those between 6 and 10 (31.4%), and 0 and 5 years (7.3%). Among nine diagnostic categories, the highest prevalence of oral and maxillofacial pathology in pediatric patients was the group of odontogenic cysts

and tumors (35.5%), followed by inflammatory and reactive lesions (17%), and salivary gland pathology (16.8%). While odontogenic cysts and tumors showed a male predilection (p<0.05), salivary gland pathology showed a female predilection (p<0.05). No statistical difference between sexes was found in the remaining diagnostic groups. With the exception of the neoplasms group, statistical differences (p<0.05) among three age groups were found. The prevalence dramatically increased after the age of 5 in all diagnostic groups (Table 1).

The top ten most common lesions were dentigerous cyst, mucocele, pyogenic granuloma, odontoma, fibrous hyperplasia, dental follicle, radicular cyst, ameloblastoma, granulation tissue, and keratocystic odontogenic tumor, respectively. These lesions constituted a major proportion (73.3%) of all the biopsies.

Of 493 odontogenic cysts and tumors, dentigerous cyst was the most common lesion, followed by odontoma and ameloblastoma (Table 2). The occurrence of dentigerous cyst accounted for almost a half (47.3%) of the oral biopsies in this category and was more frequent in males than in females (M:F = 2.06:1).

In the inflammatory and reactive lesions group, pyogenic granuloma was the most common lesion, followed by fibrous hyperplasia and granulation tissue (Table 3). These three lesions comprised a major proportion (92%) of the lesions in this group.

Of 234 salivary gland pathology biopsies, mucocele (n = 228) was the most prevalent lesion and contributed as high as 97% of the oral biopsies in this

Table 1. Distribution of oral and maxillofacial pathology with respect to sex and age groups

Diagnostic group	Total	Sex (%) Age (%)			%)			
	n (%)	Male	Female	<i>p</i> -value	0-5	6-10	11-15	<i>p</i> -value
Odontogenic cysts and tumors	493 (35.5)	295 (41.2)	198 (29.5)	< 0.001	20 (19.6)	167 (38.3)	306 (36.0)	< 0.001
Inflammatory and reactive lesions	236 (17.0)	114 (15.9)	122 (18.2)	0.603	25 (24.5)	66 (15.1)	145 (17.0)	< 0.001
Salivary gland pathology	234 (16.9)	101 (14.1)	133 (19.8)	0.036	13 (12.8)	97 (22.2)	124 (14.6)	< 0.001
Dental and periapical pathology	211 (15.2)	102 (14.2)	109 (16.2)	0.630	11 (10.8)	52 (11.9)	148 (17.4)	< 0.001
Bone pathology	75 (5.4)	38 (5.3)	37 (5.5)	0.908	10 (9.8)	19 (4.4)	46 (5.4)	< 0.001
Mucosal pathology	45 (3.2)	23 (3.2)	22 (3.3)	0.881	6 (5.9)	11 (2.5)	28 (3.3)	< 0.001
Neoplasms	44 (3.2)	21 (2.9)	23 (3.4)	0.763	11 (10.8)	13 (3.0)	20 (2.3)	0.218
Periodontal pathology	31 (2.2)	12 (1.7)	19 (2.8)	0.209	3 (2.9)	6 (1.4)	22 (2.6)	< 0.001
Miscellaneous pathology	20 (1.4)	11 (1.5)	9 (1.3)	0.655	3 (2.9)	5 (1.2)	12 (1.4)	0.035
Total	1,389* (100.0)	717 (100.0)	672 (100.0)	0.227	102 (100.0)	436 (100.0)	851 (100.0)	< 0.001

Chi-square test at p < 0.05

\* Excluded 8 normal tissues

group. The other salivary gland pathology included sialadenitis (n = 2), mucous retention cyst (n = 2) and pleomorphic adenoma (n = 2).

Among dental and periapical pathology (Table 4), dental follicle was the most prevalent

Table 2. Odontogenic cysts and tumors

Pathological diagnosis	Number of cases	% of group	% of total
Dentigerous cyst*	233	47.26	16.77
Odontoma	80	16.23	5.76
Ameloblastoma	52	10.55	3.74
Keratocystic odontogenic tumor	35	7.10	2.52
Odontogenic cyst (unclassified)	26	5.30	1.87
Calcifying cystic odontogenic tumor	23	4.70	1.66
Adenomatoid odontogenic tumor	15	3.04	1.08
Ameloblastic fibro-odontoma	7	1.42	0.50
Ameloblastic fibroma	5	1.01	0.36
Odontogenic myxofibroma	4	0.81	0.29
Calcifying epithelial odontogenic tumor**	3	0.61	0.22
Odontogenic fibroma	3	0.61	0.22
Eruption cyst	2	0.40	0.14
Cementoblastoma	2	0.40	0.14
Others***	3	0.61	0.22
Total	493	100.0	35.5

\* Included dentigerous cyst associated with odontoma (n = 9)\*\* Included calcifying epithelial odontogenic tumor associated with odontoma (n = 1)

\*\*\* Included lateral periodontal cyst, paradental cyst and primordial cyst, each with one lesion

**Table 3.** Inflammatory and reactive lesions

Pathological diagnosis	Number of cases	% of group	% of total
Pyogenic granuloma	98	41.53	7.05
Fibrous hyperplasia	79	33.47	5.69
Granulation tissue	40	16.95	2.88
Epulis granulomatosum	5	2.12	0.36
Giant cell fibroma	3	1.27	0.22
Granulomatous inflammation	3	1.27	0.22
Scar tissue	3	1.27	0.22
Sinusitis	2	0.85	0.14
Others*	3	1.27	0.22
Total	236	100.0	17.0

\* Included peripheral giant cell granuloma, eosinophilic panniculitis and reactive hyperplasia of lymph node, each with one lesion lesion, followed by radicular cyst and periapical granuloma. Table 5 presents the percentage of bone pathology. The most frequently found lesion was osteomyelitis followed by fibrous dysplasia, ossifying fibroma and necrotic bone. A male predilection (M:F = 1.85:1) was observed among pediatric patients with osteomyelitis.

Table 4. Dental and	periapical	pathology
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Pathological diagnosis	Number of cases	% of group	% of total
Dental follicle	71	33.65	5.11
Radicular cyst	69	32.70	4.97
Periapical granuloma	33	15.64	2.38
Residual cyst	8	3.79	0.57
Periapical abscess	5	2.37	0.36
Dentinogenesis imperfecta	5	2.37	0.36
Chronic hyperplastic pulpitis	4	1.90	0.29
Pulpal necrosis	4	1.90	0.29
Tooth bud	4	1.90	0.29
Chronic ulcerative pulpitis	2	0.95	0.14
Amelogenesis imperfecta	2	0.95	0.14
Others*	4	1.90	0.29
Total	211	100.0	15.2

\* Included root resorption, enamel hypoplasia, microdontia and ankylosis, each with one lesion

# Table 5. Bone pathology

Pathological diagnosis	Number of cases	% of group	% of total
Osteomyelitis	20	26.67	1.44
Fibrous dysplasia	17	22.67	1.22
Ossifying fibroma	6	8.00	0.43
Necrotic bone	6	8.00	0.43
Osteoma	5	6.67	0.36
Traumatic bone cyst	3	4.00	0.22
Garre's osteomyelitis	2	2.67	0.14
Juvenile ossifying fibroma	2	2.67	0.14
Central giant cell granuloma	2	2.67	0.14
Eosinophilic granuloma	2	2.67	0.14
Aneurysmal bone cyst	2	2.67	0.14
Others*	8	10.67	0.58
Total	75	100.0	5.4

\* Included osteoblastoma, osteochrondroma, idiopathic osteosclerosis, condylar bony hyperplasia, cherubism, venous malformation, exostosis and torus mandibularis, each with one lesion

Among mucosal pathology, oral nevus (n = 12) and squamous papilloma (n = 12) were the most prevalent lesions, followed by acanthosis and hyperkeratosis (n = 5) and non-specific ulcer (n = 5). In the category of neoplasms (Table 6), the prevalence of benign tumors accounted for over 70% of all 44 cases. Among benign tumors, hemangioma was the most common benign tumor, followed by neurofibroma. Only 12 cases were diagnosed as malignant tumors throughout the study period. Four malignant tumor types were discovered including lymphoma, malignant mesenchymal tumor, malignant schwannoma, and embryonal rhabdomyosarcoma. The most common malignant tumor was lymphoma.

Of 31 cases of periodontal pathology, only five periodontal pathology lesions were discovered. The most frequently found lesion was gingival hyperplasia (n = 13), followed by gingivofibromatosis (n = 10), drug induced hyperplasia (n = 3), gingivitis (n = 3), and gingival abscess (n = 2). The category of miscellaneous pathology included a variety of diseases that could not be classified into any diagnostic categories. In this group, non-diagnostic specimens (n = 8) was the most common biopsy, followed by hematoma (n = 2), and actinomycosis (n = 2).

#### Discussion

The present study reported the prevalence of oral and maxillofacial pathology encountering Thai

Table 6. Neoplasms

Pathological diagnosis	Number of cases	% of group	% of total
Benign			
Hemangioma	6	13.64	0.43
Neurofibroma	5	11.36	0.36
Lymphangioma	3	6.82	0.22
Lipoma	3	6.82	0.22
Solitary myofibromatosis	3	6.82	0.22
Melanotic neuroectodermal	2	4.55	0.14
tumor of infancy			
Mucosal neuroma	2	4.55	0.14
Fibrous histiocytoma	2	4.55	0.14
Others*	6	13.64	0.43
Malignant			
Lymphoma	8	18.18	0.58
Malignant mesenchymal tumor	2	4.55	0.14
Malignant schwannoma	1	2.27	0.07
Embryonal rhabdomyosarcoma	1	2.27	0.07
Total	44	100.0	3.2

\* Included benign mesenchymal tumor, hemangiopericytoma, leiomyoma, lipoblastoma, congenital epulis of the new born and schwannoma, each with one lesion children, aged 0 to 15 years, from two dental schools of Thailand. While the Faculty of Dentistry, Mahidol University is one of referral centers for the oral and maxillofacial lesions in the capital of Bangkok, the Faculty of Dentistry, Khon Kaen University is the only referral center in the northeast region of Thailand. The prevalence of oral and maxillofacial lesions among a Thai pediatric population in our study could serve as reliable representatives for Thailand.

The percentage of oral biopsies from children in our study (10.6%) was in line with that of previously published studies<sup>(8,9,12,17,18,20)</sup>, mostly ranging between 6 and 12.8%. With regard to age range, our study was mostly similar to two previous studies<sup>(10,18)</sup>. In comparison with these two studies (6% and 6.8%, respectively)<sup>(10,18)</sup>, our frequency (10.6%) of pediatric patients was relatively higher. This may be attributable to the longer study period in the present series.

In the present study, the overall occurrence of oral and maxillofacial lesions showed no statistical difference in the prevalence between sexes (M:F = 1.06:1), consistent with many previous studies<sup>(10,12,15,17,19)</sup>. Our data also showed that the occurrence of oral and maxillofacial lesions in pediatric patients increased with age. In comparison with the study conducting a similar age range stratification, the percentage (7.3%) of oral biopsies in patients aged 0-5 years in the present study was much lower than that (16.4%) of the previous study<sup>(18)</sup>. This was possibly due to different behavior of Thai parents on taking their very young children to see the doctor rather than seeing the dentist. On the other hand, this might reflect the actual prevalence of this pediatric patient group in Thailand.

The three most common lesions (dentigerous cyst, mucocele, and pyogenic granuloma) in the present study were exactly similar to those of the previous study from Thailand<sup>(19)</sup>. In addition, the two most common lesions in the present study (mucocele and dentigerous cysts) were in accordance with several studies<sup>(12,13,17,18)</sup>. Dentigerous cysts were the most commonly diagnosed lesion in the present study and in the previous study conducted in Thailand<sup>(19)</sup> whereas mucocele was the most commonly affected pediatric lesion in other studies<sup>(8,12,13,16-18,20)</sup>. The percentage of dentigerous cysts (16.77%) in the present study was relatively high in comparison with most previous studies<sup>(8,9,12,13,15,17,18,20)</sup> (ranging from 3.1-12.8%) but lower than the figure (20.7%) reported from Thailand<sup>(19)</sup>.

It is worth noting that pyogenic granuloma, ranked the third most prevalent lesion in our study as well as in the previous study from Thailand<sup>(19)</sup>. However, it was not presented in the top three most common lesions in other studies<sup>(12,13,17,18,20)</sup>. This might imply that this lesion more frequently encountered Thai children than children in other countries. Recently, Zuniga et al also reported that pyogenic granuloma is the second most commonly affected lesion in Chilean pediatric patients<sup>(16)</sup>.

Our result, showing that odontoma was the most common odontogenic tumor, is in line with many previous studies<sup>(9,10,12,13,15,17,18,20)</sup>. Only two studies<sup>(14,19)</sup> reported ameloblastoma as the most prevalent odontogenic tumor. The frequency of odontoma (5.76%) in our study was close to that of the previous study from Thailand (6.16%)<sup>(19)</sup>, and fell within the range of previous reports (2-10.4%)<sup>(8,9,12,13,15,17,18,20)</sup>.

The category of dental and periapical pathology represents the pathologic conditions directly involving the teeth and those being the consequences of pulpal infection or necrosis. This category did not exist in the majority of previous studies<sup>(8,12,13,15-19)</sup>. Only three studies<sup>(10,11,20)</sup> incorporated this category and only one previous study<sup>(20)</sup> showed detailed data of this category. Interestingly, this category was the most commonly diagnosed category in this previous study<sup>(20)</sup>, corresponding to 22% of the total biopsied specimens. Our figure (15.2%) was lower and this may be due to the much lower number of various defective lesions affecting tooth or dental pulp (such as dentinogenesis imperfecta, enamel hypoplasia, and pulpal necrosis) in the present study. In the study of Jones and Franklin<sup>(20)</sup>, these lesions accounted for 7.8% of all lesions whereas they were found at only 1.5% in the present data. The reason for the low figure in our study may be related to a rarity of sending the specimens of tooth disturbances for histopathological examination since either the patient will lose their tooth or these defects may be promptly diagnosed from clinical examination.

The bone pathology category in the present study constituted 5.4% of all pediatric oral lesions. This figure was slightly higher than that in the previous study (3.2%)<sup>(20)</sup>. Osteomyelitis was the most commonly diagnosed lesion in our study while the number of cases was fewer than in the study of Jones and Franklin<sup>(20)</sup>. Osteomyelitis is an inflammatory process affecting the jaw bone and frequently a consequence of long-term odontogenic infection. An increased prevalence of osteomyelitis is associated with several factors, for example, immunological status, systemic diseases, and malnutrition. It has been reported that this condition is more common in developing countries<sup>(1)</sup>. The higher occurrence of osteomyelitis in our study might also be due to a delay in seeking dental treatment for Thai children. This may result from either a negligence of Thai parents or difficulty in accessing dental services in Thailand, particularly in remote areas.

The data from the present study showed that neoplastic lesions, excluding odontogenic and salivary gland tumors, accounted for 3.2% of all pediatric oral lesions. Most of them (72.7%) were benign and possessed a mesenchymal origin. These results are in agreement with several previous studies<sup>(3,9,10,15,20)</sup>. Among the benign neoplasms with mesenchymal origin, hemangioma was the most common benign neoplasm in the present data, in agreement with several previous studies<sup>(2,3,15,18,20)</sup>. Interestingly, neurofibroma was the second most common benign tumor (0.36%)in our study while only one case (0.08%) was found in the previous study from Thailand<sup>(19)</sup>. However, with regard to the frequency of lesions, the frequency of neurofibroma in our study (0.36%) is in line with that of other studies<sup>(13,15,17,20)</sup></sup>, ranging from 0.2-0.45%.</sup> Oral neurofibroma is rarely involved in the oral cavity and is mostly diagnosed in teenagers and young adults<sup>(1)</sup>. The percentage of malignant neoplasm (0.9%) in the present study was very low and in accordance with most previous studies<sup>(10,12,13,17-20)</sup> showing a low occurrence of malignant neoplasm in children (0.7-2%). It is worth mentioning that no carcinoma was diagnosed from the pediatric biopsies in the present study. This emphasized the notion of previous authors<sup>(3,5)</sup> that the occurrence of oral cancer developing from epithelial cells in the pediatric population is uncommon. Owing to the small number of malignant neoplasms in each study, the most frequent malignant neoplasm found in the literature was different (9,12,13,15,17,18,20). We found that lymphoma was the most prevalent malignant neoplasm (8 from 12 cases) of all malignant neoplasms and was similar to two published reports<sup>(2,10)</sup>.

# Conclusion

Overall, most oral and maxillofacial lesions in children were benign and related to either development or tissue reaction. In comparison with previous studies from other countries, the different results discovered might be attributable to different study designs as well as socio-economic status of each country. The odontogenic cysts and tumors are the most frequently diagnosed category among Thai pediatric populations that conformed well to the fact that odontogenesis is most predominant during childhood. Although a very low frequency of malignant neoplasms was detected, they required more diagnostic consideration and intervention. These data would be helpful for general practitioners and pediatric dentists in making a provisional diagnosis and managing children who present oral and maxillofacial lesions.

## What is already known on this topic?

From a few reviews of pediatric oral lesions based on an analysis of available biopsy records, most of oral lesions found in children were predominantly inflammatory/reactive and benign types. Among these benign lesions, studies from different countries showed differences in detail that might depend on several factors for example races, behavior, and socio-economic status.

#### What this study adds?

- Comprehensive review of oral and maxillofacial lesions in Thai pediatric populations from central and northeast regions of Thailand.

- Pediatric biopsy specimens in Thailand accounted for 10.6% of all specimens submitted for histopathological diagnosis and mostly related to development and reaction of oral tissue.

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#### Potential conflicts of interest

None.

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รอยโรคในช่องปาก ขากรรไกร และใบหน้าในผู้ป่วยเด็กไทยกลุ่มหนึ่ง: การศึกษาย้อนหลังจากคณะทันตแพทยศาสตร์ 2 แห่ง

พวงวรรณ ลาภธนทรัพย์กุล, ราชัย จึงสมจิตต์, ปรมาภรณ์ กลั่นฤทธิ์, สุวิมล ทวีชัยศุภพงษ์, โสภี ภูมิสวัสดิ์

วัตถุประสงค์: เพื่อศึกษาความชุกของรอยโรคในช่องปาก ขากรรไกร และใบหน้าของผู้ป่วยเด็กไทยกลุ่มหนึ่ง

วัสดุและวิธีการ: ทำการทบทวนใบส่งตรวจชิ้นเนื้อจากผู้ป่วยเด็กอายุ 0-15 ปี ในคณะทันตแพทยศาสตร์ มหาวิทยาลัยมหิดล และ คณะทันตแพทยศาสตร์ มหาวิทยาลัยขอนแก่น ผู้ป่วยเด็กได้รับการจำแนกเป็น 3 กลุ่มอายุ คือ 0-5, 6-10 และ 11-15 ปี รอยโรค ในช่องปาก ขากรรไกร และใบหน้า นำมาจำแนกเป็น 9 กลุ่มรอยโรค โดยผลการวินิจฉัยโรคที่เป็นเนื้อเยื่อปกติจะไม่ถูกนำมาศึกษา วิเคราะห์

**ผลการศึกษา:** รอยโรคในซ่องปาก ขากรรไกรและใบหน้าของผู้ป่วยเด็กที่ได้รับการส่งตรวจชิ้นเนื้อมีจำนวน 1,389 ราย (ร้อยละ 10.6) จากรอยโรคบริเวณซ่องปากที่ส่งตรวจทั้งหมด 13,050 ราย กลุ่มรอยโรคที่พบจำนวนมากที่สุดคือ กลุ่มถุงน้ำและเนื่องอกเกิดจาก เนื้อเยื่อฟัน รองถงมาคือ รอยโรคที่เกี่ยวข้องกับการอักเสบและการตอบสนอง และความผิดปกติของต่อมน้ำลาย รอยโรคที่มีความชุก มากที่สุด 10 อันดับแรก คิดเป็นร้อยละ 73 ของชิ้นเนื้อผู้ป่วยเด็กที่ส่งตรวจ รอยโรคที่พบมากที่สุดได้แก่ ถุงน้ำเดนทิเจอรัส รองถงมา คือ ถุงน้ำเมือก และไพโอเจนิกแกรนูโถมา

สรุป: จากการศึกษาพบว่ารอยโรคส่วนใหญ่ที่พบในผู้ป่วยเด็กเป็นรอยโรคที่ไม่ร้ายแรงและเกี่ยวข้องกับการเจริญเติบโตหรือการตอบ สนองของเนื้อเยื่อ ส่วนรอยโรคที่ร้ายแรงพบในสัดส่วนที่น้อยมาก