# Relative frequency of intra-oral minor salivary gland tumors: a study of 380 cases from northern California and comparison to reports from other parts of the world

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BACKGROUND: The relative frequency of individual intra-oral minor salivary gland tumors (IMSGT) is not well documented in the literature. The aim of this study was to determine the relative frequency and distribution of IMSGT in an oral pathology biopsy service and to compare the data with similar studies from different parts of the world.

METHODS: Files from the Pacific Oral and Maxillofacial Pathology Laboratory of the University of the Pacific, San Francisco, California served as a source of material for this study. Files were systematically searched for all cases of IMSGT during a 20-year period. Tumors were classified according to the 2005 WHO classification of salivary gland tumors.

RESULTS: IMSGT were identified in 380 (0.4%) cases of 92 860 accessed. This is the largest series of IMSGT from one source reported in recent years. Of the 380 tumors, 224 (59%) were benign and 156 (41%) were malignant. Of the benign tumors, pleomorphic adenoma (PA) was the most common (39.2%), followed by cystadenoma (6.3%), canalicular adenoma (6.1%), ductal papillomas (4.4%), basal cell adenoma (1.6%), and myoepithelioma (1.3%). Of the malignant tumors, mucoepidermoid carcinoma was the most common (21.8%), followed by polymorphous low-grade adenocarcinoma (7.1%), adenoid cystic carcinoma (6.3%), adenocarcinoma, not otherwise specified (NOS; 2.1%), acinic cell carcinoma (1.6%), clear cell carcinoma, NOS (1.0%), and carcinoma ex PA (0.5%).

CONCLUSIONS: Studies related to the relative frequency of individual IMSGTs from different parts of the world are difficult to compare because many studies are outdated, the number of cases is small, the list of tumors is limited, and new entities are not included. To determine the true relative frequency, more studies should be conducted, on a large number of cases from one source, by experienced pathologists in the field of salivary gland tumors.

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#### Introduction

Tumors of the intra-oral minor salivary glands constitute an important area in the field of oral pathology as they are regularly encountered in oral pathology biopsy services. Although uncommon, these tumors are by no means rare. Epithelial tumors arising in intra-oral minor salivary glands account for 9-23% of all salivary gland tumors in major series (1–3).

The relative frequency of the individual intra-oral minor salivary gland tumors (IMSGT) is not well documented in the literature. Some studies combine tumors of major glands with minor glands and many report only malignant tumors. Studies conducted in cancer institutions are biased in favor of malignant tumors. Even the comprehensive study from the Armed Forces Institute of Pathology (3) does not represent the true frequency of these tumors because this Institute serves mainly as a referral center for pathologists and mainly problematic cases are submitted for consultation.

The best source to obtain information on the true relative frequency of IMSGT is from the records of large oral pathology biopsy services. Information gained from these files is invaluable and represents the only large source of such data presently available.

The purpose of this study was to determine the relative frequency and distribution of IMSGT in an oral pathology biopsy service and to compare these data with reports from other parts of the world.

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## Materials and methods

The files of the Pacific Oral and Maxillofacial Pathology Laboratory of the Arthur A. Dugoni School of Dentistry, University of the Pacific at San Francisco, California, USA served as a source of material for this study. This laboratory serves the communities of northern California with most biopsies received from private oral and maxillofacial surgeons. Files were systematically searched for all cases of IMSGTs during a 20-year period (1986-2005). Cases submitted for consultation from other oral or general pathologists were excluded from the study. Recurrent tumors were considered as one individual case. Intraosseous mucoepidermoid carcinomas (MEC) were excluded. Salivary gland tumors were classified according to the criteria of the WHO working group on histologic classification of salivary gland tumors published in 2005 (4). Clinical information, including patient's age, gender, and location, was obtained from biopsy submission forms.

# **Results and comments**

Intra-oral minor salivary gland tumors were identified in 380 (0.4%) cases out of 92 860 accessed during the 20year period. Table 1 shows the relative frequency of the 380 tumors. This is the largest series of IMSGT from one source reported in recent years.

Of the 380 tumors, 224 (59%) were benign and 156 (41%) were malignant. Of the benign tumors, pleomorphic adenoma (PA) was the most common (39.2%) followed by cystadenoma (6.3%), and canalicular adenoma (6.1%).

Of the malignant tumors, MEC was the most common (21.8%), followed by polymorphous low-grade adenocarcinoma (PLGA; 7.1%), and adenoid cystic carcinoma (AdCC; 6.3%).

**Table 1** Relative frequency of 380 cases of benign and malignantepithelial intra-oral minor salivary gland tumors according to therecent WHO classification (4)

	Number of cases (%)
Benign, 224 tumors (59%)	
Pleomorphic adenoma	149 (39.2)
Myoepithelioma	5 (1.3)
Basal cell adenoma	6 (1.6)
Canalicular adenoma	23 (6.1)
Ductal papillomas	
Inverted ductal papilloma	2 (0.5)
Intraductal papilloma	3 (0.8)
Sialadenoma papilliferum	12 (3.1)
Cystadenoma	24 (6.3)
Malignant, 156 tumors (41.0%)	
Mucoepidermoid carcinoma	83 (21.8)
Polymorphous low-grade adenocarcinoma	27 (7.1)
Adenoid cystic carcinoma	24 (6.3)
Acinic cell carcinoma	6 (1.6)
Adenocarcinoma, NOS	8 (2.1)
Carcinoma ex pleomorphic adenoma	2 (0.5)
Clear cell carcinoma, NOS	4 (1.0)
Basal cell adenocarcinoma	1 (0.25)
Myoepithelial carcinoma	1 (0.25)

The location of the 380 IMSGT is presented in Table 2. The palate was the most common site accounting for 54.2% of all cases followed by the upper lip (16.8%) and buccal mucosa (14.2%). Tumors arising in the upper lip were mainly benign (91%) and those in the retromolar region predominantly malignant (95%; Table 3).

#### Benign tumors

#### Pleomorphic adenoma (mixed tumor)

Overall, PA was the most common tumor. One hundred and forty-nine cases were identified comprising 39.2% of all IMSGT and 65% of benign tumors. The youngest patient was 10 years old and the eldest 92 years old. Mean age at diagnosis was 45.7 years (median 41 years). The mean age reported in other studies was similar to the present study ranging from 43.9 to 46 years (5-7). Pleomorphic adenoma occurred in 63 (42%) males and 86 (58%) females with a male-to-female ratio of 1:1.4. Female predilection was also noted in many other studies (5–8). The location of 149 PA is presented in Table 3. The most common site was the palate (64.4%)followed by the upper lip (18.8%), buccal mucosa (12.7%), lower lip (2.7%), and one case each in the retromolar region and floor of the mouth. Similar data were reported by others (5, 6, 9, 10). It is of interest to note that in the present study, no PA was identified in the tongue which concurs with most other studies. However, Waldron et al. (6) and Regezi et al. (7) each report one tongue PA in their respective series of 174 and 119 PA.

#### Myoepithelioma

Five cases of myoepithelioma were identified comprising 1.3% of all IMSGT and 2.2% of benign tumors. Three patients were males and two were females. Age at time of diagnosis ranged from 24 to 55 years with a mean of 44.5 years. Two lesions were located in the palate, two in the upper lip and one in the buccal mucosa.

Myoepithelioma is defined as a tumor composed almost exclusively of myoepithelial cells (4). It represents one extreme in the histologic spectrum of PA and the criteria to distinguish PA with a predominance of myoepithelial cells from myoepithelioma are largely subjective (9, 10). It is difficult to compare our data to other studies in the literature because most surveys do not include myoepithelioma as a separate entity, probably including it within the group of PA.

#### Basal cell adenoma

Six cases of basal cell adenoma were identified comprising 1.6% of all IMSGT and 2.7% of all benign tumors. There were five females and one male. Age at time of diagnosis ranged from 54 to 79 years with a mean of 64.2 years. Five lesions were located in the upper lip (83%) and one in the buccal mucosa.

It is difficult to compare our data on basal cell adenomas to previous studies in the literature because confusion and disagreement about the terminology exists (10) and most reports do not include basal cell adenoma as a separate entity.

Table 2 Location of 380 cases of intra-oral benign and malignant intra-oral minor salivary gland tu	mors
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	Number of cases	Palate	Upper lip	Buccal mucosa	Retromolar region	Lower lin	Floor of mouth	Tongue
Benjan (224 cases)	-,		<sub>F</sub>					
Pleomorphic adenoma	149	96	28	19	1	4	1	_
Myoepithelioma	5	2	20	1	-	-	-	_
Basal cell adenoma	6	-	5	1	_	_	_	_
Canalicular adenoma	23	_	21	2	_	_	_	_
Ductal papillomas	20		21	2				
Inverted ductal papilloma	2	_	_	2	_	_	_	_
Intraductal papilloma	3	1	_	_	_	1	1	_
Sialadenoma papilliferum	12	6	1	2	_	2	1	_
Cystadenoma	24	12	1	7	_	1	1	2
Malignant (156 cases)			-	,				-
Mucoepidermoid carcinoma	83	39	1	14	15	7	5	2
Polymorphous low-grade adenocarcinoma	27	21	2	2	_	1	_	1
Adenoid cystic carcinoma	24	18	2	1	1	_	2	_
Acinic cell carcinoma	6	_	1	2	2	1	_	_
Adenocarcinoma, NOS	8	6	_	1	_	1	_	_
Carcinoma ex pleomorphic adenoma	2	1	_	_	—	_	1	-
Clear cell carcinoma, NOS	4	2	_	_	1	_	1	-
Basal cell adenocarcinoma	1	1	_	_	_	_	_	-
Myoepithelial carcinoma	1	1	-	-		-	—	-
Total number	380	206	64	54	20	18	13	5

 Table 3
 Location of 380 benign and malignant intra-oral minor salivary gland tumors

Location	Number of cases	Benign, N (%)	Malignant, N (%)
Palate	206	117 (57)	89 (43)
Upper lip	64	58 (91)	6 (9)
Buccal mucosa	54	34 (63)	20 (37)
Retromolar region	20	1 (5)	19 (95)
Lower lip	18	8 (44)	10 (56)
Floor of mouth	13	4 (31)	9 (69)
Tongue	5	2 (40)	3 (60)

#### Canalicular adenoma

Twenty-three cases of canalicular adenoma were identified comprising 6.0% of all IMSGT and 10.3% of benign tumors. The youngest patient was 46 years old and the eldest 94 years old. Mean age at diagnosis was 70 years (median 73 years). Other studies have shown a lower mean age that varies from 61.4 to 65.6 years (5–7, 11). Canalicular adenoma occurred in seven (30%) males and 16 (70%) females with a male-to-female ratio of 1:2.3. Female predominance has been reported in most other studies (5, 6, 11).

Canalicular adenoma occurred almost exclusively in the upper lip, with 21 tumors (91.3%) identified in this location and two (8.7%) in the buccal mucosa. All studies in the literature revealed that the upper lip is the markedly predominant site, followed by the buccal mucosa (6, 10, 11). In a few studies, the palate was also involved (5, 7) and in one study 20% of 40 canalicular adenomas were located in the palate (12).

#### Ductal papillomas

According to the WHO classification (4), ductal papillomas are divided into three specific histopathologic entities referred to as inverted ductal papilloma, intraductal papilloma, and sialadenoma papilliferum. Seventeen cases of ductal papillomas were identified comprising 4.5% of all IMSGT and 7.6% of benign tumors. Two were inverted ductal papilloma, three intraductal papilloma and 12 sialadenoma papilliferum.

The two inverted ductal papillomas occurred in the buccal mucosa of two females (53 and 68 years). The three intraductal papillomas occurred in the palate of a 65-year-old male, in the lower lip of a 32-year-old female, and in the floor of the mouth of a 78-year-old male. The 12 patients with sialadenoma papilliferum had an age range of 23–74 years with a mean of 57.3 years (median of 62 years). There were seven (58.3%) males and five (41.6%) females, with a male-to-female ratio of 1.4:1. The most common location was the palate (50%) followed by the buccal mucosa (16.6%), lower lip (16.6%), and one case each in the upper lip and floor of the mouth.

It is difficult to compare our data to the literature because ductal papillomas have been inadequately reported and rarely included in surveys of IMSGT. Regezi et al. (7) reported four inverted ductal papillomas among 238 reviewed IMSGT but Waldron et al. (6) did not identify any among 425 IMSGT. It is of interest to note that sialadenoma papilliferum was more common in males while most IMSGT are more common in females. Male predominance of this lesion was also reported in a review of the literature by Brannon et al. (13).

#### Cystadenoma

Twenty-four cases of cystadenoma were identified, comprising 6.3% of all IMSGT and 10.7% of benign tumors. The youngest patient was 17 years old and the eldest 86 years old. Mean age at diagnosis was 60.9 years (median 62 years). Cystadenoma occurred in eight (33.3%) males and 16 (66.6%) females with a

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male-to-female ratio of 1:2.0. The most common location was the palate (50%), followed by the buccal mucosa (29.2%), tongue (8.3%), and one case each in the upper lip, lower lip and floor of mouth.

It is difficult to compare our data with surveys in the literature because most studies did not include cystadenoma as a separate entity. Some pathologists interpreted cystadenoma as an intraductal hyperplastic process rather than neoplastic (14) and its terminology in the literature has been inconsistent (10). However, the data of our study are generally in agreement with the study of Waldron et al. (6) on 20 cases of cystadenoma. However, in the latter study, the buccal mucosa was the most common site (35%) followed by the palate (20%).

#### Malignant tumors

#### Mucoepidermoid carcinoma

Mucoepidermoid carcinoma was the most common malignant tumor and the second most common tumor overall. Eighty-three cases were identified comprising 21.8% of all IMSGT and 53.2% of malignant tumors. The youngest patient was 14 years old and the eldest, 94 years old. Mean and median age at diagnosis was 51 years. In other studies the mean age varied from 45 to 65.6 years (5–7, 15). MEC occurred in 26 (31.7%) males and 56 (68.3%) females with a male-to-female ratio of 1:2.1. Female predominance was also reported in most other studies (5–7, 15).

The most common location was the palate (47%) followed by the retromolar region (18%), buccal mucosa (16.9%), lower lip (8.4%), floor of the mouth (6%), tongue (2.4%), and one case in the upper lip. It is of interest to note that the retromolar region was a common location for MEC and this observation is also supported by other studies (6, 15).

## Polymorphous low-grade adenocarcinoma

Polymorphous low-grade adenocarcinoma was the second most common malignant tumor and the third most common overall. Twenty-seven cases were identified comprising 7.1% of all IMSGT and 17.3% of malignant tumors. The youngest patient was 37 years old and the eldest 86 years old. Mean and median ages at diagnosis were 62 years. In other studies the mean age varied from 57.6 to 64 years (5, 7, 15). PLGA occurred in nine (33.3%) males and 18 (66.6%) females with a male-tofemale ratio of 1:2. A female predominance was also reported in most other studies (6, 16, 17).

The most common location was the palate (77.8%) followed by the buccal mucosa (7.4%), upper lip (7.4%), and one case each in the lower lip and tongue. In most studies the palate was also the predominant location followed by the buccal mucosa and upper lip (6, 17, 18). In this study, no tumor was identified in the retromolar region and floor of the mouth. However, other studies identified a few tumors in the retromolar region (5, 6).

## Adenoid cystic carcinoma

Adenoid cystic carcinoma was the third most common malignant tumor. It is of interest to note that in other studies, especially from western Europe, AdCC was found to be the most common malignant tumor (19, 20). Twenty-four cases were identified in our files comprising 6.3% of all IMSGT and 15.4% of malignant tumors. The youngest patient was 30 years old, and the eldest 91 years old. Mean age at diagnosis was 57 years (median 54 years). In other studies the mean age varied from 57.7 to 58.6 (5–7).

Adenoid cystic carcinoma occurred in eight (33.3%) males and 16 (66.6%) females with a male-to-female ratio of 1:2. Female predominance was also reported in other studies (5–7). The palate was the most common location (75%) followed by the upper lip (8.3%), floor of the mouth (8.3%), and one case each in the buccal mucosa and retromolar region. Predilection for the palate was also reported in all major studies (5–8, 20, 21). In this study, no case was identified in the lower lip and tongue but in another study (10) a few cases were reported in the lower lip.

#### Acinic cell carcinoma

Acinic cell carcinoma (AcCC) is an uncommon tumor intraorally (21). Six cases of AcCC were identified comprising 1.6% of all IMSGT and 3.8% of all malignant tumors. In other major studies AcCC accounted for 0-1.8% of IMSGT (7, 20, 22).

Age at time of diagnosis ranged from 26 to 64 years with a mean of 43.7 years. One patient was male and five were females (83%) with a male-to-female ratio of 1:5. Female predominance was also reported in another major study (6). The location of AcCC is variable. Two lesions were located in the buccal mucosa, two in the retromolar region, and one case each in the upper lip and lower lip. It is of interest to note that no tumor was found in the palate which is the most common site for most IMSGT. Moreover, no lesion was located in the floor of the mouth and tongue. However, other surveys documented a few tumors in these locations (6, 10, 23).

## Adenocarcinoma, not otherwise specified

Adenocarcinoma, not otherwise specified (NOS) is a salivary gland carcinoma that exhibits ductal differentiation but does not have sufficient histologic features compatible with any of the currently recognized categories of salivary gland carcinoma to allow a more specific designation other than 'not otherwise specified' (4, 9). The tumor is uncommon and its relative frequency in the literature varies considerably.

Eight cases of adenocarcinoma, NOS were identified in our files comprising 2.1% of all IMSGT and 8.1% of malignant tumors. Age at time of diagnosis ranged from 29 to 69 years with a mean of 49 years. One patient was male and seven (88%) were females with a male-tofemale ratio of 1:7.

Most of the lesions were located in the palate (75%) and one case each in the buccal mucosa and lower lip. It is difficult to compare our data with other studies because of the inconsistent reporting of this tumor in the literature (4, 10).

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Clear cell carcinoma, not otherwise specified

Clear cell carcinoma, NOS is an uncommon tumor composed of a monomorphous population of cells that have optically clear cytoplasm and that do not fit into other categories of carcinoma (4, 9).

Four cases of clear cell carcinoma, NOS were identified comprising 1.0% of all IMSGT and 2.6% of malignant tumors. Age at time of diagnosis ranged from 49 to 84 years with a mean of 67.5 years. Two lesions were located in the palate and one case each in the retromolar region and floor of mouth.

It is difficult to compare our data with the literature because in most surveys of IMSGT clear cell carcinoma, NOS is not recognized as a specific entity.

# Carcinoma ex pleomorphic adenoma

Two cases of carcinoma ex PA were identified comprising 0.5% of all IMSGT and 1.3% of malignant tumors. One tumor was in the palate of a 20-year-old female and the second in the floor of the mouth of a 35-year-old male.

Carcinoma ex PA is considered somewhat a controversial lesion and data varied widely in the literature (6). In most surveys the number is limited and no conclusions can be drawn.

# Miscellaneous adenocarcinomas

Two cases of rare adenocarcinomas of IMSGT were identified. One was a basal cell adenocarcinoma located in the palate of an 83-year-old female and the other was a myoepithelial carcinoma located in the palate of a 74-year-old female.

# Discussion

The present study of 380 IMSGT is the largest and most detailed study from one source published in recent years. As a group, IMSGT should be considered as an uncommon lesion, as they represent only 0.4% of all biopsy specimens submitted to an oral pathology biopsy service. In other studies from the United States, Japan, Venezuela, and Thailand, IMSGT comprised 0.28–1.4% of all biopsy specimens (7, 24–27).

In the present study, benign tumors account for 59% of IMSGT and malignant tumors for 41%. In studies from various countries, benign tumors account for 18-67% and malignant tumors for 33-82% (5-8, 25-41). The variability appears to be related to the type of cases

referred to the biopsy services or treatment centers. Studies conducted in centers for cancer treatment report a higher percentage of malignant tumors, ranging from 63% to 82% (29, 32, 41). However, studies conducted in biopsy services in the United States, show similar data to our study. In these studies, benign tumors predominate and account for 56-63% and malignant tumors account for only 37-45% (5-7, 26).

In the present study, the palate was the most common site, followed in frequency by the upper lip and buccal mucosa. These findings are consistent with other studies in the literature (6–8, 36, 40). Age and gender distribution of the most common IMSGT is summarized in Table 4. IMSGT affect mainly adult patients from the fifth through the seventh decade of life. Almost all types of IMSGT in our study were more common in females. This finding is consistent with most reports in the literature (21, 25, 27, 28, 34, 37, 38).

Review of the English-language literature reveals many studies on the relative frequency of individual IMSGT; however, it is very difficult to make a valid comparison between them for the following reasons:

- 1 some of the studies combine the data of tumors of major glands with those of minor glands;
- **2** some of the studies report only on malignant salivary gland tumors (42–44);
- **3** some of the studies do not include all the intra-oral sites (19);
- 4 some of the studies were conducted in cancer institutions and are biased in favor of malignant tumors (29, 32, 41);
- **5** some of the studies are biased because they combined their own material with consultation cases, which are often unusual, problematic, or rare and thus the true relative frequency is impossible to assess (3, 6);
- **6** some of the studies are based on a limited number of cases and thus no valid conclusions can be drawn (24, 27, 33);
- 7 some of the studies are based on the 1972 WHO classification of salivary gland tumors (45), a situation which does not allow for appropriate comparison to be made to studies based on the 1991 WHO classification (46). This is because some pathologic entities have changed their definitions and some new ones have been introduced; and

 Table 4
 Age and gender distribution of intra-oral salivary gland tumors

	Number	$A_{i}$	ge	Male-to-female
	of cases	Range	Mean	ratio
Benign				
Pleomorphic adenoma	149	10-92	45.7	1:1.4
Canalicular adenoma	23	46-94	70.0	1:2.3
Sialadenoma papilliferum	12	23-74	57.3	1:4.1
Cystadenoma	24	17-86	60.9	1:2.0
Malignant				
Mucoepidermoid carcinoma	83	14–94	51.0	1:2.1
Polymorphous low-grade adenocarcinoma	27	37-86	62.0	1:2.0
Adenoid cystic carcinoma	24	30-91	57.0	1:2.0

is shown in parenthesis

**Fable 5** Comparison of the relative frequency of individual intra-oral minor salivary gland tumors in recent studies from various countries (the percentage

**8** some of the studies were conducted by pathologists who lack experience in the field of IMSGT and therefore the possibility of misdiagnosis has to be considered. For some pathologists in various countries, benign IMSGT are represented only by PA. Thus, canalicular adenoma, myoepithelioma, ductal papillomas, and cystadenoma are all diagnosed as PA. Furthermore, the relatively new entity of PLGA, seen almost exclusively in minor salivary glands, is not yet well recognized by many general pathologists, who do not have experience with IMSGT and often diagnose it as AdCC (5, 6, 8, 10, 26).

Table 5 shows the comparison in the relative frequency of individual IMSGT in recent studies from different parts of the world, covering different ethnic groups. All studies were based on the 1991 WHO classification of salivary gland tumors (46). It is of interest to note that with the exception of the present study, most studies are limited in the number of pathologic entities identified in their material. The main limitation of these studies is in the group of benign tumors, where in many studies entities such as myoepithelioma, basal cell adenoma, canalicular adenoma, ductal papillomas (inverted ductal papilloma, intraductal papilloma, sialadenoma papilliferum), and cystadenoma were not identified. PLGA which is nowadays a well-recognized entity was also missing in several studies. It is impossible to determine whether the reason for the limited pathologic entities was because many are truly uncommon or that the pathologists were unfamiliar with these entities.

One major difference in studies from countries around the world is in the relative frequency of AdCC vs. MEC. In some studies AdCC was the most common malignant tumor (8, 20, 21, 29-31, 35-38, 41-44, 47, 48), while in others, MEC was the predominant tumor (5-7, 14, 24-28, 32, 34, 39, 40, 49, 50). Except for one major study from the United States (41), all other studies from the United States, including the present study, show that MEC is the most common malignant tumor. However, studies mainly from western Europe and South Africa found that AdCC is the most common malignant tumor. Some authors suggest that the predominancy of AdCC in certain studies may result from the fact that they were published before the time that the entity of PLGA was recognized or that pathologists in some countries were unfamiliar with PLGA and included it in the group of AdCC (5, 6, 8, 10, 26, 51). However, our review revealed that in many of these studies, the entity of PLGA was recognized (30, 33, 37, 38, 42, 47, 48) and in spite of this, AdCC remained the predominant malignant tumor. Thus, geographical and ethnic differences probably play a role in the relative frequency of AdCC and MEC.

Another issue is the relative frequency of PLGA. Studies prior to 1984 did not recognize PLGA as an entity and it has been classified frequently under the general heading of adenocarcinoma, adenocarcinoma NOS, AdCC, or PA (5, 7, 8, 26). Even after 1984, PLGA was either not diagnosed or reported in small numbers

	Present study	Libya 2006 (28)	USA 2005 (5)	Japan 2005 (8)	Thailand 2004 (24)	Uganda 2004 (30)	Brazil 1999 (32)	Japan 1997 (25)	Venezuela 1996 (27)	Brazil 1995 (34)
Total number of cases	380	75	213	82	52	88	196	129	62	164
Benign (total)	224 (59.0)	29 (38.7)	119 (55.9)	55 (67.0)	17 (32.7)	41 (45.6)	68 (34.7)	80 (62.0)	34 (54.8)	101 (61.6)
Pleomorphic adenoma	149 (39.2)	23 (30.7)	93 (43.7)	54 (65.8)	16(30.7)	28 (31.8)	65 (33.2)	74 (57.3)	24 (38.7)	87 (53.0)
Myoepithelioma	5(1.3)		×		1 (1.9)	8 (9.1)	, I	5(3.9)	) /	(1.8)
Basal cell adenoma	6(1.6)	2 (2.7)	I	Ι	-   ,	1(1.1)	3 (1.5)	, ,	2 (3.2)	2 (1.2)
Canalicular adenoma	23 (6.1)	1(1.3)	25 (11.7)	Ι	I	·	, I	Ι	,	, ,
Inverted ductal papilloma	2(0.5)		, ,	Ι	I	Ι	Ι	Ι	1(1.6)	2 (1.2)
Intraductal papilloma	3(0.8)	Ι	Ι	Ι	I	Ι	Ι	Ι	,	1(0.6)
Sialadenoma papilliferum	12 (3.1)	I	I	I	I	I	I	1(0.8)	3 (4.8)	, , 1
Cystadenoma	24 (6.3)	3 (4.0)	I	1 (1.2)	I	3 (3.4)	I	, I	4 (6.4)	6 (3.7)
Oxophilic adenoma		I	1(0.5)	I	I	1(1.1)	I	I	. 1	. I
Malignant (total)	156 (41.0)	46 (61.3)	94 (44.1)	27 (33.0)	35 (67.3)	47 (53.4)	128 (65.3)	49 (38.0)	28 (45.2)	63 (38.4)
Mucoepidermoid carcinoma	83 (21.8)	19 (25.3)	45 (21.1)	8 (9.8)	24 (46.1)	9 (10.2)	76 (38.8)	25 (19.4)	18 (29.0)	28 (17.0)
Polymorphous low-grade carcinoma	27 (7.1)	3(4.0)	18 (8.4)	I	1(1.9)	7 (8.0)	3 (1.5)	. 1		4 (2.4)
Adenoid cystic carcinoma	24 (6.3)	13 (17.3)	22 (10.3)	10 (12.2)	8 (15.4)	18 (20.5)	34 (17.3)	17 (13.1)	6(9.7)	22 (13.4)
Acinic cell carcinoma	6(1.6)	I	1 (0.4)	3 (3.7)	l	5 (5.7)	1(0.5)	. 1	. 1	6 (3.7)
Adenocarcinoma, NOS	8 (2.1)	8 (10.7)	4(1.9)	2 (2.4)	I	·	9 (4.6)	3 (2.3)	2 (3.2)	, ,
Carcinoma ex pleomorphic adenoma	2(0.5)	2 (2.7)	2(0.9)	2 (2.4)	2 (3.8)	3 (3.4)	, I	, I	, I,	1 (0.6)
Clear cell carcinoma, NOS	4(0.1)	I	i I	I	1	2 (2.3)	Ι	Ι	I	I
Miscellaneous carcinomas	2 (0.5)	1 (1.3)	2 (0.9)	2 (2.4)	I	3 (3.4)	5 (2.6)	4 (3.1)	2 (3.2)	2 (1.2)

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in the literature. It is of interest to note that in the present study, PLGA was the second most common malignancy after MEC. Other studies from the United States also found PLGA to be the second most common malignant tumor after MEC (6, 26, 52). Zarbo (51) also reports that in his experience, PLGA is more common than AdCC and in one study from South Africa (37), PLGA was found to be the most common malignant tumor. On the other hand, in several studies from Japan, no cases of PLGA were identified (8) and only in one study (38) a single case of PLGA was found. The conclusion from our review is that more studies are needed in order to clarify whether the differences in frequency are related to the criteria used for diagnosis of PLGA, as overlapping histologic features with AdCC do exist (37), or that the different frequencies are related to geographical and ethnic differences.

In conclusion, studies related to the relative frequency of individual IMSGTs from different parts of the world are difficult to compare because many are based on outdated classification, the number of cases is often small, the list of tumors is limited, and new entities are not included. To determine the true relative frequency, further studies should be conducted on a large number of cases from one source, by experienced pathologists in the field of salivary gland tumors, using current classification and accepted diagnostic criteria.

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