

## Occurrence site of canine oral lesions: a retrospective study of 659 cases

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Received March 5, 2020

Accepted April 30, 2020

### Abstract

Many types of tumorous and tumour-like lesions occur in the oral cavity of dogs. Even benign neoplasia often represents great inconvenience due to potential restrictions of therapeutic surgical approach in this area. Whereas in human medicine, there are statistical data describing areas of the oral cavity, that are more prevalent for development of particular neoplasia, in veterinary medicine, these data are not yet available. The aim of this study was to evaluate the prevalence of tumours in dogs with oral neoplasia, the occurrence site of the most common neoplastic lesions in the canine oral cavity, as well as the effect of age and sex on the prevalence of these lesions. In this study we investigated oral tumorous lesions from 659 dogs, out of which 352 lesions were diagnosed as tumours and 307 as tumour-like lesions. The most common tumours encountered were melanoma (42%, n = 148), squamous cell carcinoma (16%, n = 57) and canine acanthomatous ameloblastoma (10%, n = 35). The median age of dogs with oral neoplasia was 9.9 years, with the range of 0.2 to 17.5 years. There was no significant association between sex and the type of oral lesion (tumorous and tumour-like). Melanoma was most commonly present in the caudal maxillary region, squamous cell carcinoma on the mouth floor, canine acanthomatous ameloblastoma in the area of the rostral mandible, plasmacytoma on the tongue, osteosarcoma was most often diagnosed in the caudal parts of oral cavity and fibrosarcoma did not have a specific site of occurrence.

*Dog, canine acanthomatous ameloblastoma, oral melanoma, oral squamous cell carcinoma, plasmacytoma, tumour*

Biopsies collected from the oral cavity of dogs are one of the most commonly examined tissue samples by veterinary pathologists. The oral and pharyngeal mucosa is considered to be the fourth most common site of malignancy in dog (Maxie 2015). There are many tissue types in the oral cavity that widen the diversity of oral neoplasia. Often, the biggest pitfall for the clinician is a late diagnosis of the lesions and challenges connected with surgical treatment in the head and neck area. The most common canine neoplastic lesions are melanoma and squamous cell carcinoma (SCC) (Maxie 2015). Except for neoplastic lesions, there is a broad scale of possible tumour-like lesions arising in canine oral cavity. These lesions are mostly induced by chronic inflammation, mechanical injury or drug administration (Waner et al. 1988; Reichart et al. 1989; Head 2003; Agrawal 2015; Ullal et al. 2019).

Data from human medicine show that there are more predisposed areas in the oral cavity for development of neoplastic lesions and statistical data on the exact localization are available for some oral neoplasia, such as human oral SCC (Sundermann et al. 2018), ameloblastoma (Masthan et al. 2015) or osteosarcoma of the jaw (Chaudhary and Chaudhary 2012). Moreover, there is a relationship between the exact site of the occurrence of the neoplastic lesion in the oral cavity and the patient's survival and general prognosis (Shaw et al. 2009). In veterinary medicine, it was acknowledged that some tumours have rather poor prognosis, if occurring in the oral cavity, like melanoma (Esplin 2008; Smedley et al.

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2011; Maxie 2015) or osteosarcoma (Hammer et al. 1995). Similarly, SCC has a worse prognosis if presented in the caudal part of the oral cavity (Evans and Shofer 1988). Nevertheless, these data are available only in a small portion of the canine oral lesions.

As is the case in most neoplastic lesions, tumours in the oral cavity occur more frequently in adult and aged animals (Dorn and Priester 1976; Todoroff and Brodey 1979; Felizzola et al. 1999; Merlo et al. 2008; Nishiya et al. 2016). On the other hand, there are tumours which typically arise only in the oral cavity, and are predominantly found in younger dogs, such as compound odontoma (Head 2003).

The aim of this paper was to examine the occurrence of the most common canine oral neoplastic lesions in certain areas of the oral cavity, as well as to evaluate the frequency of canine oral tumours in relation to the patient's age and sex.

### Materials and Methods

Cases of canine oral cavity lesions submitted to the Department of Pathological Morphology and Parasitology of the Faculty of Veterinary Medicine, University of Veterinary and Pharmaceutical Sciences Brno between 2010 and 2019 were reviewed ( $n = 659$ ). Formalin fixed and paraffin embedded tissues were used to prepare histological slides. All oral lesions were classified by two veterinary pathologists based on adjusted WHO classification as cited by Head (2003) (Table 1). All biological material used in this study originated from privately owned dogs.

Data regarding detailed localization of the lesion in the oral cavity, age and sex were collected and further processed using the software Microsoft Office Excel 10 with a Data Analysis ToolPak (Microsoft Corporation, Redmond, WA). Statistical analyses, Chi-square test and Fisher's exact test were performed with the Real Statistics Resource Pack software (Release 7.0.5) in Microsoft Excel (version 16.36; Microsoft Corporation, Redmond, WA). A scheme of the canine oral cavity was used to visually depict the percentage dispersion of the neoplastic lesions which were recorded most often in this study. For this analysis, only the cases where exact localization was available were used. The oral cavity was divided into 11 compartments: the rostral mandible (the rostral aspect of the mandible including the canines), the caudal mandible, the rostral maxilla (the rostral aspect of the maxilla excluding the canines), the caudal maxilla, the mouth floor, the hard palate, the soft palate, the tongue, the tonsils, the buccal mucosa, and the lip.

### Results

#### Frequency of canine oral neoplastic lesions

Of the total number of 659 oral lesions, 53% ( $n = 352$ ) were diagnosed as neoplastic lesions (Plate V, Fig. 1), whereas 47% ( $n = 307$ ) were tumour-like lesions (Plate V, Fig. 2). The most frequent neoplastic lesions were melanoma, SCC, canine acanthomatous ameloblastoma (CAA), extramedullary plasmacytoma (EMP), fibrosarcoma, osteosarcoma, undifferentiated sarcoma, viral papilloma, mast cell tumour, lymphoma, fibroma, amyloid producing oral tumour, and chondrosarcoma (Fig. 3). The majority of melanoma cases (83%) were morphologically typical tumours with the production of melanin pigment. Cases of partially amelanotic and completely amelanotic melanomas, were also recorded (in 9% and 8% of cases, respectively). We diagnosed also neoplastic lesions, which were recorded in less than 1% of cases: odontoma, myxosarcoma, histiocytoma, granular cell tumour, infundibular acanthoma of the lip, rhabdomyosarcoma, primitive neuroectodermal tumour, haemangiosarcoma and basal cell carcinoma.

Tumour-like lesions were mostly related (in 31% of cases) to an inflammatory process in the oral cavity and most commonly included fibromatous epulis of the periodontal ligament (52%) and ossifying fibromatous epulis (12%) (Plate V, Fig. 2).

#### Site of occurrence of the most common canine oral neoplasia

Distribution of particular neoplastic lesions in the canine oral cavity varied (Plate VI, Fig. 4). Melanoma was located in the oral cavity in all of the 11 compartments, except the rostral maxilla. The caudal maxilla was affected most frequently (18%), followed by the caudal mandible and the buccal mucosa (14%). On the rostral mandible no melanomas

Table 1. Adjusted WHO classification (Head 2003).

<b>Non-odontogenic tumours</b>	<b>Odontogenic tumours</b>
Epithelial tumours	Tumours of odontogenic epithelium without odontogenic mesenchyme
Benign	Ameloblastoma
Viral filiform papilloma	Amyloid-producing odontogenic tumour
Squamous papilloma	Canine acanthomatous ameloblastoma
Viral fibropapilloma	Tumours of Odontogenic Epithelium with Odontogenic Mesenchyme
Adenoma	Ameloblastic fibroma
Malignant	Ameloblastic fibro-odontoma
Squamous cell carcinoma	Complex odontoma
Verrucous carcinoma	Compound odontoma
Adenocarcinoma	Tumours composed primarily of odontogenic ectomesenchyme
Undifferentiated carcinoma	Cementoma
Secondary carcinoma	Cementifying fibroma
Neuroendocrine tumours	Tumours derived from the tissue of the periodontal ligament
Carcinoid	Fibromatous epulis of the periodontal ligament
Melanocytic tumours	
Melanocytoma	
Malignant melanoma	
Mesenchymal tumours	
Benign	
Fibroma	
Leiomyoma	
Rhabdomyoma	
Tumours of vascular tissue	
Haemangioma	
Haemangioendothelioma	
Systemic haemangiomatosis	
Lymphangioma	
Benign peripheral nerve sheath tumour	
Malignant	
Fibrosarcoma	
Leiomyosarcoma	
Rhabdomyosarcoma	
Tumours of vascular tissue	
Haemangiosarcoma	
Haemangiopericytoma	
Malignant peripheral nerve sheath tumour	
Sarcoma associated with <i>Spirocerca lupi</i>	
Undifferentiated sarcoma	
Granular cell tumours	
Benign granular cell tumour	
Malignant granular cell tumour	
Tumours of the bone	
Benign	
Osteoma	
Ossifying fibroma	
Myxoma	
Chondroma	
Malignant	
Osteosarcoma	
Chondrosarcoma	
Multilobular tumour of bone	
Tumours of haematopoietic and related tissues	
Lymphoma	
Plasmocytoma	
Mast cell tumour	

This classifying system was adjusted according to recent studies: Ossifying fibroma and fibromatous epulis of periodontal ligament origin were classified as a tumour-like lesion in our study. Tumours that occur strictly in different species were excluded from this table.

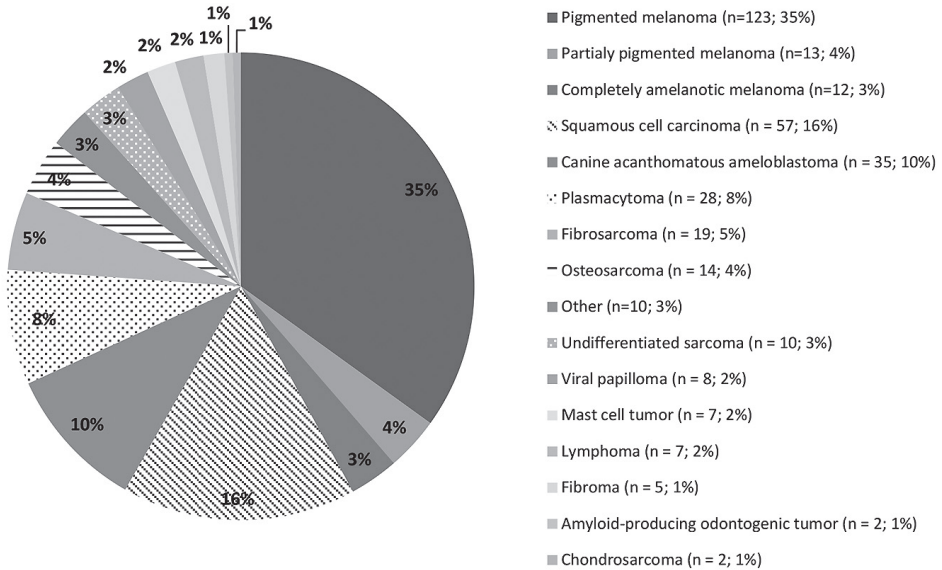


Fig. 3. Prevalence of canine oral neoplastic lesions. The total number of neoplastic lesions in the study group was 352.

were observed. Squamous cell carcinoma was mostly present on the mouth floor (17%), the tongue (14%), the rostral mandible (14%) and the tonsils (14%). Acanthomatous ameloblastoma was most commonly present in the region of rostral mandible (60%) and caudal maxilla (27%). Plasmacytoma was found most commonly on the tongue (35%) and buccal mucosa (24%). Fibrosarcoma was more commonly recorded in the maxilla, where the rostral maxilla, the caudal maxilla and the hard palate were affected at the same rate (22%), the same frequency was recorded also for the caudal mandible (22%), fibrosarcoma of the soft palate was recorded in 11% of the cases. Osteosarcoma was mostly present in caudal parts of the oral cavity – caudal mandible (38%) and caudal maxilla (38%).

#### Age and sex-related incidence of canine oral neoplasia

The age-related incidence of canine oral neoplasia is shown in Fig. 5. The incidence peak was at 9 to 12 years, where the total number of dogs with oral neoplasia was 164. For male dogs, the incidence peak was at 11 to 12 years, with a total number of 51 animals. In contrast, in female dogs the incidence peak was at 9 to 10 years, with a total number of 37 animals. Oral tumorous lesions were recorded also in young animals aged 2.4 months to 5 years in a total number of 24 animals, of which 14 were males and 10 females. Of the total number of 659 dogs with oral lesions, 53% were males and 47% females. Of the dogs with tumorous lesions, 55% were males ( $n = 193$ ) and 45% females ( $n = 159$ ) and of the dogs with tumour-like lesion, 56% were males ( $n = 172$ ) and 44% females ( $n = 135$ ). There was no significant association between sexes and the type of the oral lesion (tumour or tumour-like lesion) (Fisher's exact test:  $P = 0.31$ ). Statistical analysis showed no significant association of sex distribution in any of the oral neoplastic lesions (Pearson's chi-squared test:  $P = 0.30$ ). Melanoma was diagnosed in 83 males (57%) and 65 females (43%), SCC was diagnosed in 31 males (54%) and 26 females (46%), CAA was diagnosed in 20 males (57%) and 15 females (43%), EMPs were diagnosed in 12 males (43%) and 16 females (57%), fibrosarcoma was diagnosed in 11 males (58%) and 8 females (42%) and osteosarcoma was diagnosed in 7 males (43%) and 8 females (57%).

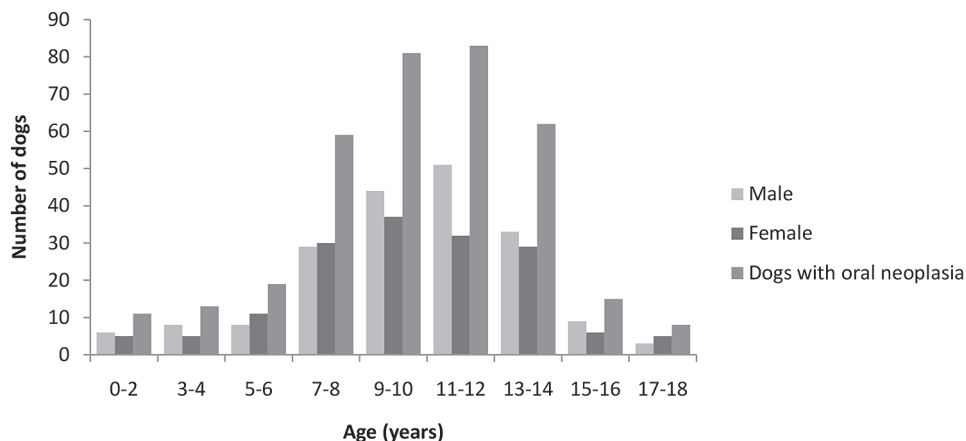


Fig. 5. Age and sex-specific incidence of canine oral neoplasia. The total number of neoplastic lesions in the study group was 352.

#### Age-related incidence of the most common canine oral neoplasia

The age related incidence of the most common oral neoplasia is shown in Fig. 6. The highest median age was recorded for melanoma with 11.4 years (range 2–17.5 years). Dogs with oral SCC were of a median age of 10.2 years (range 0.5–14 years). The lowest median age was recorded for CAA – 7.1 years (range 0.2–13 years). Dogs with oral EMPs were of a median age 10.3 years (range 2.5–16.5 years). The median age of dogs with fibrosarcoma was 10.2 years (range 4–17 years). The median age for dogs with osteosarcoma was 8.9 years (range 5–14 years).

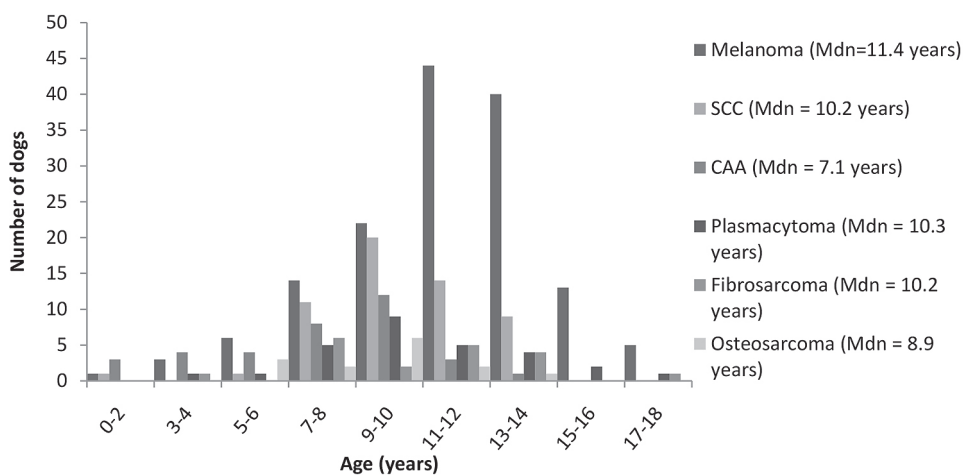


Fig. 6. Age and sex-specific incidence rates of the most common canine oral tumours. Mdn - median.

## Discussion

### Prevalence of canine oral lesions

The most frequent malignant oral lesion was melanoma, which is in accordance with reports from literature (Head 2003; Bergman 2007). We encountered a relatively high prevalence of partially pigmented (9%,  $n = 13/148$ ) and non-pigmented (amelanotic) (8%,  $n = 12/148$ ) melanomas. In dogs, SCC is considered to be the second most common malignant oral neoplasia (Todoroff and Brodey 1979; Withrow et al. 2012; Maxie 2015), which corresponds with our results, where 16% of dog patients suffered from SCC, making this tumour the second most common neoplastic lesion in our group. Other neoplastic lesions, such as CAAs are the most common odontogenic tumours in dogs (Fiani et al. 2011; Goldschmidt et al. 2017) and in our study it was the most prevalent benign tumour with a total of 10% occurrence ( $n = 35/352$ ). Extramedullary plasmacytomas are generally common in dogs (Kupanoff et al. 2006) and the oral cavity is considered to be a fairly predisposed area (Rakich et al. 1989; Kupanoff et al. 2006). Oral EMP was with an 8% occurrence ( $n = 28$ ) the fourth most common oral neoplasia in our study group. In a previously conducted study, EMPs represented only 5.2% of all oral tumours ( $n = 16$ ) (Wright et al. 2008). Regarding tumours of mesenchymal origin, the most common finding in our group was fibrosarcoma, osteosarcoma and undifferentiated sarcoma with a 5% occurrence ( $n = 19$ ), 4% ( $n = 14$ ), and 3% ( $n = 10$ ), respectively. In a similar study, osteosarcoma was more common than fibrosarcoma (Wright et al. 2008), being reported as the fourth most common oral neoplasia in the dog (Verstraete 2005).

### Occurrence site of canine oral neoplasia

The distribution of tumours in the canine oral cavity varies for each neoplasia. For some canine tumorous lesions, the most common sites of occurrence were already mapped. Melanoma was mostly recorded in the gingiva and lips or labial mucosa, but more precise description of localization is not mentioned (Ramos-Vara et al. 2000; Bergman 2007). To add to this knowledge, we observed the highest prevalence of canine oral melanoma in the gingiva of the caudal maxilla. According to the literature, canine non-tonsillar SCC arises most commonly in the gingiva (de Vos et al. 2005), however, we recorded this neoplasia most often in the area of the mouth floor; gingiva of the rostral mandible, tonsils and tongue were the second most commonly affected areas. In our study, CAA was most commonly present in the area of the rostral mandible, caudal maxilla and caudal mandible, as described in the literature (Gardner 1995; Gardner 1996; Goldschmidt et al. 2017; Malmberg et al. 2017). There is a question, whether there are different molecular or developmental conditions in the rostral mandible which enable the formation of CAA in this area with much higher probability, however, there is no mention of this issue in the literature. Canine acanthomatous ameloblastoma is considered to be an odontogenic tumour comparable to human ameloblastoma (Saffari et al. 2019). Whereas human ameloblastoma arises most commonly in the area of third mandibular molars and presumably arises from the remains of dental lamina (Masthan et al. 2015), deeper pathogenesis of CAA is unknown. Canine acanthomatous ameloblastoma often proliferates directly from the oral epithelium which undergoes odontogenic metaplasia (Head 2003). Based on our results, the process of this metaplasia might be site dependent, but further investigation of molecular mechanisms is needed. Extramedullary plasmacytomas can arise from various aspects of the oral cavity. In the study by Wright et al. (2008), the majority of EMPs were originating from the rostral aspect of the mandible, tongue, maxilla/hard palate and in the buccal mucosa. In our study, we recorded the highest presence of oral EMPs on the tongue followed by the buccal mucosa. Fibrosarcomas were found to arise most often on the caudal mandible, caudal maxilla, rostral maxilla and the rostral mandible (Frazier et al. 2012). In another study,

maxillary fibrosarcomas were much more common than those arising on the mandible or the palate (Gardner et al. 2015). In our study, this neoplastic lesion was evenly distributed in the jaws and hard palate, excluding the rostral mandible, and this tumour was also found in the soft palate. Canine osteosarcomas of the jaw were recorded to arise more often from the mandible (65%,  $n = 32/49$ ) than the maxilla in a previously conducted study (Heyman et al. 1992). In our group, the mandible and the maxilla were evenly affected; moreover, the caudal part of the jaws seemed to be more predisposed to osteosarcoma development.

#### Age and sex distribution of the canine oral lesions

Neoplastic lesions are generally considered as a disease in aging patients. In this study, we observed the highest prevalence of canine oral neoplasia in groups of animals from 9 to 12 years; however canine oral neoplasia was recorded across all age groups ranging from 2.4 months up to 18 years.

Oral melanomas are mostly found in older dogs (Head 2003; Bergman 2007). Our data correlate with other authors, who described the median age from 11 to 11.4 years (Todoroff and Brodey 1979; Ramos-Vara et al. 2000; Proulx et al. 2003; Withrow 2012). Oral SCC, fibrosarcoma and EMP had almost the same median age in our study group. The median age of dogs with oral SCC was 10.2 which is higher than the 8 to 9 years reported by some authors (Withrow 2012).

Dogs with oral fibrosarcoma in this study were of a median age of 10.2 years which is higher than reported by other studies, where the median age ranged from 7 (Head 2003; Gardner et al. 2015) to 9.4 years (Frazier et al. 2012). Taking the actual representation in the age groups into consideration, fibrosarcoma in the canine oral cavity is most likely to occur at the age of 7 to 8 years and then in older animals 11 to 14 years old. Fibrosarcoma was more often diagnosed in males, which was previously reported (Gardner et al. 2015; Head 2003), the biological basis to this sex specificity remains unknown. Oral EMPs are most commonly found in middle-aged to older dogs (mean 8 to 10 years) (Rakich et al. 1989; Wright et al. 2008). In our study, the median age of 10.3 years was rather higher than previously reported. This tumour was more often recorded in females. In veterinary medicine, there are no comparable data for sex distribution of oral EMPs and in human medicine, males are more prone to this lesion (Dores et al. 2009). The reason for this sex specificity is unknown. Dogs with CAA in our group were of a median age of 7.1 years, which is in agreement with other authors (Malmberg et al. 2017). This could lead to the conclusion that this tumour occurs in relatively young animals, however, the highest prevalence was found in the age group of 9 to 10 years. Some studies report an even higher age for dogs with CAA, with the median age of 11.0 years (Kelly et al. 2010). The mean age for the diagnosis of canine osteosarcoma of the jaw is reported to be from 9 to 10 years of age (Kosovsky et al. 1991; Schwarz and Withrow 1991; Wallace et al. 1992; Straw et al. 1996), which is in accordance with our results. Osteosarcoma was more often diagnosed in females. There is inconsistent information in the literature about the sex distribution of oral osteosarcoma. Some studies report males to be predisposed (Hillers et al. 2005; Egenvall et al. 2007), some claim contrary (Ru et al. 1998; Sapierzynski and Czopowicz 2017) and according to other authors there is no sex predisposition (Anfinsen et al. 2011). We did not find a difference between the sexes in the occurrence of melanoma, SCC and CAA, which is in accordance with the literature (Malmberg et al. 2017; Ramos-Vara et al. 2000).

There is a common phenomenon of different biological behaviour of neoplasia depending on the location. In veterinary medicine, there is insufficient information on the most prevalent sites of occurrence of the canine oral neoplastic lesions. This study brings more insight into the canine oral lesion prevalence and the anatomical site occurrence of the most common canine oral neoplasia.

### Acknowledgements

This work was supported by the Internal Grant Agency of University of Veterinary and Pharmaceutical Sciences Brno (104/2018/FVL). Authors would like to thank Dr. Diana Frenclová for her kind cooperation.

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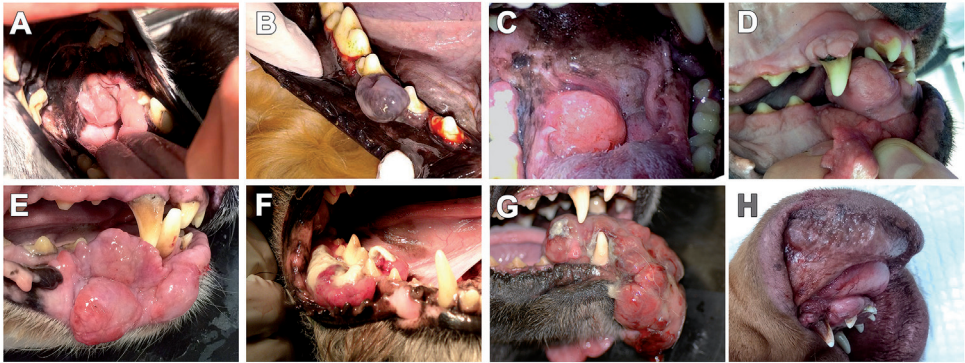


Fig. 1. Most common canine oral neoplasia. A - amelanotic melanoma of the soft palate; B - pigmented melanoma of the gingiva; C - tonsillar squamous cell carcinoma; D - canine acanthomatous ameloblastoma; E - plasmacytoma of the buccal mucosa and gingiva; F - fibrosarcoma of the gingiva with ulceration; G - osteosarcoma of the mandible; H - undifferentiated sarcoma of the rostral maxilla.

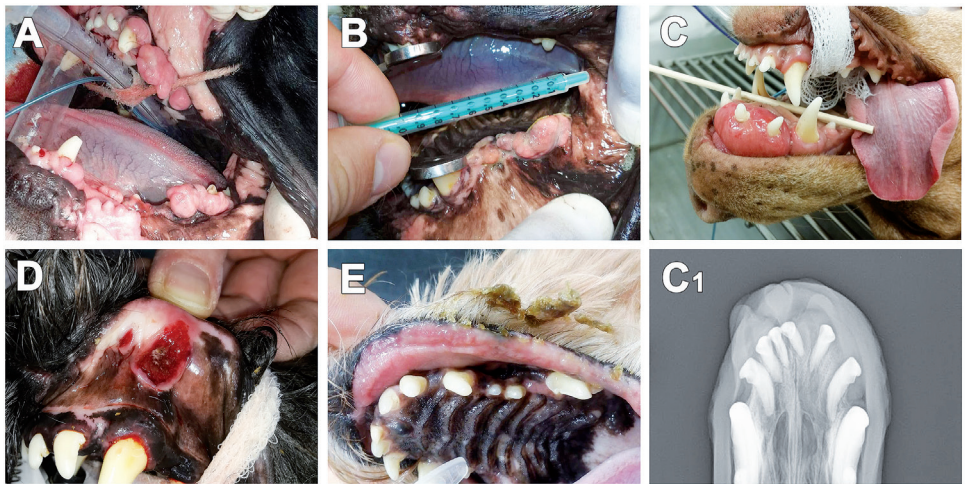


Fig. 2. Most common canine tumour-like oral lesions. A - ossifying fibromatous epulis; B - fibromatous epulis of periodontal ligament; C - presarcomatous proliferative lesions induced by the foreign body, with X-ray findings showing deviation of the maxillary incisors (C1); D - ulcerative stomatitis; E - generalized chronic active stomatitis.

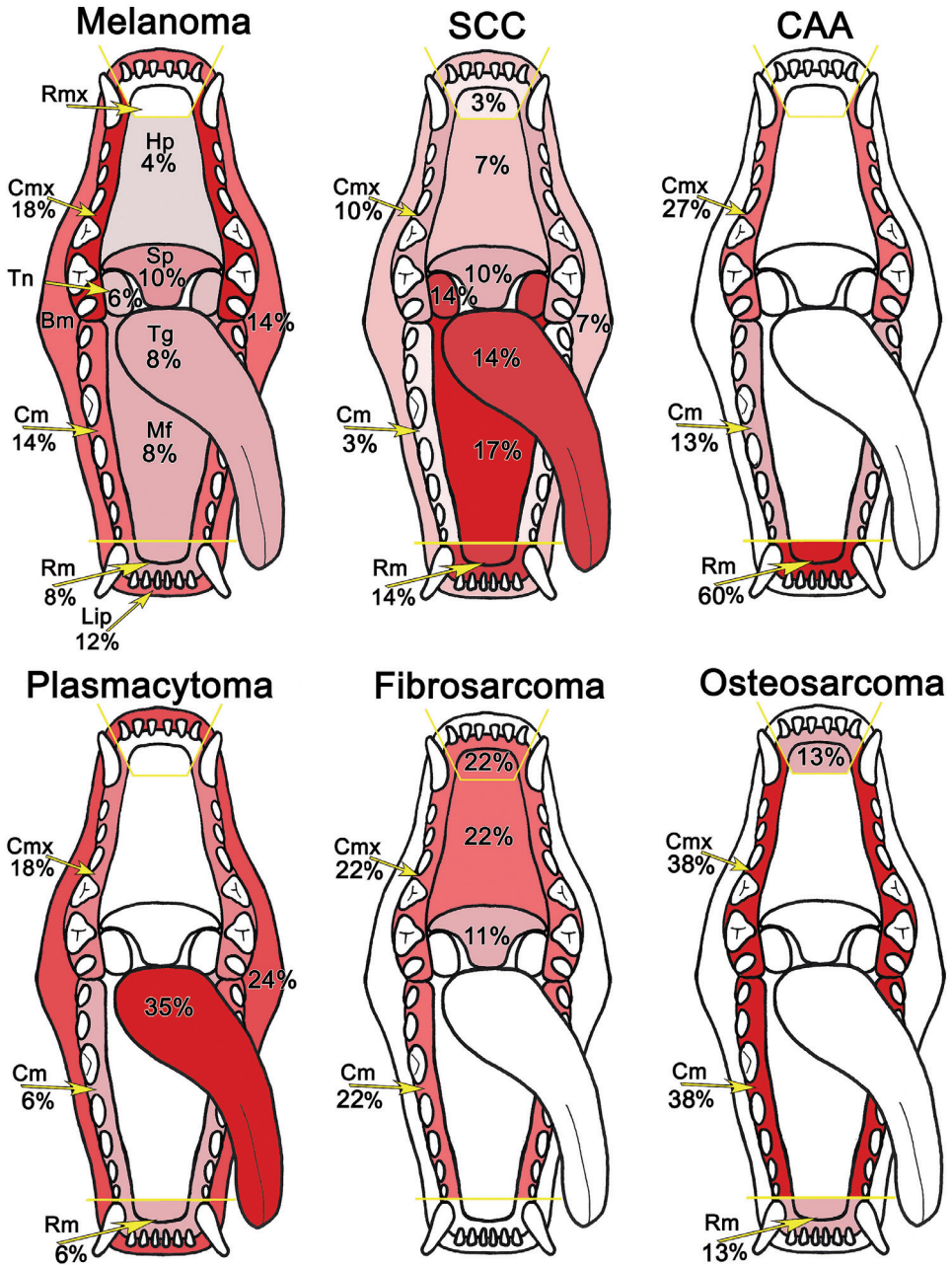


Fig. 4. The site of occurrence of the most common canine oral neoplasia. The colour code was used for a better depiction. Counts of lesions used for this analysis are: melanoma n = 51, SCC n = 29, CAA n = 15, plasmacytoma n = 17, fibrosarcoma n = 9, osteosarcoma n = 8. Mb - buccal mucosa, Mf - mouth floor, Tg - tongue, Hp - hard palate, Sp - soft palate, Tn - tonsils. Areas with 0% occurrence are not marked. Image: Barbora Putnová