

Canine Head Tumours Evaluated by CT-scan

A retrospective study (20-11-2007 till 19-4-2013)

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Contents

Abstract 3

Introduction..... 4

 Canine head tumours 4

 Tumours of the skull and jaws..... 4

 Tumours of the skin..... 5

 Tumours of the oral space..... 6

 Tumours of the nose and nasal sinuses 7

 Tumours of the ears 7

 Tumours of the eye 8

 Tumour staging..... 9

Materials and methods 10

 Patients list 10

 Patient characteristics 10

 Statistics 10

Results 11

 Effects of gender on the type of tumour and histological type. 12

 Effects of breed and breed groups on the type of tumour and histological type..... 12

 Effects of age on the type of tumour and histological type. 12

 Effects of localization on the type of tumour and histological type. 12

 Effects of tumour, histological type and localization on lung metastases..... 13

 Effects of tumour, histological type and localization on osteolysis 14

Discussion..... 15

Abstract

Many tumours can manifest on the canine head. These tumours come from different origins and have different behaviours. Even the same tumour can behave differently on different sites (for example squamous cell carcinomas). The goal of this study was to give an insight in the type of tumours presented at the University Clinic of the Faculty of Veterinary Medicine of Utrecht University and their prevalence and behaviour.

By using the patients databases of the division of diagnostic imaging and the university clinic a list was made of patients who were presented for CT-scan of the head to evaluate a tumour of the head. From these patients an overview was made containing information about the patient (patients number, gender, age, breed and breed group), the tumour (final diagnosis, histological type, localization and the presence of osteolysis) and whether or not a scan (radiograph or CT-scan) of the thorax was made and the outcome of this scan (whether or not there were any lung metastases found).

358 patients were presented for a CT-scan of the head for evaluation of a tumour. Fifty-six (15.64%) patients were crossbreeds and 305 (84.36%) were pure breeds. Thirty-four different tumours were found in 242 patients. The most common tumours were squamous cell carcinoma (58; 16.20%), malignant melanoma (31; 8.66%), adenocarcinoma (24; 6.70%), sarcoma (20; 5.59%), fibrosarcoma (16; 4.47%), carcinoma (15; 4.19%), acanthomatous ameloblastoma (15; 3.91%) and osteosarcoma (9; 2.51%). In 182 cases a CT-scan (160) or radiograph (20) of the thorax was performed. In 18.1% (33) of the cases lung metastases were found.

Only the breed groups seemed to have a significant influence ($P < 0.0005$) on the type of tumour. The other variables did not have a significant influence on the type of tumour or the n was too small for statistical analysis. Age (young versus old) seems to have a significant ($P = 0.017$) influence on sarcoma. Location seems to have a significant ($P = 0.008$) influence on osteosarcoma. In case of malignant melanoma the age ($P < 0.0005$) and location ($P = 0.009$) seem to be of influence.

No significant effects of tumour, histological type or localization were seen on the presence of lung metastases. Although it seems that melanocytic tumours were the most malignant histological type and no lung metastases were seen in tumours located at the ear, sarcomas and acanthomatous ameloblastoma. Localization and histological type seem to have a significant influence on the occurrence of osteolysis. Tumours in the oral space most frequently cause osteolysis. Between the histological types this were the epithelial tumours.

In conclusion this research gives an overview of the tumours of the canine head that were presented at the University Clinic and their behaviour as to cause osteolysis and metastatic disease to the lungs.

Introduction

Canine head tumours

At least 50 different tumours of the head have been described in the dog⁽¹⁻⁵⁾, originating tumours originate from different tissues and growing at different sites⁽³⁾. These tumours show a broad variety in characteristics, such as metastatic pattern, speed of growth, invasiveness and prognosis⁽¹⁻⁹⁾. In the literature a number of different classifications of canine head tumours have been described, such as division into groups according to localization or tissue of origin^(3,10). The following locations are used: intra-cranial, the skull and jaws, the skin and soft tissues, the oral space, the nose and nasal sinuses, the eye and the ears⁽³⁾. Intra-cranial tumours are not included in this study.

The aim of this study is to determine which canine head tumours are commonly seen at the University Clinic of Veterinary Medicine of Utrecht University. Furthermore, how often these tumours metastasize to the lungs and their tendency to cause osteolysis at the site of origin are examined. These facts have a major influence on the prognosis and the choice of therapy. By comparing collected data, correlations between different variables and tumours are sought. The possible correlation between tumour type and its tendency to metastasize to the lungs and its tendency to cause osteolysis are examined.

Tumours of the skull and jaws (table 1.1)

All primary bone tumours can manifest on the skull and jaws originating from the bone and cartilage (and occasionally from other cells, for example fibrosarcoma and haemangiosarcoma) of the skull and jaws. The most common primary bone tumour is osteosarcoma^(9, 11, 12). Osteosarcoma is most frequently seen in older, larger breed dogs and metastasize in early stage of the disease. Metastases occur mainly in the thorax but can also be seen at other bones or soft tissues. These metastases are often too small to be detected by diagnostic imaging when the patient is presented⁽¹³⁾. Two distinct osteosarcomas of the skull are known: multilobular osteochondrosarcoma and mandibular osteochondrosarcoma⁽³⁾.

Mandibular osteochondrosarcoma is the most common skull and jaw tumour and arises in the ramus of the mandibular. This tumour is slow to metastasize.

Multilobular osteochondrosarcoma is an osteoproliferative, invasive tumour arising from the calvarium and causing local osteolysis. In at least 50% of the dogs not euthanized for problems caused by the primary mass metastases are seen⁽¹⁴⁾.

Tumours of the skeleton.

Primary tumours of bone

Benign

- Osteoma
- Chondroma (rare)
- Enchondroma
- Monostotic osteochondroma
- Polyostotic osteochondroma (multiple cartilagenous exostoses)

Malignant

- Osteosarcoma
- Parosteal osteosarcoma
- Chondrosarcoma
- Fibrosarcoma
- Haemangiosarcoma
- Liposarcoma
- Anaplastic sarcoma
- Giant cell tumour (of bone)

Table 1.1,⁽⁹⁾**Tumours of the skin (table 1.2) and soft tissues (table 1.3)**

Tumours of the skin and soft tissues account for approximately one third of all canine tumours⁽³⁵⁾ and can arise from any type of cell present in the skin. Two thirds of the skin tumours known in dogs are benign⁽¹⁵⁻¹⁷⁾. The type of tumour and location have an influence on the characteristics of the tumour. Skin tumours Kaldrymidou et al. found that 18.4% of the skin tumours are located on the head and the neck and there are more than thirty different skin tumours known^(15, 16). However the ten most common types of skin tumours account for approximately 80% of all skin tumours^(15, 18, 19).

Classification of tumours affecting the skin.

Epithelial tumours	Papilloma	
	Basal cell tumour/ carcinoma	
	Adnexal tumours	
	- Sebaceous gland tumours	- Sebaceous gland adenoma - Sebaceous epithelioma - Sebaceous gland adenocarcinoma
	- Tumours of parianal glands	- Perianal gland adenoman/ adenocarcinoma
	- Sweat gland tumours	- Adenoma/ adenocarcinoma
	- Tumours of hair follicles	- Pilomatricoma
	- Intracutaneous cornifying epithelioma	- Trichoepithelioma
Melanocytic tumours	Benign melanoma	
	Malignant melanoma	
Mast cell tumours	Well, intermediate and poorly differentiated	
Cutaneous lymphoid neoplasia	Plasmacytoma	
	Primary cutaneous T cell lymphoma	
	Epitheliotrophic lymphoma (mycosis fungoides)	
	'Histiocytic' lymphoma	
	Lymphomatoid granulomatosis	
Histiocytic and granulomatous skin conditions	Canine cutaneous histiocytoma	
	Cutaneous histiocytosis	
	Sterile pyogranulomatous/ granulomas dermatoses	
	Systemic histiocytosis	

Table 1.2,⁽⁶⁾

In dogs tumours of soft tissues account for approximately 15% of all "skin" tumours⁽²⁰⁾. Tumours of the soft tissues originate from different types of tissues. These tumours are both benign and malignant. Soft tissue sarcomas are more frequently seen in large breed dogs. They are usually locally invasive but are relatively slow to metastasize⁽²⁰⁻²²⁾.

Classification of soft tissue tumours.

Fibrous tissue	Benign
	Fibroma
	Malignant
	Fibrosarcoma
	Canine haemangiopericytoma

Fibro-histiocytic	Benign -
	Malignant Malignant fibrous histiocytoma/ malignant histiocytosis
Adipos	Benign Lipoma
	Malignant Liposarcoma
Muscular-skeletal	Benign Leiomyoma/ fibroleiomyoma
	Malignant Leiomyosarcoma
Muscular-smooth	Benign (rhabdomyoma)
	Malignant Rhabdomyosarcoma
Synovial	Benign -
	Malignant Synovial (cell) sarcoma
Vascular	Benign Haemangioma (lymphangioma)
	Malignant Haemangiosarcoma (lymphamngiosarcoma)
Peripheral nerve	Peripheral nerve sheath tumours: Terminology ambiguous
Other	Benign Myxoma
	Malignant myxosarcoma

Table 1.3, ⁽⁷⁾

Tumours of the oral space (table 1.4)

The oral cavity is a very common site for tumours to emerge, with about 6% of all canine tumours being malignant oral tumours. However not all oral tumours are malignant. Oral tumours occur more often in males than females⁽²³⁾, affecting more often older dogs⁽³⁾. Between those tumours there is a lot of variety in characteristics. The most common oral space malignant tumours are squamous cell carcinoma, malignant melanoma, and fibrosarcoma^(1, 24). Gingival squamous cell carcinoma is slow to metastasize⁽²⁵⁾, whereas oral malignant melanomas are known to metastasize quickly⁽¹⁾. The most common benign tumours are adenoma, polyps and fibroma⁽¹⁾.

Tumours of the oropharynx.

Gingiva and dental arcade	Benign/non-metastatic <ul style="list-style-type: none"> - Papilloma - Peripheral odontogenic fibroma (osseus/ fibrous epulis) - (Giant cell epulis) - Odontoma
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	<ul style="list-style-type: none"> - Ameloblastoma - Basal cell carcinoma (acanthomatous epulis)
	Malignant <ul style="list-style-type: none"> - Squamous cell carcinoma - Malignant melanoma - Fibrosarcoma - Other sarcomas
	(Epitheliotropic lymphoma) (Plasmacytoma)
Mandible (maxilla)	Osteosarcoma Fibrosarcoma
Tongue	Squamous cell carcinoma (Rhabdomyosarcoma, Granular cell myoblastoma)
Tonsil	Squamous cell carcinoma Lymphoma
Salivary glands	Mixed salivary tumour Adenocarcinoma
Cheek and lips	Squamous cell carcinoma Mast cell tumour Melanoma Plasmacytoma Epitheliotropic lymphoma

Table 1.4,⁽³⁾

Tumours of the nose and nasal sinuses (table 1.5)

Tumours of the nasal cavity and paranasal sinuses represent 1-2% of all canine tumours⁽²⁶⁻²⁸⁾, occurring more frequently in mesaticephalic or dolichocephalic dogs of older age⁽²⁹⁻³²⁾. Tumours arise mainly from the glandular epithelium, but also squamous cell carcinomas are not uncommon at this site^(31, 32). About 80% of tumours of the nasal cavity and sinuses are malignant⁽²⁸⁾ and locally aggressive, with a general slow tendency to metastasize^(27, 30, 32).

Tumours of the nasal cavity and paranasal sinuses.	
Carcinoma	Adenocarcinoma Squamous cell carcinoma Undifferentiated carcinoma (including transitional cell carcinoma)
Sarcoma	Fibrosarcoma Chondrosarcoma Osteosarcoma Undifferentiated sarcoma
Other	Lymphoma Transmissible venereal tumour Melanoma Neuroblastoma

Table 1.5,⁽³⁾

Tumours of the ears (table 1.6)

Ear tumours are uncommon in the dog, with approximately 2-6% of the tumours in dogs. They occur most frequently in mostly older animals with a history of chronic otitis. The cocker spaniel is overrepresented^(3, 33-35). The tumours originate from the sebaceous glands and ceruminous glands. Up to 60% of the tumours of the ears in dogs (excluding polyps) are malignant^(36, 37), growing locally

aggressive⁽³⁾ with a low tendency to metastasize⁽³⁵⁾. Ceruminous gland adenocarcinoma, squamous cell carcinoma, and carcinoma of undetermined origin are the most common malignant tumours⁽³³⁾.

Tumours of the ears	
Benign	Ceruminous gland adenoma Poliepen Basal cell tumours Papillomas
Malignant	Ceruminous gland adenocarcinoma (most common) Squamous cell carcinoma Carcinoma of unknown origin

Any cutaneous tumour may, on occasion, arise in the ear canal.

Table 1.6,⁽³⁾

Tumours of the eye (table 1.7)

Extraocular tumours are tumours of the eyelids (common), third eyelid (rare), conjunctiva (rare), orbit (see tumours of the skull and jaws) and optic nerve (very rare)^(8, 38). Tumours of the eyelids are approximately 85% benign adenomas⁽³⁹⁾. Tumours that arise of the conjunctiva and third eyelid are often squamous cell carcinomas but other neoplasms also occur⁽³⁸⁾. Behaviour varies between different tumours⁽⁴⁰⁾.

The most common primary intraocular tumour in the dog is the melanoma⁽⁴¹⁾ occurring mostly in older dogs⁽⁴⁰⁾ with a slow metastasizing pattern⁽⁴²⁾. Tumours of the uvea can be divided into primary tumours, generalized tumours and metastases. The primary tumours mostly arise from the iris and seldom from the ciliary body or choroid⁽³⁸⁾. Tumours of the cornea, sclera, retina and choroid are uncommon^(38,41).

Tumours affecting the eye and orbit.		
Extra ocular	Eyelids	Squamous cell carcinoma and basal cell carcinoma Meibomian/sebaceous gland adenoma (adenocarcinoma) Melanoma MCT and other skin tumours
	Third eyelid	Primary tumours <ul style="list-style-type: none"> - Melanoma - Haemangioma - Squamous cell carcinoma and basal cell carcinoma - Adenoma/adenocarcinoma - Viral papilloma
		Secondary <ul style="list-style-type: none"> - Lymphoma
	Conjunctiva	Squamous cell carcinoma Melanoma Systemic histiocytosis
	Orbit	Primary connective tissue tumours Primary tumours of skull Local invasion
	Optic nerve	Optic nerve meningioma
Ocular	Cornea and sclera	Melanoma (limbal or epibulbar) Squamous cell carcinoma
	Iris and ciliary body	Ciliary body adenoma/adenocarcinoma Multicentric lymphoma Melanoma

		Medulloepithelioma Metastatic tumours (mammary carcinoma, haemangiosarcoma, malignant melanoma)
	Retina and choroid	Retinoblastoma Melanoma

Table 1.7, ⁽⁸⁾

Tumour staging

Tumour staging is used for evaluation of the tumour and possible metastases and gives an insight in the extent and seriousness of the disease. Tumour staging consists of clinical staging and histopathological staging ^(23, 29, 43).

Clinical staging is used to gain an insight in the extent of the tumour and possible metastases, helping to determine the prognosis and best treatment plan. This method evaluates the primary tumour (T), the local and regional lymph nodes (N) and distant metastases (M) ⁽⁴⁴⁾. This TNM anatomical staging is a widely used tumour staging system that helps staging the tumour in an objective way. The evaluation of the primary tumour focusses on the extent of the primary tumour, including size and infiltration in adjacent tissues. The clinical staging is performed by physical examination, different diagnostic imaging techniques and biopsies. Diagnostic imaging of the head can be performed by radiograph, CT, MRI and ultrasound. Which technique is advised depends on tumour type, location, money of the owner and availability. CT and MRI are the best techniques for evaluation of the bony and soft tissue of the head, each technique having its advantages and disadvantages. In the University Clinic often CT is performed, because it is superior for the evaluation of the bony structures, the lungs, is cheaper and has shorter examination times ⁽⁴⁵⁾. The evaluation of the regional lymph nodes is used for establishing metastatic disease ⁽²³⁾. Evaluation of the lymph nodes is usually performed by physical examination, diagnostic imaging techniques and biopsy or aspiration. The evaluation of distant metastases is performed by physical examination, imaging techniques and laboratory investigations ⁽⁴⁴⁾. Evaluation for pulmonary metastases is performed by thoracic radiographs or CT-scan. Thoracic radiographs are significantly less sensitive in detecting lung metastases than a CT-scan of the thorax ⁽²³⁾.

Histological staging gives insight in the behaviour expected from the tumour ^(23, 43). The most accurate method for tumour diagnosis is by histology of a representative biopsy or of the whole tumour. When using cytology the coherence of the cells is lost, so the diagnosis may be less accurate ⁽⁴³⁾.

Materials and methods

Patients list

Using the patient administration program (PACS) of the division of diagnostic imaging and the patient administration program (Vetware) of the University Clinic of the Faculty of Veterinary Medicine of Utrecht University, a list was made of all dogs that were diagnosed with a tumour of the head and of which a CT-scan of the head was performed. Using PACS a list was made of all patients who were presented for a CT-scan of the head. The search terms used were: schedel (skull), neus (nose), maxilla, mandibula (mandibular) and thorax. Thorax was added because often CT examination of the head and thorax are combined and sometimes both examinations are saved under one denominator.

The patients on the list obtained by this first search were looked up in Vetware. With the use of Vetware it was determined what the final diagnosis of each patient was and whether or not they were suitable for this study.

Patient characteristics

The patients suited for this research were added to an excel file. The patients were evaluated for different characteristics. Those characteristics were about the patient (patients number, gender, age, breed and breedgroup), the tumour (final diagnosis, histological type, localization and osteolysis) and the outcome of the examination of the thorax when a CT-scan or radiograph of the thorax was taken (whether or not there were any lung metastases found). The breeds were categorized into the different breed groups (group 1: Sheepdogs and Cattle Dogs, group 2: Pinscher and Schnauzer - Molosoid Breeds, group 3: Terriers, group 4: Dachshunds, group 5: Spitz and Primitive types, group 6: Scenthounds and Related Breeds, group 7: Pointing Dogs, group 8: Retrievers - Flushing Dogs - Water Dogs, group 9: Companion and Toy Dogs) of the Fédération Cynologique Internationale (FCI). The histological types are epithelial, mesenchymal, hematopoietic and melanocytic. The localization was divided in the nose and nasal sinuses, the oral space, the ears, the skin and soft tissues and a remainder group (enclosing among other intraocular tumours). Tumours of the jaws were included in the tumours of the oral space. The other tumours of the skull were included in the remainder group. All CT-images were evaluated for lysis of one of the bony structures of the head.

Statistics

Using the Fisher's exact test it was explored if there was a relation between the type of tumour or histological type and the different characteristics listed (gender, age, breed, breed group and localization). In an attempt to get more significant results only the most common tumours were used. The most common breeds were also selected for the same reason. Age was split into young (1-5 years) and old (6 years and older) in order to fit into the Fisher's exact test.

In an attempt to get more significant data a logistic regression was used investigating the same characteristics per tumour. Also using a logistic regression it was explored which characteristics (localization, histological type and final diagnosis) have an influence on the chance of metastases or the presence of osteolysis.

Results

A total of 358 cases were admitted to this study. The age of the dogs ranged from 4 months to 16 years old with an average of 8 years. There were 87 different breeds and 56 (15.64%) patients were crossbreeds. The most common breeds were the labrador retriever (32; 8.94%), the golden retriever (30; 8.38%), the Jack Russel terrier (18; 5.03%), the Rottweiler (8; 2.23%), the Balgian shepherd (7; 1.96%), the beagle (7; 1.96%), the Rhodesian ridgeback (7; 1.96%), the West Highland white terrier (7; 1.96%) and the German shepherd (7; 1.96%). The female/male ratio was 153/204 (0,75).

In 108 (30.17%) cases the final diagnosis was neoplasia based on physical examination and a CT-scan and in 8 (2.23%) cases the final diagnosis was tumour or inflammation based on histology or cytology. In the remaining 242 patients 34 different tumours were found. The most common tumours were squamous cell carcinoma (58; 16.20%), malignant melanoma (31; 8.66%), adenocarcinoma (24; 6.70%), sarcoma (20; 5.59%), fibrosarcoma (16; 4.47%), carcinoma (15; 4.19%), acanthomatous ameloblastoma (15; 3.91%) and osteosarcoma (9; 2.51%). Squamous cell carcinoma is a single histological diagnosis, but behaves differently at different sites⁽²³⁾. This means that the group of squamous cell carcinomas should be divided in squamous cell carcinomas of the nose (23; 6.42%), squamous cell carcinomas of the oral space (27; 7.54%) and squamous cell carcinomas of the skin (8; 2.23%). In the group of the squamous cell carcinomas of the nose a sub-group can be made of the squamous cell carcinomas that arise from the planum nasale and the nasal septum (11; 3.07). Table 3.1 shows the number of tumours of the different histological types (epithelial, mesenchymal, hematopoietic and melanocytic). 241 cases could be sorted into these groups. The remainder of the cases the diagnosis was not accurate enough to determine the tissue of origin. Twenty (5.59%) tumours were located in the ears, 45 (12.57%) in the skin and soft tissues, 128 (35.75%) in the oral space and 155 (43.30%) in the nose and nasal sinuses. The remainder group counted 10 (2.79%) tumours.

In 182 cases a CT-scan (160) or radiograph (20) of the thorax was performed. In 18.1% (33) pulmonary metastases were found. In the group of the CT-scan this percentage was 19.38% and in the radiograph group it was 10%. This difference was not significant according to the Fisher's exact test.

Histological type	Number of patients	Number of different tumours
Epithelial	134	15
Mesenchymal	71	15
Melanocytic	31	1
Hematopoietic	5	2
Total	241	33

Table 3. 1

Osteolysis was found in 249 (69.55%) cases. In 28 tumour types at least one case with osteolysis was found. In most tumour types 50% or more of the patients had osteolysis. The exception is malignant melanoma, with osteolysis in only 36.67% of the cases.

Effects of gender on the type of tumour and histological type.

Using the Fisher's exact test no significant correlation was found between the gender and the type of tumour or histological type. The incidence of fibrosarcoma and carcinoma was approximately two times higher in the female population (respectively 4.3% versus 9.7% and 3.6% versus 8.7%). No significant relations were found using logistic regression.

Effects of breed and breed groups on the type of tumour and histological type.

No significant correlation was demonstrated between the breeds and the tumour type or histological type. The breed groups seem to have a significant ($P < 0.0005$) influence on the tumour type but not on the histological type. The prevalence of squamous cell carcinomas is higher in all the breed groups (17,2% - 34,4% within breed group) in comparison to the crossbreeds (13,9%). The Sheepdogs and Cattle Dogs were the most effected by adenocarcinomas (20,7%), Pinscher, Schnauzer and Molossoid Breeds by sarcomas (16,7%) and Retrievers, Flushing Dogs and Water Dogs by acanthomatous ameloblastomas (11,5%). Carcinomas mostly affected Pinscher, Schnauzer and Molossoid Breeds (10,0%), Sheepdogs and Cattle Dogs (10,3%) and crossbreeds (11,1%). Surprisingly the prevalence of fibrosarcomas was higher in the crossbreeds (16,7%) than in all the breed groups (0,0% - 7,7%). Using the logistic regression no significant relations were found.

Effects of age on the type of tumour and histological type.

In six out of eight tumours the majority was older than 5 years (the two exceptions are sarcoma and acanthomatous ameloblastoma). The largest differences were found in malignant melanoma (4.7% of the tumours from dogs of 0 to 5 years of age and 14.6% of the tumours from the dogs older than 5 years), sarcoma (16.3% 0-5 years and 6.5% older than 5 years) and carcinoma (2.3% 0 to 5 years and 7.0% older than 5 years). The melanocytic histological type also showed a considerable difference between the age groups, as can be expected from the results of the analysis of the effect of age on the type of tumour. However there was no significant relation found between age and the type of tumour or histological type.

Using the logistic regression a significant relation between age and malignant melanoma and age and sarcoma were found. Age (young versus old) seems to have a significant ($P = 0.017$) odds ratio of 3.253 (young animals having 3.253 times greater chance of getting a sarcoma) in case of sarcoma. Although the odds ratio in case of age used as linear quality is not significant. In case of malignant melanoma the odds ratio for age is 1.320 ($P < 0.0005$). Meaning every year of live the chance of a dog getting malignant melanoma is 1.320 times bigger than the year before.

Effects of localization on the type of tumour and histological type.

No significant result came from the statistical analysis of the effects of localization on the type of tumour or on histological type. Squamous cell carcinoma mainly occurred at the oral space and the nose and nasal sinuses and did not occur in the ear or the remainder group. Malignant melanoma occurred mainly in the oral space and the skin and soft tissues and not in the ear. Adenocarcinoma was mostly found in the ear and the nose and nasal sinuses. Sarcoma did not occur in the ear or the remainder group and fibrosarcoma also did not occur in the remainder group. Carcinoma was found mostly in the nose and nasal sinuses and not in the ear or the remainder group. Acanthomatous ameloblastoma was only found in the oral space. Osteosarcoma was not found in the ear or at the skin and soft tissues.

No epithelial tumours were found in the remainder group, opposed to mesenchymal tumours which were mainly found in the remainder group. The melanocytic tumours occurred mainly in the oral space and at the skin and soft tissues and did not occur in the ear. Hematopoietic tumours only occurred in the nose and nasal sinuses and (especially) the ear.

Using the logistic regression a significant relation was found between localization and malignant melanoma and between localization and osteosarcoma. For location of malignant melanoma the nose is a very uncommon location. The most common locations for malignant melanoma are the oral space (OR: 43.825; $P < 0.0005$, the odds ratio is in comparison to the nose and nasal sinuses), the skin and soft tissues (OR: 36.105; $P: 0.001$) and the remainder group (OR: 52.019; $P: 0.002$). In case of malignant melanoma all the tumours in the remainder group were located intraocular. Location seems to have a significant ($P = 0.008$) influence on osteosarcoma. Although it seems that the most common location falls into the remainder group (presumably the skull).

	Exp(OR)	Sig. (P)
Age	1,320	,000
Location (nose and nasal sinuses)		,009
Oral space	43,825	,000
Skin and soft tissues	36,105	,001
Ears	,000	,999
Remainder group	52,019	,002
Constant	,000	,000

Table 3. 2 Logistic regression Malignant melanoma

Effects of tumour, histological type and localization on lung metastases.

The tumour type, histological type and localization did not seem to have a significant effect on the presence of lung metastases. However there are some (not significant) interesting outcomes. First none of the patients with a tumour located at the ear had lung metastases (in contrast to 11,5% - 33,3% of the patients with tumours at the other locations) and none of the patients with sarcoma or acanthomatous ameloblastoma had lung metastases. From the patients with osteosarcoma 50% had lung metastases. Although the influence of histological type was also insignificant, the melanocytic type seems to be the most malignant histological type (in 25% of the patients lung metastases were found). It should be remembered that all these results were not significant (probably because n was too small).

<u>Tumour</u>	Lung metastases		
	None	One or more	Total
Squamous cell carcinoma	32 (84,21%)	6 (15,79%)	38 (100,00%)
Malignant melanoma	21 (75,00%)	7 (25,00%)	28 (100,00%)
Fibrosarcoma	13 (92,86%)	1 (7,14%)	14 (100,00%)
Sarcoma	8 (100,00%)	0 (0,00%)	8 (100,00%)
Carcinoma	5 (71,43%)	2 (28,57%)	7 (100,00%)
Adenocarcinoma	5 (83,33%)	1 (16,67%)	6 (100,00%)
Osteosarcoma	3 (50,00%)	3 (50,00%)	6 (100,00%)
Acanthomatous ameloblastoma	4 (100,00%)	0 (0,00%)	4 (100,00%)
Total	91 (81,98%)	20 (18,02%)	111 (100,00%)

Histological type			
epithelial	54 (84,38%)	10 (15,63%)	64 (100,00%)
mesenchymal	34 (87,18%)	5 (12,82%)	39 (100,00%)
melanocytic	21 (75,00%)	7 (25,00%)	28 (100,00%)
hematopoietic	1 (100,00%)	0 (0,00%)	1 (100,00%)
Total	110 (83,33%)	32 (16,67%)	132 (100,00%)
Localization			
Oral space	67 (79,76%)	17 (20,24%)	84 (100,00%)
Nose and nasal sinuses	46 (88,46%)	6 (11,54%)	52 (100,00%)
Skin and soft tissues	25 (75,76%)	8 (24,24%)	33 (100,00%)
Ears	5 (100,00%)	0 (0,00%)	5 (100,00%)
Remainder	4 (66,67%)	2 (33,33%)	6 (100,00%)
Total	147 (81,67%)	33 (18,33%)	180 (100,00%)

Table 3. 3

Effects of tumour, histological type and localization on osteolysis

Significant correlations were found between the occurrence of osteolysis and histological type ($P < 0.005$) and the occurrence of osteolysis and the localization ($P < 0.0005$). In comparison with the nose and nasal sinuses osteolysis appeared more often in the oral space ($P = 0.001$; $OR = 4.058$) and less often in the ears ($P = 0.024$; $OR = 0.151$). Osteolysis occurred less often in melanocytic tumours ($P < 0.0005$; $OR = 0.112$) than epithelial tumors. Table 3.4 shows the results of the logistic regression of the occurrence of osteolysis.

	Exp(OR)	Sig. (P)
Nose and nasal sinuses		0.000
Oral space	4.058	0.001
Skin and soft tissues	0.468	0.101
Ears	0.151	0.024
Remainder	1.578	0.618
Epithelial		0.000
Mesenchymal	0.766	0.484
Melanocytic	0.112	0.000
Hematopoietic	0.313	0.349
Constant	1.920	0.008

Table 3. 4 Logistic regression of the occurrence of osteolysis

Discussion

The collected data give an insight in the type of head tumours presented to the University Clinic. The literature concurs with the significant results^(3, 6, 7, 13, 35, 46). This is different on the insignificant, although pronounced outcomes. In case of the influence of gender on fibrosarcomas the literature describes a 2:1 male: female ratio⁽³⁾ whereas this study found a 1:2 male: female ratio. In this study no pulmonary metastases were found in tumours of the ears and sarcomas. However according to the literature tumours of the ears can metastasize to the lungs, although this does not happen often⁽³⁾. In case of sarcomas the literature describes pulmonary metastases in up to 25% of the cases^(7, 47). In case of osteosarcomas and the melanocytic tumours the literature does concur with the results of this study^(19, 47, 48).

In this study only the dogs of which a CT-scan of the head was made were included in this study. This might give an inaccurate idea of the distribution and prevalence of some tumours, because not all tumours are accurately represented. In the case of the intraocular tumours this becomes very clear. Of only 2 patients with intraocular tumours a CT-scan of the head was made. However it seems very unlikely that those were the only patients presented with an intraocular tumour at the University Clinic during six years. This is probably due to the fact that an ultrasound is a more logical choice of diagnostic imaging in case of an intraocular tumour.

Caution should also be taken in the interpretation of the data of the scans of the lungs. Owners may decline to make the extra cost for an additional CT-scan of the lungs because for example changes in the CT-scan of the head are so dramatic that there are no treatment possibilities. This scenario occurred especially often in cases of nasal tumours. By the time nasal tumours are presented at the University Clinic, the CT-scan of the head shows extensive osteolysis and invasion into the nasal sinuses or even the intra-cranial space. Based on this information owners frequently decide to euthanize the dog and further examination is ceased. This may cause a wrong image of the frequency of lung metastases in relation to tumours of the nose and nasal sinuses.

Furthermore it should be noted that in this study only the thoracic scans made on first time examination of a dog were included in the data. Some tumours are slow to metastasize and could give a negative result for lung metastases at first whilst in a later stadium lung metastases can indeed be found. Also metastases may be present without showing on the radiograph or CT-scan.

Tumours can behave differently when they arise on different locations. In case of squamous cell carcinomas this is taken into account when performing the logistic regression. However this may also be the case with different tumours. Unfortunately dividing the data into more groups would mean even smaller groups. As the groups were too small to begin with, this was not attempted in this study.

Finally a problem in this study is that the results were mostly insignificant. This was probably due to the fact that the number of cases was too small. This was definitely the case when looking at the thoracic scans. Also the great number of different final diagnosis (34) causes groups to contain few patients. This can also be said for different breeds (84). By creating larger groups it was tried to evade this problem but unfortunately this was not enough. For further research it might be wise to use all the dogs with a tumour of the head presented at the University Clinic of the Faculty of Veterinary Medicine or even include patient information from other veterinary clinics in the Netherlands.

References

1. Bronden LB, Eriksen T, Kristensen AT. Oral malignant melanomas and other head and neck neoplasms in danish dogs - data from the danish veterinary cancer registry. *Acta Veterinaria Scandinavica*; 2009.51: 54, (18 December 2009). 2009.
2. Oral en perianal tumors (proceedings) [Internet]. Available from: <http://veterinarycalendar.dvm360.com/avhc/article/articleDetail.jsp?id=771450&sk=&date=&%0A%09%09%09&pageID=2>.
3. Morris J, Dobson J. Head and neck. In: *Small Animal Oncology*. 1st ed. Oxford: Blackwell Science Ltd; 2001. p. 94-124.
4. Neumann ZL, Fan TM, Looper J. Canine and feline nasal tumors. *Veterinary Medicine*; 2011.106: 8, 402-404, 406-410, 412, 416. 2011.
5. Sanchez J, Buendia AJ, Vilafranca M, Velarde R, Altimara J, Martinez CM, et al. Canine carcinosarcomas in the head. *Veterinary Pathology*; 2005.42: 6, 828-833. 2005.
6. Morris J, Dobson J. Skin. In: *Small Animal Oncology*. 1st ed. Oxford: Blackwell Science Ltd; 2001. p. 50-68.
7. Morris J, Dobson J. Soft tissues. In: *Small Animal Oncology*. 1st ed. Oxford: Blackwell Science Ltd; 2001. p. 69-77.
8. Morris J, Dobson J. The eye and orbit. In: *Small Animal Oncology*. 1st ed. Oxford: Blackwell Science Ltd; 2001. p. 252-61.
9. Morris J, Dobson J. Skeletal system. In: *Small Animal Oncology*. 1st ed. Oxford: Blackwell Science Ltd; 2001. p. 78-93.
10. Withrow SJ. Chapter 3: The pathology of neoplasia. In: *Small Animal Clinical Oncology*. Missouri: Saunders; 2007. p. 54-67.
11. Brodey RS. Canine osteosarcoma. A clinicopathologic study of 194 cases. *Clin Orthop*. 1969;62:54-64.
12. Heyman SJ, Diefenderfer DL, Goldschmidt MH, Newton CD. Canine axial skeletal osteosarcoma. A retrospective study of 116 cases (1986 to 1989). *Veterinary surgery*. 1992;21(4):304-10.
13. Withrow SJ. Chapter 23: Tumors of the skeletal system. In: *Small Animal Clinical Oncology*. Missouri: Saunders; 2007. p. 540-82.
14. Dernell WS, Straw RC, Cooper MF, Powers BE, LaRue SM, Withrow SJ. Multilobular osteochondrosarcoma in 39 dogs: 1979-1993. *J Am Anim Hosp Assoc*. 1998;34(1):11-8.

15. Kaldrymidou H, Leontides L, Koutinas AF, Saridomichelakis MN, Karayannopoulou M. Prevalence, distribution and factors associated with the presence and the potential for malignancy of cutaneous neoplasms in 174 dogs admitted to a clinic in northern greece. *Journal of veterinary medicine.Series A.* 2002;49(2):87-91.
16. Mukaratirwa S, Chipunza J, Chitanga S, Chimonyo M, Bhebhe E. Canine cutaneous neoplasms: Prevalence and influence of age, sex and site on the presence and potential malignancy of cutaneous neoplasms in dogs from zimbabwe. *J S Afr Vet Med Assoc.* 2005;76(2):59-62.
17. Priester WA, Mantel N. Occurrence of tumors in domestic animals. data from 12 united states and canadian colleges of veterinary medicine. *J Natl Cancer Inst.* 1971;47(6):1333-44.
18. North SM, Banks TA. CHAPTER 18 - tumours of skin and subcutaneous tissues. In: *Small Animal Oncology.* Edinburgh: W.B. Saunders; 2009. p. 173-82.
19. Vail DM, Withrow SJ. Chapter 18 - tumors of the skin and subcutaneous tissues. In: Stephen J. Withrow A2DVM A2DACVS A2DACVIM (Oncology), David M. Vail, DVM,DACVIM (Oncology), editors. *Withrow & MacEwen's Small Animal Clinical Oncology (Fourth Edition).* Saint Louis: W.B. Saunders; 2007. p. 375-401.
20. MacEwan EG. Soft tissue sarcomas. *Small Animal Clinical Oncology.* 2001:283-304.
21. Mauldin GN. Soft tissue sarcomas. *The Veterinary clinics of North America.Small animal practice.* 1997;27(1):139-48.
22. Thrall DE. Soft-tissue sarcomas. *Semin Vet Med Surg Small Anim.* 1995;10(3):173-9.
23. Verstraete FJM, Lommer MJ. Section 8: Management of maxillofacial tumors and cysts. In: *Oral and Maxillofacial Surgery in Dogs and Cats.* Saunders Elsevier; 2012. p. 373-494.
24. Todoroff RJ, Brodey RS. Oral and pharyngeal neoplasia in the dog: A retrospective survey of 361 cases. *J Am Vet Med Assoc.* 1979;175(6):567-71.
25. White. Mandibulectomy and maxillectomy in the dog: Long term survival in 100 cases. *J Small Anim Pract.* 1991;32(2):69-74.
26. Brodey RS. Canine and feline neoplasia. *Adv Vet Sci Comp Med.* 1970;14:309-54.
27. MacEwen EG, Withrow SJ, Patnaik AK. Nasal tumors in the dog: Retrospective evaluation of diagnosis, prognosis, and treatment. *J Am Vet Med Assoc.* 1977;170(1):45-8.
28. Madewell BR, Priester WA, Gillette EL, Snyder SP. Neoplasms of the nasal passages and paranasal sinuses in domesticated animals as reported by 13 veterinary colleges. *Am J Vet Res.* 1976;37(7):851-6.

29. Avner A, Dobson JM, Sales JI, Herrtage ME. Retrospective review of 50 canine nasal tumours evaluated by low-field magnetic resonance imaging. *J Small Anim Pract.* 2008;49(5):233-9.
30. Ladue TA, Dodge R, Page RL, Price GS, Hauck ML, Thrall DE. Factors influencing survival after radiotherapy of nasal tumors in 130 dogs. *Veterinary Radiology and Ultrasound.* 1999;40(3):312-7.
31. Morris. Radiological assessment of severity of canine nasal tumours and relationship with survival. *J Small Anim Pract.* 1996;37(1):1-6.
32. Patnaik. Canine sinonasal neoplasms: Clinicopathological study of 285 cases. *J Am Anim Hosp Assoc.* 1989;25(1):103-14.
33. London. Evaluation of dogs and cats with tumors of the ear canal: 145 cases (1978-1992). *J Am Vet Med Assoc.* 1996;208(9):1413-8.
34. Moisan PG, Watson GL. Ceruminous gland tumors in dogs and cats: A review of 124 cases. *J Am Anim Hosp Assoc.* 1996;32(5):448-52.
35. Withrow SJ. Chapter 18: Tumors of the skin and subcutaneous tissues. In: *Small Animal Clinical Oncology.* Missouri: Saunders; 2007. p. 375-401.
36. Rogers KS. Tumors of the ear canal. *Veterinary Clinics of North America - Small Animal Practice.* 1988;18(4):859-68.
37. Sula MJM. Tumors and tumorlike lesions of dog and cat ears. *Vet Clin N Am : Small Anim Pract.* 2012 11;42(6):1161-78.
38. Stades FC, Wyman M, Boevé MH, Neumann W, Spiess B. *Ophthalmology for the veterinary practitioner.* second ed. Germany: Schlütersche; 2007.
39. Roberts, S M Severin, G A Lavach, J D. Prevalence and treatment of palpebral neoplasms in the dog: 200 cases (1975-1983). *J Am Vet Med Assoc.* 1986;189(10):1355-9.
40. Withrow SJ. Chapter 30: Ocular tumors. In: *Small Animal Clinical Oncology.* Missouri: Saunders; 2007. p. 686-98.
41. Diters, R W Dubielzig, R R Aguirre, G D Acland, G M. Primary ocular melanoma in dogs. *Vet Pathol.* 1983;20(4):379-95.
42. Wilcock BP, R. Adenocarcinoma of the gland of the third eyelid in seven dogs. *J Am Vet Med Assoc.* 1988;193(12):1549-50.
43. Morris J, Dobson J. Diagnosis and staging. In: *Small Animal Oncology.* 1st ed. Oxford: Blackwell Science Ltd; 2001. p. 15-30.
44. TNM classification of tumours in domestic animals. ===. 1980:53pp.

45. Thrall. A comparison of radiographic and computed tomographic findings in 31 dogs with malignant nasal cavity tumors. *Vet Radiol.* 1989;30(2):59-66.
46. Ehrhart N. Soft-tissue sarcomas in dogs: A review. *J Am Anim Hosp Assoc.* 2005;41(4):241-6.
47. Withrow SJ. Chapter 20: Soft tissue sarcomas. In: *Small Animal Clinical Oncology.* Missouri: Saunders; 2007. p. 425-54.
48. Coyle VJ, Rassnick KM, Borst LB, Rodriguez CO, Northrup NC, Fan TM, et al. Biological behaviour of canine mandibular osteosarcoma. A retrospective study of 50 cases (1999-2007). *Veterinary and comparative oncology.* 2013.