# Oral Tumours in Dogs & Cats

Oral tumours in dogs are characterised by locally-aggressive disease. Obtaining a good prognosis for your patient hinges around good local control of the primary tumour. Although the metastatic rate varies with the diagnosis (and in the case of melanoma the metastatic rate is very high), the possibility of metastasis is entirely academic if good local control cannot be effected; due to the pain of the primary tumour euthanasia will be necessary long before metastatic disease threatens the dog's life.

A finite list of differential diagnoses will cover the vast majority of canine oral tumours; melanoma is the commonest, followed by squamous cell carcinoma, followed by fibrosarcoma and acanthomatous ameloblastoma. Osteosarcomas and round cell tumours occur rarely. The diagnostic investigation is reasonably stereotyped, and involves haematology, serum biochemistry, urinalysis, imaging of the oral cavity and thorax, fine needle aspiration of the local lymph nodes (bilaterally) and biopsy of the mass. The use of 3-dimensional imaging like CT is very useful since conventional radiography will not detect osteolysis unless 40% of the bone cortex has been destroyed. 3-dimensional imaging also helps to plan the surgical approach or radiation therapy. Here is a summary of the necessary margins and suggestion of sensitivity to different therapies:

| Diagnosis | Surgical Response | RT Response | Chemo Response |
|---|---|---|---|
| Melanoma | +++ 2cm Margins | +++++ | Poor |
| SCC | +++ 2cm Margins | +++ | Poor |
| Fibrosarcoma | +++ 3cm Margins | +/- | Poor |
| Acanthomatous Epulis | +++ Just complete Excision | +++ | Poor |
| (Osteosarcoma) | +++ 2cm Margins | +/- | Poor |

Table 1: response characteristics of oral tumours

Considerable care has to be taken in counselling an owner of a dog where you are proposing a mandibulectomy or maxillectomy procedure. Most hemimandibulectomy procedures are not especially disfiguring but may result in increased salivation, drooping of the tongue out of the side of the mouth, or messy eating (which usually improves with time). They may pose a risk of mandibular drift however, which can be addressed by use of a special elasticated trainer. Rostral maxillectomies and orbitectomies are the most likely surgeries to be disfiguring, but are still associated

with good long-term function in most cases. Although dogs may appear different, the key feature of canine radical jaw surgeries is that dogs adapt and tolerate their new facial conformation beautifully in the vast majority of cases. To open-minded owners who can be convinced of this, mandibulectomy / maxillectomy / orbitectomy procedures can be curative for their dog. Still, there remains a significant group of owners who would prefer euthanasia over a potentially-curative and radical surgery. Outcomes may be improved by use of implant-based reconstruction in the latter category.

Discussion with specialists, and making use of forums with other onco-surgeons is to be encouraged when considering discussing challenging surgeries with owners. A useful resource is the Veterinary Society of Surgical Oncology, VSSO: https://vsso.org.

## *Oral Melanoma*

Melanomas of the oral cavity in dogs are aggressive tumours, with a high rate of metastasis. Survival times for oral melanomas treated with surgery alone range from 5-17 months, with 1 year survival rates 21-35%. If the local disease in the mouth is adequately addressed, most dogs with oral melanomas are later euthanased because of metastatic disease.

As for all oral tumours, local therapy is the keystone in good melanoma management. Surgery is usually the first consideration but for locations which are not amenable to surgery melanomas respond well (80% response rate) to hypofractionated radiation therapy; often responses are complete (tumours almost disappearing). Following surgery there are two main options for systemic management of potential metastatic disease in canine melanoma: immunotherapy (Merial Melanoma Vaccine) and systemic drug therapy.

Immunotherapy involves treating with the Merial melanoma vaccine (Oncept). This is a DNA vaccine consisting of xenogeneic (human) tyrosinase DNA in a bacterial plasmid vector. The aim of the vaccine is to trigger an immune response against canine tyrosinase (expressed in melanocytes but not in other cells) and thus it represents a specific therapy. This vaccine is administered intradermally every 2 weeks for 4 treatments and then every 6 months thereafter. It has to be imported from the USA on a named patient basis, and is only available to veterinary oncology or internal medicine specialists currently. The vaccine appears to be safe with minimal adverse effects. Occasional erythema (redness) can be seen at the vaccination site and momentary discomfort can be experienced during administration. Vitiligo (depigmentation) of the skin has been seen in a few patients. There are studies indicating potential benefit in increasing survival in melanoma patients. One study showed a significant benefit in survival in vaccinates compared to historical controls. The median survival for controls was 324 days and the median was not reached for vaccinates at the time of publication. The time beyond which

75% of the population was expected to survive was 156 days for historical controls and 464 days for vaccinates.

However there is some controversy over the vaccine's efficacy. In one recent independent randomised study, no survival benefit was seen in vaccinated dogs, and response to the vaccine in the majority of dogs, anecdotally, seems to be disappointing. Nonetheless *there are definitely some dogs who respond very favourably to the vaccine and for these individuals the vaccine represents a highly-effective treatment*.

In general, canine melanomas are poorly responsive to systemic drug therapy (as is the situation in human medicine), however MTD chemotherapy with carboplatin, metronomic chemotherapy or targeted therapy with toceranib have been used with varying levels of success. Whichever therapy is chosen, monitoring would be performed by regular physical examination (particularly assessing the local tumour site and lymph nodes, as well as restaging with a CT scan or radiographs approximately every 3 months, to assess for the presence of any distant metastatic lesions.

## *Canine Oral Squamous Cell Carcinomas*

Oral squamous cell carcinomas (SCCs) in dogs are usually very locally invasive, but the metastatic rate is in the order of 20-30%. When metastasis occurs, it is usually to the regional lymph nodes, or the lungs. Managing the local disease in the jaw can be difficult as surgical excision with adequate margins is extremely hard to achieve in the oral cavity. For this reason, surgery may be followed with radiation therapy to try to sterilise the surgical margins. If surgery is not possible, radiation therapy can be used in the gross disease setting; many SCCs of the dental arcades will respond well to radiation however not perhaps to the same extent as melanomas, and a hyperfractionated protocol is required (with consequent greater expense).

In cases which involve metastasis, or where margins of surgical excision are incomplete and adjunctive radiation therapy is not possible, adjunctive chemotherapy is usually offered. Chemotherapy can also be used palliatively in the absence of any local therapy, but any duration of response will sadly be short here. Carboplatin is probably the best-evidenced drug to use in this setting, and the client should understand that it is still not as effective for local control as surgery or radiation therapy. Metronomic chemotherapy may also be considered from a “first-principles” point of view. Responses have been observed to toceranib but responses are typically finite and it should be remembered that providing it works this is an ongoing treatment (not a course).

Dogs receiving appropriate local control of a mandibular squamous cell carcinoma (effected by appropriate surgery with or without radiation therapy) have achieved a good quality of life for an extended period (in the region of 2 years or more). Dogs

with maxillary SCCs typically have shorter survival times, likely a reflection of the greater difficulty in achieving complete excision in this area.

SCCs of the tonsil are much more aggressive than those associated with the gingiva or buccal mucosa. They are typically much more resistant to radiation therapy and have a very high metastatic rate (approximately 73%). This difference in aggression may not be directly related to the anatomic location; tonsillar SCCs have shown to be much more likely to be of higher grade than the SCCs of other areas in the mouth. Tongue-based SCCs are reported to be intermediate in their aggression between the gingival SCCs and the tonsillar SCCs.

Due to the higher rate of metastasis for tonsillar SCCs, both local therapy (surgery and / or radiation therapy) and systemic chemotherapy are indicated for these tumours. Although earlier reports suggested very short survival times, we may now expect survival in the order of 6-10 months if both local and systemic therapy are given. In this way, tonsillar SCCs are not that different to appendicular osteosarcomas, and our attitude to treatment of osteosarcomas is often very different !

Finally, all oral SCCs may be associated with hypercalcaemia. Although most gingival SCCs are not a diagnostic challenge, a detailed examination of pharynx and tonsils is indicated in the investigation of a hypercalcaemic patient.

## *Canine Oral Fibrosarcomas*

Oral fibrosarcomas are the most invasive oral tumour. Up to a third of cases metastasize (to local lymph nodes or lungs) but local disease is nearly always the cause of euthanasia. Complete resection of such a tumour will necessitate a radical rostral maxillectomy or mandibulectomy procedure, involving removal of the tumour and at least 3cm of healthy “margins.” Early reports of recurrence after this surgery stated a 40-60% local recurrence rate, more recent reports are of 20-25% recurrence. For this reason, surgery is best followed by adjunctive radiation therapy, even in the cases that are resected with clean margins.

If surgery is not possible, there are no equally-effective alternatives. Oral fibrosarcomas are generally resistant to chemotherapy and only have a modest response to radiation therapy in the gross setting (although they are more responsive to radiation therapy when surgically “debulked” first).

## *Acanthomatous Ameloblastomas*

Acanthomatous Ameloblastomas (AAs) are the tumours formerly known as acanthomatous epulides, adamantinomas, or basal cell carcinomas. Any guesses for what they will be called next ?!

These are benign tumours (not considered to have a metastatic risk), derived from the periodontal ligament. What sets them apart from the peripheral odontogenic

fibromas (“POFs” previously referred to as fibromatous or ossifying epulides), is that AAs invade and destroy bone, POFs don’t.

Complete excision is all that is necessary to control the expansion of an AA, and is usually curative. If surgery is not possible then good responses have been reported to radiation therapy or intralesional bleomycin therapy (NB the author doesn’t recommend the use of intralesional cytotoxic drugs on health and safety grounds !).

## *Feline Oral Tumours*

Feline oral tumours are even harder to treat than their canine counterparts, partly because smaller jaws and more delicate anatomy makes complete surgical resection difficult in many cases, and partly because cats often tolerate oral surgery, particularly mandibulectomy procedures, poorly. After oral surgeries, cats typically have to be fed by an oesophagostomy tube for at least 2-4 months, and in at least 12% cases, this is permanently. Maxillectomies are often much better tolerated than mandibulectomies due to the bracing effect of the upper jaw and nose; mandibulectomies are often associated with mandibular drift, malocclusion and self-traumatisation by lower teeth. Counselling the owner of a feline oral tumour patient is therefore much harder; whereas most dogs have excellent return to function long-term, the opposite is true with cats.

The diagnostic approach to oral tumours is very similar for cats as per dogs, and the list of differential diagnoses covering 99% of tumours is even smaller – most tumours are oral SCCs, with fibrosarcomas making up the remainder.

Oral SCCs in cats are usually fast growing and locally invasive, carrying a poor prognosis. Interestingly, the feline oral SCCs are much less sensitive to radiation or drugs than their canine counterparts (they are more akin to the canine tonsillar SCCs than canine mandibular SCCs). Although feline oral SCCs metastasize infrequently to regional lymph nodes, and rarely to distant sites, the morbidity associated with the local disease in the mouth often brings people to elect euthanasia on welfare grounds within months of diagnosis. Managing the local disease of a feline SCC is challenging because surgical excision with adequate margins cannot be achieved in the oral cavity. Thus, a combination of some or all of: surgery, radiation therapy, and chemotherapy represents the most common attempt for definitive therapy, the precise treatment being tailored to the specific details of each individual case. These treatment options rarely effect adequate long term local control however, and are limited by a very poor response to radiation therapy. The one-year survival rate is generally less than 10%, with a median survival time of about three to six months for most treatment regimes.

Oral fibrosarcomas in cats share the radiation resistance of their canine counterparts, and of the feline oral SCC – in fact all oral tumours in cats are generally very radiation resistant. The oral fibrosarcoma is extremely invasive and so complete resection is hard to achieve, local recurrence is common, and despite

having a low metastatic rate, the prognosis is guarded to poor. Chemotherapy is frequently used, often in the gross disease setting but most cases I have treated have experienced a survival in the order of 4-8 months. Doxorubicin and carboplatin, or metronomic chemotherapy are the most popular choices for chemotherapy but insufficient cases have been treated to establish the optimal medical treatment.

# Further Reading:

## *Useful Websites & Societies:*

- Veterinary Society of Surgical Oncology: https://vsso.org
- Veterinary Cancer Society (US): http://vetcancersociety.org
- European Society of Veterinary Oncology: https://www.esvonc.com
- Julius Liptak's Website: http://www.animalcancersurgeon.com

## *Reference Texts:*

- Withrow & MacEwen's Small Animal Clinical Oncology; Vail, Thamm, Liptak; 6th Ed.; Saunders
- Tumors in Domestic Animals; Ed. Meuten; 5th Ed.; Wiley Blackwell
- Textbook of Veterinary Diagnostic Imaging; Ed. Thrall; 7th Ed.; Saunders
- Veterinary Surgical Oncology; Ed. Kudnig, Seguin; Wiley Blackwell
- Veterinary Computed Tomography; Ed. Schwartz & Saunders; Wiley Blackwell
- Veterinary Drug Handbook; Plumb; 9th Ed.; Wiley Blackwell

## *Papers:*


- Burton JH[1], Mitchell L, Thamm DH, Dow SW, Biller BJ. "Low-dose cyclophosphamide selectively decreases regulatory T cells and inhibits angiogenesis in dogs with soft tissue sarcoma." J Vet Intern Med. 2011 Jul-Aug;25(4):920-6.
- PJ Bergman, JD Wolchok; Of mice and men (and dogs): development of a xenogeneic DNA vaccine for canine oral malignant melanoma; Cancer Therapy Vol 6; 817-826; 2008
- Smedley et.al; Prognostic Markers for Canine Melanocytic Neoplasms: A Comparative Review of the Literature and Goals for Future Investigation; Veterinary Pathology 48(1); 54-72; 2011
- Tuohy et.al; Outcome following curative-intent surgery for oral melanoma in dogs: 70 cases (1998–2011)J Am Vet Med Assoc 2014;245:1266–1273
- Verganti et.al; Use of Oncept melanoma vaccine in 69 canine oral malignant melanomas in the UK; J Small Anim Pract 2017 Vol. 58 Issue 1 Pages 10-16
- Riggs et.al; Outcomes following surgical excision or surgical excision combined with adjunctive, hypofractionated radiotherapy in dogs with oral squamous cell carcinoma or fibrosarcoma; (*J Am Vet Med Assoc* 2018;253:73–83