INTRODUCTION:

Radiation therapy is commonly the treatment of choice in the primary and/or post-surgical management of several common types of tumors in dogs and cats. In addition, there are many less common and/or tumors lesser known for responsiveness to radiation for which radiation therapy is not always the first-line but should be a consideration.

An emerging area where radiation is proving efficacious is in the treatment of benign diseases. Historically, concerns regarding toxicity and carcinogenesis have limited investigation into these benefits but the risks for these are likely extremely low. Extensive experience outside of North America has shown substantial benefit in treatment of benign and inflammatory diseases such as osteoarthritis. There is emerging experience and data that similar benefits can be seen in dogs and cats.

COMMON INDICATIONS FOR RADIATION THERAPY IN DOGS AND CATS

Although not the primary focus of this lecture, some of the most commonly irradiated types of tumors are:

- Soft Tissue Sarcoma
- Mast Cell Tumor
- Nasal Tumor
- Oral Tumor (Melanoma, Squamous Cell Carcinoma, Fibrosarcoma)
- Brain Tumor
- Bone Tumor

LESSEER KNOWN TUMORS THAT CAN BE EFFECTIVELY TREATED WITH RADIATION THERAPY

Genitourinary tumors (prostatic and bladder carcinomas) were long concerned poorly radiation responsive tumors. In 2004, a pilot study evaluated hypofractionated radiation (6 fractions x 5.75 Gy) in combination with piroxicam and mitoxantrone showed a 90% clinical improvement rate and median survival time of 11 months. As this was not superior to outcomes with chemotherapy and piroxicam alone, this confirmed these long held beliefs. However, a 2012 study evaluating full-course IMRT (20 fractions of 2.7-2.85 Gy) showed a median event-free survival of 11 months and median overall survival of 22 months which would represent a noteworthy improvement over previous studies. The protocol was well tolerated but some important gastrointestinal and urinary toxicities were seen. This approach warrants additional investigation and consideration for dogs with bladder tumors.

Anal sac adenocarcinomas are most commonly treated surgically for primary and nodal disease. Narrow excision of the primary tumor is common as is eventual development of nodal disease. In the primary treatment setting, the best reported outcomes are the result of multi-modal therapy with surgery of the
primary mass and/or involved lymph nodes followed by postoperative radiotherapy and chemotherapy with a reported median survival time of >2.5 years. In the advanced disease setting, there are 2 studies in 2016 evaluating hypofractionated radiation for these patients and both report good rates of symptomatic relief and median durations of local control for 9-11 months, which was superior to surgery in the study that also evaluated surgical management of advanced nodal disease.

Epulides are common odontogenic tumors that can be treated successfully with wide surgical excision. However, when wide surgery requires extensive mandibular and/or maxillofacial reconstruction, radiation therapy can be an effective alternative or adjunct therapy with a reported 3-year progression free survival rate of 80% for acanthomatous epulides.

Invasive thyroid tumors can be risky to remove surgically and likely to recur due to a lack of resectable tissue planes in the surrounding area. While freely movable or encapsulated thyroid tumors are excellent surgical candidates, invasive thyroid tumors are good candidates for radiation therapy instead of surgery or as a follow-up to incomplete or narrow excision with reported median progression-free survival times of >2 years.

Infiltrative lipomas are an unusual disease entity with frequent local recurrence but essentially no risk for metastasis. There is only one study evaluating radiation therapy for this indication but showed an 80% progression-free survival at 3-years post-irradiation. Radiation is beneficial for macroscopic and for narrowly excised infiltrative lipomas.

Canine hemangiosarcoma is often visceral and treated with surgery and/or chemotherapy. However, radiation therapy can be an effective palliative treatment in cases of hemangiosarcoma, particularly in subcutaneous and retroperitoneal locations with a reported response rate of 70%. However, all hemangiosarcomas have high metastatic potential and frequently progress at distant sites within months.

Lymphoma can present in a wide variety of ways in dogs and cats. The role of radiation for the multicentric form of lymphoma seen most commonly in dogs remains unclear. For solitary extra-nodal forms of lymphoma such as nasal or nasopharyngeal lymphoma, radiation therapy appears to be the most effective treatment although it is best if combined with chemotherapy. In one recent study, abdominal radiation as a rescue therapy (after failing chemotherapy) for feline gastrointestinal lymphoma had a 90% response rate with a median survival of 7 months after radiation.

Thymomas are seen sporadically in dogs, cats, and rabbits and are often difficult to address surgically. Cats and rabbits have reported median survival times of 2 years after radiation therapy with dogs having shorter durations of tumor control with a median of 8 months.

Other tumors that the role for radiation remains poorly defined but there appears to be a moderate-to-high rate of response and tumor control include extramedullary plasmacytomas, histiocytic sarcomas, and heart-based tumors (chemodectoma).

**RADIATION TREATMENT OF “BENIGN” DISEASE**

The use of low-dose radiation to treat benign disease is controversial in human medicine. Although significant evidence exists to support its use, it is very difficult to quantify or estimate the risks associated with exposure to low-dose radiation. Particularly in the United States, this has resulted in a lack of established protocols and fear of radiation-induced tumors and potential litigation. As a result, there is an opportunity for veterinary medicine to lead the way. Unfortunately, evidence thus far is lacking.
Even at doses far lower than are needed in cancer treatment, radiation has a strong local anti-inflammatory effect through a variety of mechanisms including direct toxicity to inflammatory cells and changes to cell adhesion and cytokine expression\textsuperscript{14}.

Osteoarthritis is one of the most common diseases seen in humans, dogs, cats, and other species. A 2013 study out of Germany evaluated over 1000 people with painful gonarthritis and found a response rate of 80\% with over half of the responders having a duration of improvement of greater than 1 year\textsuperscript{15}. Through personal communication and my own anecdotal experience, I estimate that 80\% of dogs treated with radiation therapy (3 fractions x 2 Gy) will improve and this can be increased to 90\% by re-treating the non-responders 2-3 weeks later. 40\% will maintain improvement for 12 months. This can be repeated many times without significant toxicity.

In cats, this is particularly appealing because they often are not suitable for long term NSAID use. A recent case-report describes the success of low-dose radiation therapy in managing the inflammatory processes associated with osteochondrodysplasia in Scottish Fold cats\textsuperscript{16}.

Granulomatous meningoencephalitis can be a debilitating neurologic condition that is challenging to treat medically. One study showed a median survival time of 400 days in dogs treated with radiation and steroids compared to only 40 days with steroids alone\textsuperscript{17}.

Acral lick dermatitis (canine neurodermatitis) is another inflammatory condition of dogs that has been reported to have an 80-90\% response rate to radiation.

The other potential indications are little more than anecdotes but a significant number cases of chronic rhinitis have been treated with hypofractionated radiation protocols and high rates of clinical improvement, typically for 8-12 months duration. I recently evaluated and treated a cat with refractory feline stomatitis despite having all teeth extracted and exhaustive medical management with a marked clinical response. Other conditions for which I may consider the use of low-dose, anti-inflammatory radiation include refractory inflammatory bowel disease and/or pancreatitis.

REFERENCES