Non-resectable and metastatic tumors present a difficult challenge for veterinarians and pet owners. The relatively limited efficacy of intravenous chemotherapy for macroscopic disease, and the cost and morbidity associated with radiation therapy have stimulated the search for additional therapeutic options. While surgery can be successfully performed in the head and neck, this area provides unique challenges such as the proximity to important neurovascular structures, high motion environment, the nasal, oral and sinus cavities, the rich and abundant blood supply providing frequent opportunities for massive hemorrhage and limited visualization, and the owners’ reliance upon cosmetic results. These limitations often prevent clean margins from being achieved resulting in combined modalities needed to treat, or rather palliate, the often large tumors presented in this region.

Similar difficulties in human oncology have inspired various creative, image-guided, regional tumor therapies in the continuously developing subspecialty of interventional radiology (IR). IR involves the use of contemporary imaging techniques such as fluoroscopy and ultrasonography to selectively access vessels and other structures in order to deliver different materials for therapeutic reasons. In the past two decades, IR techniques have expanded considerably with both vascular and non-vascular procedures being performed routinely in humans. Specifically, IR techniques are being increasingly utilized to help palliate humans with cancer (interventional oncology) in which traditional therapies have failed or have been demonstrated to provide little benefit. These techniques are particularly useful in cases of regional disease in order to maximize local therapy and minimize systemic toxicity.

While results have been variable, regional techniques such as percutaneous tumor ablation, intra-arterial chemotherapy, transcatheter arterial embolization/chemoembolization, and/or palliative stenting have been demonstrated to improve survival times, disease-free intervals, recurrence rates, or completeness of tumor necrosis (Additional references available from author upon request). All of these techniques are currently in their infancy in veterinary oncology, however not unlike the situation in our human counterparts, Interventional Oncology is poised to become the fourth pillar of veterinary oncology.

A number of minimally invasive options exist for use in dogs with head and neck tumors. Most of these are still considered experimental in veterinary patients and include stenting for malignant obstructions, local delivery of chemotherapy (intra-arterial chemotherapy), transarterial embolization (TAE) for hemorrhage or tumors, transarterial chemoembolization (TACE) with or without drug-eluting brads (DEBs), and percutaneous ablation.

**STENTING FOR MALIGNANT OBSTRUCTIONS**

While nasopharyngeal stenting has been reported in veterinary patients for benign nasopharyngeal stenosis\(^1\), similar techniques could be used for malignant obstructions.
when airway patency is lost or severely diminished. The author has placed stents within the nasopharynx and nasal cavity for complete airway obstructions including bare and covered stents. Experience with benign cases would suggest bare stents are better tolerated than covered stents (due to lack of stent integration and continued inflammation/discharge with the covered stents) and that complete (benign) obstructions necessitating creating a new nasopharyngeal lumen are more likely to grow through the stent interstices than incomplete obstructions. Complications experienced with benign disease include stent migration (uncommon), stenosis recurrence through the stent (uncommon but more likely with complete obstructions), continued nasal discharge (more common with covered stents), stent collapse, and oronasal fistulas through acquired palate defects.

**INTRA-ARTERIAL CHEMOTHERAPY, TRANSARTERIAL EMBOLIZATION (TAE), AND TRANSARTERIAL CHEMOEMBOLIZATION (TACE)**

Intravascular techniques such as intra-arterial delivery of chemotherapy and transarterial chemoembolization (TACE) have been developed in order to increase local chemotherapy concentrations and dwell times within the tumor, reduce subsequent systemic toxicities, reduce tumor blood supply and oxygenation, and improve local tumor control rates in those cancers that have demonstrated to have poor responses following systemic chemotherapy. IA chemotherapy involves superselective catheterization of the blood supply to the tumor. TAE requires the same access but instead of chemotherapy delivery, particle or beads are delivered to cause tumor ischemia to reduce tumor growth or control hemorrhage. TACE involves selective intra-arterial chemotherapy delivery in conjunction with subsequent particle embolization followed by delivery of particles or beads to reduce the tumor bloodflow causing subsequent ischemia. More recently, arterial ports have been described providing sustained local delivery of chemotherapy into the tumors over time. Routine use of these devices would be difficult and expensive in animals. For this reason and others, the author has preferred the use of TACE if access to the tumor vasculature has been achieved and deemed safe (sparing blood supply to the internal carotid artery and ophthalmic arteries). More recently, drug-eluting beads that bind to various chemotherapeutics have been evaluated to enhance the concentration and extend the duration of tumor-chemotherapy exposure.

**PERCUTANEOUS ABLATION THERAPIES**

The use of ablation devices to damage tissues is not a new one. Radiofrequency waves have been known to heat tissues when passing through them since the late 1800’s and cryotherapy had been used in the nineteenth century as well. Most surgeons have probably used some type of thermal ablation perhaps without even knowledge of it. The “Bovie knife” used for cauterization and cutting of tissues uses radiofrequency waves, the same type of heat generation now being used to perform percutaneous tumor ablation.

There are number of different types of ablation therapies, most of which harness heat or cold (“Thermal ablation”) to damage the tissues. Other ablation therapies include chemical ablation such as alcohol. Percutaneous ethanol injection (PEI) was the first local ablation therapy described in the 1980s. This procedure was effective for HCC within cirrhotic livers but less effective for other tumors in which the tumors did not
contain a clear tumor capsule (to contain the ethanol, acetic acid, or hot water). PEI has been described in veterinary patients for use in thyroid and parathyroid tumors. To improve results in other tissues, devices harnessing thermal tumor damage were investigated. Radiofrequency ablation (RFA) has been the most investigated of these techniques. In the 1990’s RF currents generated through needle tips became available. The further advancement of these techniques using cool-tip needles (to avoid charring), multi-pronged needle tips or needle clusters, more powerful generators, etc. have enabled more controlled, larger areas of tumor destruction. In humans, RFA for liver tumors smaller than 3cm in diameter have the same recurrence rates as open surgical resection.

Cryotherapy is another common used ablation therapy and many veterinarians are familiar with the use of freezing tumors from experience with ophthalmologists or for superficial tumors in horses and even occasionally in companion animals. Mammalian tissues receive lethal freezing when temperatures reach -20 to -25 degrees Celsius. Some tumors may be able to withstand lower temperatures but -40 degrees Celsius is generally accepted to be lethal to all mammalian tissues. Unlike other traditional therapies such as radiation, some tumors are radiation sensitive and others are not. ALL tissues die at -40 degrees Celsius. There are both direct and indirect methods of cellular death when exposed to freezing temperatures. The mechanism of death is multifactorial but includes ischemia due to blood vessel freezing/thrombosis, and cellular membrane breakdown due to intra- and extracellular ice crystal formation with subsequent osmotic differences.

Historically, cryotherapy was performed using liquid nitrogen to produce freezing temperatures. A slow thaw is followed by another freezing cycle to provide the maximal effect on the tumor. The large probes limited the use to superficial tumors and the slow freeze-thaw cycles meant the procedures were fairly prolonged. Recent advances in cryotherapy technology include changing from a liquid to gas medium. Utilizing the Joule-Thomson Law, argon gas passed through a cryoprobe expands at the tip resulting in reduced temperature. The use of gas allows much smaller probes (17 gauge) that can be placed into organs within the body using ultrasound, CT, and/or MRI guidance (FIGURE 1). Due to different gas properties, the same Law predicts helium expanding at the probe tip will result in temperature increases. Rapid argon freezing with rapid helium thaws now permit small probes to be placed within the body and rapid freeze-thaw cycles to be performed. Different probes are available to provide different ablation margins with reported “isotherm” tables describing temperatures reached at different depths within the iceball.

More recently, other thermal ablation techniques such as laser and microwave ablation and electric field ablation techniques (irreversible electroporation) are advancing the science of percutaneous tumor ablation and will likely play a larger role in the minimally-invasive treatment of tumors in humans and animals.

FIGURE 1: Cryoprobe in a canine nasal FSA under CT guidance
In general, ablation therapies may be best suited for non-surgical patients with a limited number of small tumors. There are currently no randomized controlled trials comparing different ablation modalities in humans and even fewer scientific reports in animals in naturally-occurring diseases (although a lot of experimental data exists). Ablations that cannot achieve a clean margin around the tumor should not be suggested to provide curative intent; different modalities and different probes will change the lethal zone of ablation. There are also technical modifications that can be used to reduce the incidence of local tissue damage such as hydrodissection, artificial pneumothorax/pneumoperitoneum. In addition, thermal ablation therapies can be combined with vascular procedures (TACE) to reduce tumor bloodflow and the heat-sink effect associated with larger blood vessels. The author is currently exploring the use of cryotherapy for treatment of head and neck tumors and a series of case examples will be presented.

REFERENCES

SUGGESTED REFERENCES