EMERGING TREATMENT OPTIONS: INTERVENTIONAL ONCOLOGY
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Key Points

• Interventional oncology is a rapidly developing specialty in veterinary medicine that focuses on utilizing image-guided therapies in the minimally invasive treatment of neoplastic disease.
• Several new therapies involving the locoregional delivery of chemotherapy and embolic agents, tumor ablation and stenting are being discovered in veterinary medicine and early results are promising.

Interventional oncology has been a mainstay in human medicine for many years, and this specialty is progressively being integrated more regularly into veterinary medicine. Stenting of malignant strictures is being performed commonly, and more advanced procedures, such as local delivery of chemotherapy and embolic agents, are also gaining traction as well. These procedures still require more investigation to evaluate efficacy and outcomes, and other procedures are emerging and being attempted in companion animals as well.

Locoregional Therapies

Intra-arterial Chemotherapy: Conventional chemotherapy involves administration of drug into a peripheral vein resulting in systemic dosing of the drug. When given intravenously, the drug also undergoes dilution prior to reaching the tumor. (Vogl 2008) The administration of intra-arterial chemotherapy by interventional oncologists is common practice in human medicine. The major reason for administration of chemotherapy directly into the arterial supply of a tumor is that a higher concentration of drug can be accumulated locally (at the tumor site), with less systemic side effects. (Mortimer 1988)

Intra-arterial chemotherapy is being performed in some veterinary clinics in the treatment of urothelial neoplasia. As the treatment options for bladder, urethra and prostate tumors have limited success, chemotherapy is often selected as a primary treatment. One emerging option is the local delivery of chemotherapy directly to the arterial blood supply of the tumor (vesicular or prostatic arteries). This procedure is performed via an approach to the carotid artery or femoral artery, and superselection of the blood supply of the tumor allows for targeted chemotherapy delivery.

In humans, intra-arterial chemotherapy is often administered in conjunction with radiotherapy in an attempt to achieve better outcomes. (Mokarim 1997, Furutani 2002) This concept has also been exploited in clinical veterinary cases of bladder carcinoma and in osteosarcoma. (McCaw 1988, Heidner 1991, Powers 1991, Withrow 1993) In a study evaluating the combination of intra-arterial chemotherapy (cisplatin) with radiation therapy for treatment of bladder cancer, two dogs demonstrated an objective reduction in tumor size. (McCaw 1988) Side effects and toxicity were minimal in these two dogs. (McCaw 1988) The potential is vast for this treatment combination in veterinary medicine and currently this therapy is being considered for treatment of bone, nasal and bladder/prostate neoplasia.
Transarterial Embolization/Chemoembolization: Transarterial embolization (TAE) and transarterial chemoembolization (TACE) are well-established treatment modalities in human medicine. TAE and TACE are generally not considered first-line therapies when other standard treatments such as surgery remain as a viable option. (Stuart 2003)

TACE has been promoted for several reasons. Eliminating the blood flow to an area that has received chemotherapy will reduce the wash-out of that drug. (Gunvén 2008) Additionally, vessels that are exposed to chemotherapy will also become ischemic (secondary to the embolization), making them more susceptible to the toxic effects of the drug. The embolization may also cause the drug to be retained in the tumor for an extended period of time. (Gunvén 2008) As the chemotherapy is given directly into an artery that is feeding the tumor, the systemic side effects may be less. (Gunvén 2008) TAE may be used as the definitive treatment of neoplastic disease but also has the advantage of being used preoperatively to decrease blood loss during surgical removal of a tumor. (Kadir 1983)

The effects of TACE and TAE have been most studied in the liver. There are several factors that make the liver particularly suitable for these techniques. First, the liver has a unique dual blood supply that allows for embolization, while still maintaining an adequate blood supply to healthy tissue. The portal vein supplies the majority of the liver’s blood supply (75-85%) with the hepatic artery supplying the rest. (Zhou 2009) Second, the hepatic artery is the major blood supply to most primary hepatic tumors (85-100%) and tumors that metastasize to the liver (80-100%). (Breedis 1954) This unique arterial blood supply allows for occlusion of the blood supply to the tumor without causing ischemia to normal liver tissue. (Stuart 2003) Third, many drugs have an increased ability to concentrate in the liver and this limits the systemic toxicity that can be seen with conventional chemotherapy. (Stuart 2003) Lastly, the arterial vascular supply to the liver is easily accessible with selective and superselective catheterization. (Pentecost 2006)

Clinical veterinary literature documenting both TAE and TACE therapies is limited, and those available have demonstrated mixed results. The embolization of hepatocellular carcinoma, hepatocellular adenoma, fibrosarcoma, nasal adenocarcinoma and metastatic osteosarcoma has been attempted. (Sun 2002, Weisse 2002, Cave 2003, Marioni-Henry 2007) In the report evaluating two cases of hepatocellular carcinoma, one dog received TAE and one dog received TACE. (Weisse 2002) In those cases, the survival times post embolization were approximately four months and 28 days, respectively; however, subjective decrease in the size of the tumor in the dog undergoing TAE was noted and blood flow to the embolized region was decreased. (Weisse 2002)

The author is currently performing embolization of hepatic and nasal tumors, and early results are promising. For these procedures the femoral artery is approached and selection of the main arterial supply of the tumors (hepatic arterial branches for hepatic neoplasia and generally the infraorbital artery or sphenopalatine artery for nasal neoplasia) is performed. Bland embolization or chemoembolization has been delivered and post-procedure CT scans are demonstrating tumor response in many cases. The embolization of prostatic neoplasia is also in the early investigational stages in the author’s practice.

Ablative Therapies

The most commonly used forms of tumor ablation include radiofrequency ablation, cryoablation, microwave ablation, and laser ablation. Additionally, high-intensity focused ultrasound is showing promise in successful treatment of certain tumors, including prostatic
neoplasia. (Rebillard 2008) These procedures can be performed with minimally-invasive image-guided techniques. Multiple tumor types have been treated with ablation and the research invested into the use of tumor ablation is vast and growing infinitely. As many human tumors are diagnosed at a stage when resection is not possible, tumor ablation offers an alternative option for treatment and this therapy may also benefit our veterinary patients.

Radiofrequency ablation (RFA) has been the most studied form of ablative therapy. Radiofrequency waves are converted to heat and this thermal damage causes subsequent tissue destruction. (D’Ippolito 2002, Kunkle 2008) Most clinical experience with RFA has been with treatment of hepatic malignancies, particularly, hepatocellular carcinoma. RFA is considered the treatment of choice for early-stage, non-resectable hepatocellular carcinoma. (Lencioni 2009) Treatment of metastatic colonic disease has also been reported. (Lencioni 2009, Padma 2009) RFA has been used to treat canine primary hyperparathyroidism (Pollard 2001) and feline hyperthyroidism (Mallery 2003), but the clinical use of RFA to treat malignant neoplasia in companion animals has yet to be investigated.

Cryoablation utilizes alternating freeze-thaw cycles that cause intracellular ice crystal formation, cellular dehydration and microcirculatory failure that results in ischemia and cytotoxicity. (Vestal 2005, Raman 2009) Microwave and laser ablation are newer ablation strategies but the use of these systems is growing quickly as the clinical utility is being discovered. Microwave ablation works by heating the water molecules in tissues with resultant coagulation necrosis and cell death. (Abbas 2009) Microwave ablation has been evaluated in the treatment of liver, lung, kidney, adrenal gland and bone neoplasia in humans. (Lencioni 2008, Moser 2008, Abbas 2009) Laser ablation is performed with a Neodymium-YAG laser. This device elevates the temperature of tumor tissue and also results in coagulative necrosis. Clinical reports of laser ablation are lacking but proposed applications include liver, lung and bone tumors. (Pacella 2001, Lencioni 2008, Moser 2008)

Stenting

Recent advances in stent technology have included development of drug-eluting stents, removable stents, radioactive stents and absorbable stents. Drug-eluting stents are used commonly in human medicine and drugs such as paclitaxel have been embedded into the coating on the stent. (Ong 2005, Lewis 2008) Drug-eluting stents are most commonly utilized for cardiovascular disease in humans (Lewis 2008), although, clinical cases of hepatobiliary malignancy have been treated with drug-eluting stents. (Suk 2007) Additionally, paclitaxel-eluting stents have been evaluated in the urinary tracts of pigs and dogs. (Shin 2005, Liatsikos 2007) Removable and absorbable stents are being utilized in human interventional radiology (Lootz 2001, Tammela 2003, Grabow 2005, Lewis 2008, McLoughlin 2008, Kotsar 2010); however, the application for removable and absorbable stents in veterinary interventional oncology is likely to be limited. Further research is needed to evaluate the use of radioactive stents, but early research and clinical results are hopeful. (Liu 2007, Liu et al. 2009) These stents provide an intraluminal source of brachytherapy with the goal of local tumor control. (Balter 1998, Liu 2007, Liu 2009)
References