Hepatic Chemoembolization: A Novel Regional Therapy

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Nonresectable and metastatic liver tumors are difficult challenges in veterinary patients. As such, these animals have traditionally been treated conservatively and symptomatically. The relatively limited efficacy of routine (intravenous) chemotherapy for macroscopic disease, and the cost and potential deleterious side effects associated with radiation therapy have led investigators to evaluate increasingly novel therapeutic modalities. Similar difficulties in human oncology have inspired various creative, image-guided, regional tumor therapies in the continuously developing subspecialty of interventional radiology termed “interventional oncology.” Regional tumor therapies, as suggested by the name, have been designed to increase local tumor control without increasing systemic toxicities and side effects. These techniques are not indicated for all oncology patients, just those patients in whom surgery and radiation are not indicated, and where systemic therapies have failed to control the local disease. Regional techniques, such as percutaneous tumor ablation (including radiofrequency ablation, microwave ablation, laser thermal ablation, cryoablution, and percutaneous ethanol injection), and transcatheter arterial chemoembolization have been demonstrated to improve response rates and local control, and enhance tumor necrosis when compared with traditional therapies. Percutaneous tumor ablation techniques used in the liver of humans tend to be most effective in patients with a few (<3), small (<4 cm diameter) lesions. Because these circumstances are less commonly encountered in the author’s clinical experience in veterinary medicine, patients are more commonly candidates for chemoembolization for the palliative treatment of nonresectable and metastatic liver neoplasia.

In general, “embolotherapy” involves the use of fluoroscopy and other advanced imaging modalities to access specific vascular structures selectively to deliver embolic materials to control hemorrhage, occlude vascular malformations, or reduce tumor growth. These techniques are commonly used in human medicine for
embolization of arteriovenous malformations, intractable epistaxis or gastrointestinal bleeding, and uterine artery embolization for symptomatic uterine fibroids in women.

Chemoembolization involves selective intra-arterial chemotherapy delivery in conjunction with subsequent particle embolization. This technique has been demonstrated to result in a 10- to 50-fold increase in intratumoral drug concentrations when compared with systemic intravenous chemotherapy administration. The subsequent particle embolization results in tumor cell necrosis and paralyzes tumor cell excretion of chemotherapy resulting in minimized systemic toxicity. This procedure is most commonly used in the treatment of diffuse hepatocellular carcinoma in humans but has also been used to treat other tumors of the liver and elsewhere in the body. Most hepatic tumors rely on hepatic arterial blood supply (up to 95%) for growth in contrast to the normal liver parenchyma, which receives most of its blood supply by the portal vein (approximately 80%). Hepatic artery embolization should theoretically cause more ischemia to the liver tumor while the remaining normal hepatic parenchyma obtains sufficient oxygenation from the portal venous system. In addition, the chemotherapy is often mixed with Lipiodol, a carrier agent that is an oily substance that supplies radiographic contrast to the chemotherapy and acts as a tumor localizer. Because hepatic tumors lack Kupffer cells, which are important for metabolizing oily substances in normal hepatic parenchyma, the Lipiodol and accompanying chemotherapy are concentrated in the liver tumor rather than the surrounding healthy hepatic parenchyma. 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.

Although often performed under conscious sedation in humans, the veterinary patients in the author’s interventional radiology service are placed under general anesthesia and the entire chemoembolization procedure is performed in an angiography suite. Arterial access is usually achieved by cut-down to the femoral artery and the procedure is performed under fluoroscopic guidance using a combination of appropriately sized sheaths, catheters, and guidewires. Microcatheters and microwires are passed coaxially through the larger catheters to superselect very small vessels when necessary.

An intimate knowledge of vascular anatomy is required to ensure the tip of the catheter is beyond any branch points that may supply normal tissue. Once appropriate catheter placement has been confirmed angiographically, a slurry of chemotherapy (standard systemic dose) and Lipiodol, and appropriately sized particulate material

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![Fig.1](https://example.com/fig1.png)

**Fig.1.** Prechemoembolization and postchemoembolization CT scans of a cat with hepatocellular carcinoma. (A) Prechemoembolization axial CT demonstrating primary tumor (arrows) and metastatic lesion (arrowheads) within the liver. (B) Postchemoembolization axial CT demonstrating enhanced uptake of oily chemotherapy mixture (asterisks) caused by enhanced vascularity of tumor versus normal liver parenchyma.
(typically polyvinyl alcohol particles), are injected under fluoroscopic guidance until complete stasis of blood flow is achieved. Repeat selective and nonselective angiograms are performed to document complete embolization (Fig. 2). The vascular sheaths are removed and hemostasis is typically achieved by ligation of the femoral artery or direct manual compression for 20 minutes.

Reported complications in the human literature include hemorrhage at the vascular access site; nontarget embolization complications (skin necrosis, damage to normal parenchyma); hepatic infarction and abscessation; and postembolization syndrome, a collection of clinical signs characterized by malaise, fever, and pain. It is premature to speculate if similar complications will occur in the veterinary population; however, the author has not yet identified other, unreported complications in patients. The goal of these therapies is generally palliative (reduced tumor growth); however, some tumors can shrink (Fig. 3) and chemoembolization may play a role in neoadjuvant therapy for larger solitary liver tumors.

Regional tumor therapies, such as chemoembolization, offer a new option for treatment of nonresectable and diffuse metastatic tumors. In human patients, chemoembolization of diffuse hepatocellular carcinoma has been shown to improve survival rates. Median survival times of 3 to 6 months are expected, with systemic chemotherapy response rates of only approximately 20%. Chemoembolization has improved median survival times to 1 to 2 years with positive biologic response (as determined by decreasing alpha fetoprotein levels) in 70% to 85% of subjects and morphologic response in 36%.

In veterinary medicine, patients with relapsed tumors or progressive disease comprise a population for which few therapeutic options exist. Interventional radiology

![Hepatic Artery Pre-Chembo](image1)

![Hepatic Artery Post-Chembo](image2)

**Fig. 2.** Prechemoembolization arteriogram by a catheter placed from the femoral artery into the common hepatic artery demonstrating branching and arborization of hepatic artery branches and gastroduodenal artery (*top*). Postchemoembolization arteriogram demonstrating complete embolization of hepatic artery branches with patent gastroduodenal artery (*bottom*).
techniques offer the potential to prolong survival times and quality of life in these patients with minimal systemic toxicity risks. In the author’s interventional radiology service, these techniques have been performed and reported on for diffuse hepatocellular carcinoma, metastatic bone tumors, and uterine fibroids among others.6

REFERENCES


Fig. 3. Prechemoembolization and postchemoembolization abdominal ultrasonography images in a dog with recurrent hepatocellular carcinoma at the porta hepatis. (Left panel) Notice defined hepatic tumor with approximate 3.6 × 4.7 cm measurements. (Right panel) Six weeks following single chemoembolization treatment demonstrating similar appearance of tumor but with 1.4 × 2.1 cm measurements (partial remission). This dog had subsequent surgery to remove this mass as much as possible.