The typically compromised patients combined with high vascularity, difficult access, and poor suture holding all contribute to making liver surgery challenging for the veterinary surgeon. Risks can be reduced by careful planning, appropriate pre-operative patient preparation, knowledge of the anatomy and physiology, and alternative plans should they become necessary. While many solitary massive HCC tumors can be surgically excised with median survival times greater than 3 years, there is a 29% surgical complication rate and this does not include the many liver tumors defined as nodular or diffuse that are not resectable. While the surgical mortality rate was only 5% in this population of dogs, right-sided tumors were associated with a 40% mortality rate!! In addition, up to a third of dogs with massive HCC in another study were identified to have distant metastases making invasive surgery a less optimal solution. It is generally agreed that easily resectible, isolated massive left-sided (and pedunculated central and right-sided) HCC cases should receive surgical excision; this leaves a fairly large proportion of HCC cases for which surgery may not be the ideal treatment. Surgical resection of these tumors is addressed in another lecture so this presentation will be limited to the discussion of alternative options for those cases in which surgical excision would be associated with excessive risk of considerable morbidity or mortality or cases in which surgery is not indicated.

A number of minimally invasive options exist for use in dogs with liver tumors and liver disease. Most of these are still considered experimental in veterinary patients but each will be briefly discussed. These techniques include transjugular liver biopsy, 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), portal vein embolization (PVE), and percutaneous ablation.

**TRANSJUGULAR LIVER BIOPSY (TJLB)**

Transjugular liver biopsy is a minimally invasive technique for obtaining non-selective liver samples for biopsy. Patients best suited for this technique are those with severe coagulopathies and ascites, both of which could contribute to potentially life-threatening biopsy associated hemorrhage. The principle is that a tru-cut type biopsy needle is passed transvenously from a percutaneous transjugular approach. The biopsy needle device is advanced into the hepatic vein under fluoroscopic guidance and fired into the hepatic parenchyma. Using this technique, the liver capsule is not punctured and therefore any subsequent hemorrhage though the biopsy tract occurs into the venous system and is therefore not associated with any morbidity. This technique has not been performed in client owned animals by the author but is currently being evaluated in cadavers.

**STENTING FOR MALIGNANT OBSTRUCTIONS**

Occasionally liver tumors can lead to caudal vena cava (CVC) obstruction or multiple hepatic vein obstructions. Chronic, tumor-related CVC obstruction in dogs is
often not associated with clinical signs due to the capacity of the systemic venous system to find collateral circulation over time. Hepatic vein obstructions are also not typically associated with clinical signs although when multiple HVs are obstructed or if the CVC is obstructed cranial to the HVs entrance, the patient can develop portal hypertension and subsequent ascites. If venous obstruction is the cause of the ascites, HV and/or CVC stenting has been demonstrated to relieve venous obstructions and resolve the portal hypertension in dogs.3

INTRA-ARTERIAL CHEMOTHERAPY

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 is not routinely performed in dogs with nonresectable HCC. While local delivery of certain chemotherapy drugs in humans have been demonstrated to result in elevated tumoral drug concentrations and even improved biological tumor responses, improved survival times were not necessarily routinely achieved. More recently, hepatic arterial ports have been placed providing sustained local delivery of chemotherapy into the liver 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.

TRANSARTERIAL EMBOLIZATION (TAE)

TAE involves superselective catheterization of the blood supply to the tumor (as for IA chemotherapy) followed by delivery of particles or beads to reduce the tumor bloodflow causing subsequent ischemia. This technique may be safer than TACE as the risk of chemotherapy effects are spared. The author has used this technique rather than TACE for more debilitated patients in whom excessive morbidity was hoping to be avoided, in patients with benign liver tumors, and in a patient with hemorrhage occurring from diffuse HCC.

TRANSARTERIAL CHEMOEMBOLIZATION (TACE)

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 to systemic intravenous chemotherapy administration.5 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 as well as elsewhere in the body. Most hepatic tumors rely
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 as well as acting as a tumor localizer. As hepatic tumors lack Kupfer cells that 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 (*Figure 1*). 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.

While often performed under conscious sedation in humans, the veterinary patients in our I.R. service are placed under general anesthesia and the entire chemoembolization procedure is performed in an angiography suite. Arterial access is usually achieved via cut-down to the femoral artery and the procedure is performed under fluoroscopic guidance using a combination of appropriately sized sheaths, catheters and guidewires. Micro-catheters and micro-wires are passed coaxially through the larger catheters in order to super-select 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 (typically polyvinyl alcohol particles) are injected under fluoroscopic guidance until complete stasis of bloodflow is achieved. Repeat selective and non-selective angiograms are performed to document complete embolization (*Figure 2*). The vascular sheaths are removed and hemostasis is typically achieved via 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, non-target embolization complications (skin necrosis, damage to normal parenchyma), hepatic infarction/abscessation, and post-embolization 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 authors have not yet identified other, unreported complications in our patients. The goal of these therapies is generally palliative.

![Figure 1](image1.png) Pre- and Post chemoembolization CTs of a cat with hepatocellular carcinoma. A. Pre-chembo axial CT demonstrating primary tumor (arrows) and metastatic lesion (arrowheads) within the liver. B. Post-chembo axial CT demonstrating enhanced uptake of oily chemotherapy mixture (asterisks) due to enhanced vascularity of tumor versus normal liver parenchyma.

![Figure 2](image2.png) Pre-chembo arteriogram via a catheter placed from the femoral artery into the common hepatic artery demonstrating branching and arborization of hepatic artery branches and gastroduodenal artery (above). Post-chembo arteriogram demonstrating complete embolization of hepatic artery branches with patent gastroduodenal artery (below).
(reduced tumor growth), however some tumors can shrink and chemoembolization may play a role in neoadjuvant therapy for larger solitary liver tumors.

PORTAL VEIN EMBOLIZATION (PVE)

Liver regeneration starts within hours of surgical removal and peeks within 3 days, reaching near complete compensatory hypertrophy and hyperplasia after 6 days following 70% hepatectomy but can take as long as 6-10 weeks. This is believed to occur through compensatory hypertrophy and hyperplasia. The increased liver volume results from the change in liver blood flow, especially portal blood flow. During partial hepatectomy, the splanchic blood flow remains unchanged through the portal vein so the perfusion through the remaining portal branches is increased resulting in marked hypertrophy of the remaining parenchyma. Portal vein embolization (PVE) involves obstruction of the ipsilateral portal vein perfusing the segment of liver to be resected pre-operatively (before resection takes place). This procedure results in hypertrophy of the contralateral segment of liver and is currently being used in humans before massive liver tumor resections that might otherwise result in subsequent liver failure due to inadequate remaining hepatic volume or portal hypertension. Portal vein embolization is reportedly effective in dogs as liver volumes increased 25-33% following PVE. Using a different technique, portal vein arterialization via splenic arterio-venous shunting has been shown to improve liver function in dogs after extended hepatectomy.

PERCUTANEOUS ABLATION THERAPIES

Percutaneous tumor ablation techniques such as radiofrequency ablation, microwave ablation, laser thermal ablation, cryoablation, and ethanol ablation are expanding in human medicine. These techniques seem most effective in human patients with a few (<3 lesions), small (<4cm diameter) lesions. Unfortunately, veterinary patients have historically been diagnosed much later in the stage of the disease. As such, it appears that the intravascular techniques may be more appropriate in the majority of animals with liver tumors deemed non-resectable (or diffuse). Intravascular techniques such as intra-arterial delivery of chemotherapy, trans-arterial embolization (TAE), and trans-arterial 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.

REFERENCES