

## Liver Cancer

Around the world, primary liver cancer, known as hepatocellular carcinoma (HCC), is one of the five most common cancers. The cancer begins in the main cells of the liver (hepatocytes) and most frequently occurs in those persons who have liver disease and scarring called cirrhosis. Cirrhosis typically occurs in patients who have chronic infection with hepatitis B or C, or in patients who have a long history of alcohol abuse. While HCC is not quite as common in the United States as it is in other parts of the world, particularly in Asia and Africa, where it is the most common type of cancer, its incidence continues to rise in the U.S., presumably coinciding with the ever-increasing number of cases of hepatitis B and C infections.

The liver is also a common site of spread of many cancers from other parts of the body (metastases). The most common cancer to spread to the liver is colon cancer, although virtually any cancer can spread to the liver. Some liver metastases are detected at the time the original cancer is diagnosed, while others may not be found for many years as the cancer cells may spread but may grow so slowly as to only be seen on x-ray studies many years later. Liver metastases are many times more common in the United States than hepatocellular carcinoma.

In cases of HCC, the treatment of choice is liver transplantation. Because cirrhosis typically causes scarring of the entire liver, simple surgical removal of the liver tumor leaves the patient at high risk of developing a new tumor in the liver. Unfortunately most patients are not candidates for transplantation due to tumor size (over 5-6 cm), location in the liver, or poor health making the patient unable to tolerate major open surgery. Only about 20% of patients are offered a transplant option. Unfortunately treatment options for HCC with traditional chemotherapy or radiation therapy are very limited and not very successful. Without treatment, average survival in patients with HCC is about 6-9 months.

Patients with metastatic tumor to the liver are generally not felt to be transplant candidates due to the spread of tumor from other parts of the body. However, surgical removal of metastatic tumor has been considered the standard of care for these patients when possible, as about 1 in 10 patients with metastatic tumor that are surgical candidates may be cured with surgery. Again, however, only about 10-20% of patients with liver metastases are felt to be surgical candidates because of an excessively large number of tumors within the liver, large size or poor location of the tumors, or poor general health of the patient. While traditional radiation therapy is not useful in the liver, some metastatic cancers do respond favorably to chemotherapy, particularly some of the most recently developed chemotherapy regimens.

Interventional radiologic treatments have developed to offer options to patients who may not be surgical candidates or do not desire surgical care, and also to those patients who do not respond favorably to chemotherapy, or respond incompletely. The mainstays of interventional treatment include radiofrequency ablation and chemoembolization.

## Chemoembolization

Chemoembolization, formally known as transhepatic arterial chemoembolization or TACE, is typically used for the treatment of hepatocellular carcinoma but can also be useful in the treatment of metastatic tumor to liver. It can be used alone if the tumor is too large in size or in a poor location to allow other treatment options. It can also be used in conjunction with surgery to shrink tumor prior to surgical removal, or with radiofrequency ablation to affect better cell death in the treated tumor.

TACE takes advantage of the fact that the liver has a dual blood supply, getting blood from both the hepatic artery and the portal vein that carries blood from the stomach and bowel to the liver. Normal liver gets the greatest amount of its blood and nutrients from the portal vein, while tumor, on the other hand, gets nearly all of its blood supply from the hepatic artery. As such, TACE can be performed with significant effect on tumor tissue after closure of tumor branches from the hepatic artery, with little effect, in most cases, upon normal liver tissue.

In the TACE procedure, a tiny catheter is guided, under x-ray visualization, from the femoral artery at the top of the leg into the blood vessels that supply the liver tumor (figure 1). A mixture of chemotherapy drugs and small particles is then injected into the tumor. The particles act to keep the chemotherapy drugs in the tumor and allow much higher doses of drugs to be delivered to than could typically be achieved with standard chemotherapy (figure 2) given through an IV line – as much as 200-400 times higher doses. Even with the higher chemotherapy dose to the liver, the associated side effects of the chemotherapy are decreased as less chemotherapy drug is circulating in the bloodstream. TACE is typically performed as a short-stay procedure with patients admitted to the hospital the morning of the procedure and discharged the following morning. Most patients typically experience some fatigue as the most common side effect, usually lasting for 1-2 weeks.

Chemoembolization by itself is felt to be a palliative procedure, as permanent cure is only rarely achieved. However, it can be extremely effective in controlling liver cancer and may be even more effective when combined with other treatment options such as ablation.

## Radiofrequency Ablation

Radiofrequency ablation (RFA) offers patients an option for treatment when a traditional surgical option may not exist. Under CAT scan or ultrasound guidance, the ablation needle is advanced through the skin, into the liver, with the tip of the needle probe positioned in tumor. An electric current is then administered through the needle to cause heating and death of the tumor cells (figure 3)

The procedure is generally very well tolerated by the patient and most are discharged the following morning with little residual discomfort. Because the ablation effect is localized

to the area of tumor, the procedure can usually be repeated as needed, particularly if new areas of tumor arise. Complication rates are low, typically in the range of 2-3%.

While transplantation will always offer the best chance of cure with any liver tumor, RFA may provide an option with equal effectiveness to surgical removal of tumor. As the procedure is relatively new, surgical removal of tumor remains the treatment of choice. However, early studies of RFA are quite promising. Some studies have shown RFA in the treatment of some hepatocellular carcinomas to have a five-year survival rate in the range of 40-50% while studies on treatment of metastatic disease have shown 3-year survival rates in the range of 45-50%. These outcomes compare very favorably to surgical removal of tumor as a treatment option, possibly with less associated complications and shorter post-procedure recovery time.

Of course, as with all cancer treatments, close follow-up examination is required. Typically with TACE and RFA, follow-up CAT scans and/or MRI are performed every 3 months for at least one or two years. Any regrowth of tumor or new tumors are best treated at the smallest size possible.

### Micro-Sphere Therapy

Treatment with radioactive micro-spheres is, in some ways, similar to chemoembolization or TACE described above. The procedure again takes advantage of the fact that the liver has dual blood supply, getting blood from both the hepatic artery and the portal vein that carries blood from the stomach and bowel to the liver. Normal liver gets the greatest amount of its blood and nutrients from the portal vein, while tumor, on the other hand, will get nearly all of its blood supply from the hepatic artery. A tiny catheter is again directed into the tumor blood vessels that arise from the hepatic artery. The micro-sphere particles are then injected and directed preferentially to the tumor tissue.

SIR-sphere micro-sphere particles developed by Sirtex Medical (see Links page) are tiny plastic beads that are not much larger than the size of a few blood cells and are combined with yttrium-90 radioisotope. Each particle that is trapped in the vascular bed of the liver tumor delivers radiation that penetrates only about 2.5mm of tissue, minimizing effects upon normal healthy tissue. This targeted radiation has its effects over a period of about two weeks.

Patients treated with micro-spheres can often go home and resume normal activities the same day. As with all treatments for cancer, close follow-up care is utilized to determine tumor response and any possible recurrence. Micro-sphere therapy may be an option in cases of recurrence or regrowth of tumor, or may be used in conjunction with other types of treatments to control tumor growth.

