Bridging Procedures Prior to Liver Transplantation

- Several interventional radiology procedures are available as bridging techniques to treat hepatocellular tumors prior to liver transplantation:
  - Transarterial chemoembolization (TACE)
  - Radiofrequency ablation (RFA)
  - Microwave ablation
  - Cryoablation
  - Percutaneous ethanol injection (PEI)

The only definitive cure for patients with hepatocellular cancer (HCC) is liver transplantation, a treatment suitable for patients whose tumor(s) do not exceed a certain size and who meet certain other criteria. However, available organs are in short supply, and wait times can be long. In the US, wait times vary depending on the region of the country as defined by the United Network for Organ Sharing (UNOS) and range from a median of 2.7 to 20.1 months. Many patients on the waiting lists become disqualified due to tumor progression; the dropout rate is 8.7%, 16.9%, and 31.8% at 3, 6, and 12 months respectively in patients who do not receive treatment to limit progression.

Interventional radiologists work alongside hepatologists, oncologists, and transplant surgeons to minimize the dropout rate by performing various image-guided interventional procedures to limit tumor progression. In this article, we describe several available therapies to control tumors during the waiting period. These treatments, which are regarded as bridging therapies, may be beneficial for patients who are on the waiting list for liver transplantation for long periods of time. In addition, patients who do not initially meet the accepted criteria for transplantation may receive these treatments as neoadjuvant therapies to downstage their cancer and, in some cases, make them eligible for transplantation.

Transarterial Chemoembolization (TACE)

TACE is the mainstay of bridging therapies. In this procedure, a catheter is positioned in the hepatic artery under image guidance to deliver chemotherapeutic agents followed by microparticles into the tumor vasculature (Figure 1). The microparticles lodge in the capillaries and simultaneously cause tumor ischemia while providing a high, localized dose of chemotherapy (10–25 times higher than the systemic dose). Systemic toxicity is minimal. The procedure has been shown to reduce the waiting list dropout rate significantly, from 15% to 3%. In addition, TACE with drug-eluting beads can raise post-transplantation survival significantly in those who spend four to nine months on the waiting list, although it may not be beneficial for those with longer wait times.

Disadvantages of TACE include the need for multiple treatment sessions and its dependence on factors such as tumor vascularity. TACE also has several contraindications including serum bilirubin >3mg/dL, severe coagulopathy, ascites on diuretic therapy, and albumin <28 g/L.
Figure 1. TACE. Pre-treatment MRI of a 43-year-old man with hepatitis C shows (A) a 4 cm T2-hyperintense solitary mass (arrow) in segment VI of the liver with enhancement features compatible with hepatocellular carcinoma. The patient was treated with TACE with drug-eluting beads (B). A follow-up MRI six months after TACE shows intrinsic T1 peripheral hyperintensity (C) within the treated lesion with no residual internal enhancement (D), confirmed on subtracted imaging (E).

Radiofrequency ablation (RFA)

In RFA, a probe is positioned within a tumor under image guidance, and radiofrequency energy is applied to heat the tissue and ablate it. In cirrhotic livers, this treatment is particularly effective because the cirrhotic liver and the tumor capsule act as an insulator, creating an oven effect. The rate of complete tumor necrosis in a single session is as high as 63% in tumors <3 cm, but the procedure can be effectively employed in tumors up to 5 cm. Multiple overlapping ablations may be necessary to achieve the desired zone of ablation.

RFA has advantages over TACE in that percutaneous access is relatively easy in most cases, tumor necrosis is more predictable, post-procedure patient discomfort is generally less, and it can be an outpatient treatment in some cases. RFA also offers the benefit of creating a “surgical margin” around the tumor (Figure 2), which helps minimize the risk of residual or recurrent disease. Repeat procedures can be performed, if necessary. The major limitation of RFA is the risk of non-target organ injury, which makes it unsuitable when the tumor is in close proximity to structures such as bile duct, bowel, or heart. In addition, blood flow in large vessels can act as a heat sink, limiting the effectiveness of RFA. RFA is contraindicated in cases of severe, decompensated cirrhosis (Child-Turcotte-Pugh Class C).
Figure 2. RFA. Contrast-enhanced CT shows a solitary 3.5 cm enhancing mass (A) in segment II of the liver in a 58-year-old man with hepatitis C. Follow-up CT one month after RFA shows a zone of ablation that encompasses the tumor and a margin of normal tissue surrounding the tumor (B).

Microwave Ablation

Microwave ablation (Figure 3) is similar to RFA in that it employs heat to destroy tissue but the means of heat generation differs. It heats tissues more quickly and evenly, making it less susceptible to heat-sink effects and thus offering a significant advantage over RFA. Microwave ablation also has potential for shorter procedure times and larger ablation volumes than RFA. It is a relatively new technique and is regarded as a method that is still under investigation.

The disadvantages of microwave ablation are similar to those of RFA.

Figure 3. Microwave Ablation. T1-weighted gadolinium-enhanced MRI (A) shows a solitary hyperintense mass (arrow) in segment II of the liver in a 63-year-old woman with hepatitis C. A follow-up MRI one month after microwave ablation (B) demonstrates a zone of ablation (arrow) that is larger than the original lesion.
Cryoablation

In cryoablation, multiple cryoprobes are placed in the tumor(s) and freeze-thaw cycles are used to lower the temperature (−20° to −40° C) and cause cell death. The ice ball that develops can be monitored with MRI, CT, or ultrasound to ensure that it encompasses both the lesion and a margin of normal hepatic tissue. Since multiple probes are used, the size of the ice ball can be large. In addition, the ice ball can conform to an irregularly shaped tumor.

Potential complications can include hemorrhage, seen in 0.6% of patients, and severe systemic reactions. The systemic reactions have been correlated with the release of cytokines and other biochemicals from the necrotic tissue. Minor complications were observed in 14.3% of patients.

Percutaneous Ethanol Injection (PEI)

PEI is the oldest of the interventional therapies and its use is now mostly limited to treatments of tumors that are close to structures at risk for thermal damage. It is most effective for tumors <3 cm and has the advantage of low cost. Treatment of larger lesions is more challenging because of the need for repeated injections over multiple sessions.

Combination Therapies

Recent evidence has indicated that the combination of TACE and RFA is synergistic and improves the survival of HCC patients compared with either treatment alone. If RFA precedes TACE, the hyperemic rim surrounding the ablated region may be more effectively targeted by TACE. Conversely, TACE prior to RFA can generate a larger ablation area because embolization reduces the heat-sink effect.

In addition, PEI can be useful in selected cases prior to thermal ablation to treat tumor tissue adjacent to structures that could be damaged by heat.

Further Information

For further information on bridging interventions prior to liver transplantation, please contact Ronald S. Arellano, MD, Interventional Radiology, Department of Radiology, Massachusetts General Hospital, at 617-726-3937.

We would like to thank Dr. Arellano and Nazanin H. Asvadi, MD, for their assistance and advice on this issue.
References


