Ablation Basics and liver RFA

Koichiro Yamakado, MD, PhD
Department of Radiology, Hyogo College of Medicine, Japan

A. Ablation Basics

Tumor ablation

The term tumor ablation is defined as the direct application of chemical (ie, nonenergy) or energy-based (ie, thermal and nonthermal) therapies to eradicate or substantially destroy focal tumors[1].

Patient Selection

Based on some guidelines such as Barcelona Clinic Liver Cancer (BCLC) staging system[2] and other guidelines, Radiofrequency ablation (RFA) is considered a curative treatment, and is applied to patients with 3 or fewer hepatocellular carcinomas (HCCs) 3cm or smaller. This concept is usually applied in other organs. Combination of RFA with arterial embolization expands indication even in large tumors, because perfusion mediated tissue cooling (heat-sink effect) diminish the ablative zone size[1]. Development of technology such as multiple needle insertion and high-power microwave ablation also helps to create larger ablative zone. Function of each organ and coagulability are important factors to decide the indication. In general, a platelet count of 50,000 to 60,000 /mL, and an international normalized ratio (INR) of prothrombin time of less than 1.5 are used. The other factors to decide indication are patients' performance status, age, and tumor location, tumor visibility, and safe approach to the target tumor. When the target tumor is adjacent to the critical organs such as bowel and nerve, and it is impossible to separate the tumor from the critical organ, there is a risk of collateral damage when using energy-based ablation.

Technique

US, CT including real-time CT fluoroscopy, and MR imaging are used when placing needles, electrodes, antenna, and probes in the target tumor. US is the most frequently used modality in the liver. But not all liver tumors are visible on US images. Contrast-enhanced US images, and fusion-images with CT and MRI are used to depict inconspicuous liver tumors.

CT images are used as a preferable image- guide modality in many organs such as lung, kidney, adrenal glands, and bone and soft tissue.

Placement of RF electrodes depends on tumor size and tumor shape. Overlapping ablation is sometimes required to achieve enough ablative margin that is 5mm or greater than tumor diameter.

Chemical Ablation

Chemical ablation can be performed using imaging-guided percutaneous direct injection of either ethanol or acetic acid into liver, thyroid, adrenal, and pancreatic tumors using several small (19-22 gauge) needles under CT, real-time CT fluoroscopy or ultrasound guidance[1]. Chemical ablation works by protein denaturation that causes coagulative necrosis and thrombosis of small vessels.

An important benefit of chemical ablation is that it causes much less collateral damage to adjacent organs. A shortcoming is the small ablative zone obtained by one treatment session. More frequent treatment sessions are required than for RFA[3].

Energy-based Ablation

This category includes modalities that destroy a tumor either through thermal (heat or cold) or nonthermal mechanisms.

Radiofrequency ablation

Radiofrequency ablation (RFA) has received increasing attention as a promising technique for treatment of focal malignant diseases in the liver, lung, kidney, adrenal gland, breast, thyroid gland and bone, and other organs has been established as a standard therapy in some areas such as, liver, lung and kidney.

Alternating electric current operated in the range of RF can produce a focal thermal injury in living tissue. Currently available devices traditionally designated for "radiofrequency ablation (RFA)" function in around 450 KHz range. The tip of the electrode conducts the current, which causes local ionic agitation and subsequent frictional heat[4]. Temperatures in excess of 50°C produce coagulative necrosis. But tissue cells become more susceptible to chemotherapy or radiation when their temperature is increased to 42°C (ie, hyperthermia), and heating tissues at 45°C for several hours produces irreversible cellular damage. Heating of tissue at 50°-55°C markedly shortens the duration necessary to irreversibly damage cells to 4-6 minutes. Near immediate coagulation of tissue is induced at temperatures between 60°C and 100°C and is manifest as irreversible damage to mitochondrial and cytosolic enzymes of the cells. At more than 100°-110°C, tissue vaporizes and carbonizes. A 2-5 cm spherical thermal injury can be produced with each ablation.

Microwave Ablation

Microwave ablation works using electromagnetic energy with frequencies of 30 MHz to 30 GHz to agitate water molecules and cause frictional heating and cell death by coagulative necrosis. The benefits of microwave ablation are its more rapid increase in temperature, higher local temperature, large ablation volume in a shorter ablation time, and the obviation of grounding pads.

Laser ablation

All types of ablation with light energy such as Nd: YAG, erbium, and holmium is laser ablation. Laser ablation is used for the treatment of liver, lung, kidney, breast, and prostate, and other organs.

Cryoablation

Cryoablation causes cell death by the application of alternating cycles of freezing and thawing. Expansion of the argon forced through the small internal aperture in the probe reaches temperatures of –80°C to –150°C by the Joule–Thomson effect. Thawing is achieved by the application of helium. The alternating cycles of freezing and thawing cause mechanical stress on the cellular membranes from intracellular ice crystal formation, hypotonic cell disruption, and microvascular thrombosis.

The advantage of cryoablation is visualization of the ice ball during treatment procedure on CT and MR images. Therefore, the area of thermal injury can be monitored and damage to adjacent organs can be avoided. Cryoablation also causes less periprocedural pain than RFA. The shortcomings of cryoablation are its increased risk of hemorrhage caused by microvascular thrombosis and inability to coagulate tissue, as can be done with RFA and microwave ablation.

Irreversible electroporation

Those technologies and devices that cause cell death through the repeated application of short-duration high-voltage electrical pulses that create "irreversible" injuries to cellular membranes[4]. While there may be some hyperthermic ablative changes with higher-power applications, the mechanism of cell death with IRE is thought to be predominantly nonthermal[5]. IRE is less influenced by heat sink effect, and causes less damages to nerve and fibrous tissue.

B. Liver RFA

Local therapeutic effect after liver RFA

Local tumor progression is usually evaluated by contrast-enhanced CT or MRI. Anticancer effect becomes stronger as the tumor size becomes smaller. Complete disappearance of tumor enhancement can be achieved in 90% of small HCCs (≤3cm), 60% of medium-sized HCCs (3.1-5cm), and 24% of large HCCs (>5cm) (3,6).

The local tumor progression rate has been reported to be 2.4%-19.5% at 3 years when the maximum tumor size is 3cm or smaller[7]. Infiltrating tumor morphology, previous treatment history, subphrenic tumor location, vicinity to the vessels, and ablative margin have been reported to be significantly worse factors affecting local tumor progression[7].

Some of these limitations can be overcome. When the tumor is in the liver dome, it

is sometimes difficult to depict the whole tumor by ultrasonography, and almost half of the subphrenic tumors recurs at 3 years after RFA[8]. The usefulness of artificial pleural effusion, artificial ascites, and real-time virtual sonography have been reported to depict tumors that are invisible by conventional ultrasonography[9]. On the other hand, there is no blind spot when using CT as an image guide, in particular, iodized-oil is accumulated in the tumor after chemoembolization[10]. The local tumor progression rate is as low as 3% at 5 years after the combination therapy of RFA and chemoembolization[10].

Survival after RFA

Superiority of RFA to PEI in prolonging patients' survival has been shown in a randomized controlled trial[11]. The 3-year survival rates were 48%-67% following PEI and 63%-81% following RFA.

Chen, et al. performed randomized control trial between RFA and hepatectomy in patients who had HCC measuring 5 cm or smaller, and found the same overall and recurrence-free survival between the two patient groups[12].

Combination therapy of RFA and chemoembolization also provides HCC patients the same survival as surgical intervention does. Yamakado et al. retrospectively compared overall and recurrence-free survival between this combination therapy and hepatectomy in Child-Pugh grade-A patients who had HCC lesions within Milan criteria (13). There were no significant differences found in either the 5-year overall (75% vs. 81%) or recurrence-free survival (27% vs. 26%) rate. Combination therapy of RFA and chemoembolization is useful in treating HCC nodules larger than 5cm. Takaki et al. performed combination therapy in 20 patients who had 3 or less HCC nodules with a maximum diameter of 5.1-10cm and reported the 5-year survival rate of 41% that is almost equal to that following hepatectomy[14].

Recently, survival rates up to 10 years have started to be reported[15,16]. Shiina et al. treated 1,170 patients by RFA and reported the 5- and 10-year survival rates to be 60.2% and 27.3%, respectively[15]. They combined chemoembolization in patients with 4 or more tumors or those with even one tumor larger than 3 cm. Age, hepatitis C, Child-Pugh grade, tumor diameter, tumor number, des-γ-carboxy-prothrombin (DCP), and lectin-reactive α-fetoprotein level (AFP-L3) were significant prognostic factors. Fujimori et al. performed combination therapy of RFA and chemoembolization in 277 naïve HCC patients, and reported the 5- and 10-year survival rates of 56.3% and 23.5% [16]. Those results are almost comparable to those following hepatectomy.

References

1) Ahmed M, Solbiati L, Brace CL, et al. Image-guided tumor ablation: standardization of terminology and reporting criteria--a 10-year update. Radiology. 2014; 273(1):241-60.

2) European Association For The Study Of The Liver; European Organisation For Research And Treatment Of Cancer: EASL-EORTC clinical practice guidelines: Management of hepatocellular carcinoma. J Hepatol. 2012; 56: 908-943.
3) Livraghi T, Goldberg SN, Lazzaroni S, Meloni F, Solbiati L, Gazelle GS. Small hepatocellular carcinoma: treatment with radio-frequency ablation versus ethanol injection. Radiology 1999; 210(3): 655–661.
4) Golberg A, Yarmush ML. Nonthermal irreversible electroporation: fundamentals, applications, and challenges. IEEE Trans Biomed Eng 2013; 60 (3): 707–714.
5) Faroja M, Ahmed M, Appelbaum L, et al. Irreversible electroporation ablation: is all the damage nonthermal? Radiology 2013; 266 (2): 462-470.
6) Livraghi T, et al. Hepatocellular carcinoma: radio-frequency ablation of medium and large lesions. Radiology 2000; 214: 761-768.
7) Takaki H, et al. Radiofrequency Ablation Combined with Chemoembolization for the Treatment of Hepatocellular Carcinomas Measuring 5 cm or smaller: Risk Factors for Local Tumor Progression. J Vasc Interv Radiol. 2007; 18(7): 856-61.
8) Kim PN, et al. Planning ultrasound for percutaneous radiofrequency ablation to treat small (≤ 3 cm) hepatocellular carcinomas detected on computed tomography or magnetic resonance imaging: a multicenter prospective study to assess factors affecting ultrasound visibility. J Vasc Interv Radiol. 2012; 23(5): 627-34.
9) Nam SY, Ret al. Percutaneous radiofrequency ablation for hepatic tumors abutting the diaphragm: clinical assessment of the heat-sink effect of artificial ascites. AJR Am J Roentgenol. 2010; 194(2): W227-31.
10) Yamakado K, et al. Subphrenic versus nonsubphrenic hepatocellular carcinoma: combined therapy with chemoembolization and radiofrequency ablation. AJR Am J Roentgenol. 2010; 194(2): 530-5.
11) Lin SM, et al. Randomized controlled trial comparing percutaneous radiofrequency thermal ablation, percutaneous ethanol injection, and percutaneous acetic acid injection to treat hepatocellular carcinoma of 3 cm or less. Gut. 2005; 54(8):1151-6.
12) Chen MS, et al. A prospective randomized trial comparing percutaneous local ablative therapy and partial hepatectomy for small hepatocellular carcinoma. Ann Surg. 2006; 243(3): 321-8.
13) Yamakado K, et al. Early-stage hepatocellular carcinoma: radiofrequency ablation combined with chemoembolization versus hepatectomy. Radiology. 2008; 247(1): 260-6.
14) Takaki H, et al. Radiofrequency ablation combined with chemoembolization for the treatment of hepatocellular carcinomas larger than 5 cm. J Vasc Interv Radiol. 2009; 20(2): 217-24.
15) Shiina S, et al. Radiofrequency ablation for hepatocellular carcinoma: 10-year outcome and prognostic factors. Am J Gastroenterol. 2012; 107(4): 569-577.

16) Fujimori M, et al. Survival with up to 10-year follow-up after combination therapy of chemoembolization and radiofrequency ablation for the treatment of hepatocellular carcinoma: single-center experience. J Vasc Interv Radiol. 2013; 24(5): 655-66.