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Ablation of hepatocellular carcinoma

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ABSTRACT

Radiofrequency ablation (RFA) has gained a wide acceptance as a first-line therapeutic option for small hepatocellular carcinoma (HCC). For very early-stage HCC, despite a higher rate of local tumour progression, RFA is considered as a viable alternative to surgical resection owing to its comparable long-term survival, reduced morbidity, and greater preservation of hepatic parenchyma. For HCCs larger than 2 cm, RFA can contribute to near-curative therapy when combined with chemoembolization. RFA can be used as part of a multimodal treatment strategy for more advanced or recurrent cases, and could be a useful bridging therapy for patients who are waiting for liver transplantation. However, the use of RFA is still limited in treating large tumours and some tumours in high-risk locations. To overcome its current limitations, other ablation techniques are being developed and it is important to validate the role of other techniques for enhancing performance of ablation therapy for HCC.

Hepatocellular carcinoma (HCC) occurs predominantly in patients with chronic liver diseases and limited hepatic functional reserve. For this reason, surgical removal of HCC is feasible only in 15–20% of cases and non-surgical modalities play a relatively large role in the treatment of HCC. Commonly used non-surgical methods include ablation therapy, transcatheter arterial chemoembolization (TACE),

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radiation therapy, and systemic chemotherapy. In particular, ablation therapy has become a mainstay, especially for early-stage HCC, because of its superb local control capability and high safety profile.

Currently-adopted or emerging ablation modalities include percutaneous ethanol injection (PEI), radiofrequency ablation (RFA), microwave ablation (MWA), cryoablation, and high-intensity focused ultrasound (HIFU) ablation. Among these, RFA has been most frequently used worldwide, therefore there are abundant data regarding its clinical outcomes as compared with other ablation techniques or with hepatic resection.

This review evaluates the role of RFA in the management of HCC. Optimal candidates who would benefit from RFA and its contribution in multimodal therapeutic strategy will be discussed. In addition, important facts about other ablation techniques will be summarized.

Bioeffects of RFA

Alternating electrical current (300–1,000 kHz) emitted from the RF electrode tip induces heat reaching temperatures of 60–100 °C. When the tumour is exposed to this heat, near immediate coagulation necrosis occurs as irreversible damage. The size of the ablation zone achieved by one application of commercially-available RF devices is up to 3–5 cm in diameter [1]. Because of the possible microvascular invasion, as well as microscopic satellite nodules of HCC, the ablation zone needs to contain not only the entire target tumour but also ablative margins of 0.5–1.0 cm of peritumoral tissue in order to 'completely' treat HCC.

This heat effect is also able to shut down microvascular flow. However, blood flow in larger vessels is often not affected, and maintenance of blood flow limits heat deposition and prevents the ablation zone from being further enlarged, in what is called the heat-sink effect [1,2]. The shut-down of blood flow by RFA can be easily assessed using contrast-enhanced ultrasound (US), computed tomography (CT), or magnetic resonance imaging (MRI) by demonstrating avascular zones where the target tumour was present. However, the results of radiological examinations have shown discrepancies as compared to those of pathologic examinations, with a tendency of overestimation [3]. This overestimation might be attributed to residual microscopic viable cell nests that are impossible to detect with current imaging studies and are a source of subsequent local tumour progression (LTP). On the other hand, the discrepancy might be due to limitation of conventional histopathological analysis, which cannot assess heat fixation or apoptosis and could result in underestimation.

Advances in RFA techniques

Techniques for larger ablation zones

A conventional RF electrode could induce coagulation necrosis of no greater than 1.6 cm in diameter [1]. This limitation is worsened by vaporization and/or carbonization that act as an insulator of electrical currents. To overcome this inherent limitation, several adaptations have been adopted for currently available RF devices, including expandable multi-tined designs, internal cooling by chilled saline, clustered design, pulsing of RF energy, and concomitant saline infusion into the tissue. These techniques have contributed to enlarging the RFA zone to 3–4 cm. Multiple overlapping ablations or simultaneous application of multiple electrodes can enlarge the ablation zone further [1]. Taking these techniques into consideration, in theory at least, HCC up to 4–5 cm in diameter can now be ablated 'technically'.

Techniques for accurate targeting

Another crucial limiting factor is the difficulty of accurate targeting in some situations. US is the most commonly used guiding modality for RFA. Visibility of HCC by US is hindered by a difficult location with a poor acoustic window, which is more likely to be present in a cirrhotic liver, or by small tumour size in a background of macronodular cirrhosis. In a study by Kim et al [4], US-guided percutaneous RFA was unfeasible in 33.1% of cases, and tumour invisibility was the most common reason for this. Several techniques have been suggested to overcome this limitation.