Quality Improvement Guidelines for Radiofrequency Ablation of Liver Tumours

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Abstract The development of image-guided percutaneous techniques for local tumour ablation has been one of the major advances in the treatment of liver malignancies. Among these methods, radiofrequency ablation (RFA) is currently established as the primary ablative modality at most institutions. RFA is accepted as the best therapeutic choice for patients with early-stage hepatocellular carcinoma (HCC) when liver transplantation or surgical resection are not suitable options [1, 2]. In addition, RFA is considered a viable alternative to surgery (1) for inoperable patients with limited hepatic metastatic disease, especially from colorectal cancer, and (2) for patients deemed ineligible for surgical resection because of extent and location of the disease or concurrent medical conditions [3]. These guidelines were written to be used in quality-improvement programs to assess RFA of HCC and liver metastases. The most important processes of care are (1) patient selection, (2) performing the procedure, and (3) monitoring the patient. The outcome measures or indicators for these processes are indications, success rates, and complication rates.

Definitions

Ablative Margin
This is the region ablated beyond the borders of the tumour to achieve complete tumour destruction. Ideally, it should measure 0.5–1.0 cm wide.

Complete Ablation
This is the nonenhancing area, including the tumour and the ablative margin, on contrast-enhanced imaging modalities.

Complications

Complications can be stratified on the basis of outcome by using the society of interventional radiology (SIR) standard table. Major complications result in admission to a hospital for therapy (for outpatient procedures), an unplanned increase in the level of care, prolonged hospitalization, permanent adverse sequelae, or death. Minor complications result in no sequelae, and they may require nominal therapy or a short hospital stay for observation (generally overnight). Major and minor complications and side effects should be reported on the basis of the number of ablation sessions on a per-session basis.

Electrode (Radiofrequency Applicator)
One or multiple electrodes are inserted directly into the tumour to deliver RF energy current. Electrodes can be monopolar or bipolar, and they can have different designs (multitined expandable, internally cooled, perfused).
- **Monopolar Electrode** This has a single active electrode applicator, with current dissipated at one or several return grounding pads.
- **Bipolar Electrode** This consists in two electrode applicators or in a single array containing both the active and return electrodes.
- **Multitined Expandable Electrode** This has multiple electrode tines that expand from a larger needle cannula.
- **Internally Cooled Electrode** This electrode has an internal lumen that is perfused by saline without coming into direct contact with patient body tissue.
- **Perfused Electrode** The tip of the electrode has small apertures that allow the fluid (usually saline) to come in contact with the tissue.

Heat-Sink Effect

This is convective cooling by adjacent blood vessels, usually \( \geq 3 \) mm, when ablated tissues are heated. It can negatively affect the results of RFA because it can potentially remove heat before complete tumour ablation is achieved.

Hydro/Gas Dissection

This is the instillation of liquid (dextrose 5%, sterile water) or gas (air, carbon dioxide) between the area of ablation and the structure vulnerable to heating damage (usually the bowel).

Incomplete Ablation

This is the presence of residual unablated tumour, which is seen as peripheral irregular enhancement at imaging. It often grows in a scattered, nodular, or eccentric pattern.

Local Tumour Progression

This is the appearance at follow-up of foci of untreated disease in tumours that were previously considered to be completely ablated.

Overall Survival

This is the time from inclusion in the study to death. Patients who are alive at the end of follow-up are censored.

Radiofrequency Ablation

This is coagulation induction from all electromagnetic energy sources with frequencies \(<30 \text{ MHz}\). For tumour ablation purposes, the frequency is usually in the range of 375 to 500 kHz.

Technical Success

This is considered when treatment of the tumour was performed according to protocol and complete tumour coverage is assessed either during or immediately after the procedure.

Transient Hyperechoic Zone

This is the transient (\( >30–90 \) min) zone of increased echogenicity seen at US within and surrounding a tumour during and immediately after RFA.

Indications

**HCC**

RFA is the therapy of choice in very early and early HCC according to the Barcelona Clinic Liver Cancer (BCLC) classification (Table 1) when patients are not candidates for either liver resection or transplantation. Patients are required to have a single tumour smaller or as many as three nodules \(<3 \text{ cm}\) each, no evidence of vascular invasion or extrahepatic spread, performance status test of 0, and liver cirrhosis in Child-Pugh class A or B.

**Liver Metastases**

**Primary Tumour Histotype**

RFA is generally indicated for nonsurgical patients with colorectal cancer oligometastases isolated to the liver. Selected patients with limited hepatic and pulmonary colorectal metastatic disease, however, may qualify for percutaneous treatment if extrahepatic disease is deemed curable. In patients with hepatic metastases from other primary cancers, promising initial results have been reported in the treatment of breast and endocrine tumours.

**Number of Lesions**

The number of lesions should not be considered an absolute contraindication to RFA if successful treatment of all metastatic deposits can be accomplished. Nevertheless, most centres preferentially treat patients with \( \leq 5 \) lesions.

**Tumour Size**

The target tumour should not exceed 3 cm at its longest axis to achieve best rates of complete ablation using most of the currently available devices.
Pretreatment imaging must carefully define the location of each lesion with respect to surrounding structures as follows:

- Lesions located on the surface of the liver can be considered for RFA, although their treatment requires adequate expertise and may be associated with a higher risk of complications.
- Thermal ablation of superficial lesions that are adjacent to any part of the gastrointestinal tract must be avoided because of the risk of thermal injury of the gastric or bowel wall. The colon appears to be at greater risk than the stomach or small bowel for thermally mediated perforation. Gastric complications are rare, most likely owing to the relatively greater wall thickness of the stomach or the rarity of surgical adhesions along the gastrohepatic ligament. Mobility of the small bowel may also provide the bowel with greater protection compared with the relatively fixed colon. The use of special techniques, such as intraperitoneal injection of dextrose to displace the bowel, can be considered in such instances.
- Treatment of lesions adjacent to the hepatic hilum increases the risk of thermal injury of the biliary tract. This tumour location represents a relative contraindication to RFA. In experienced hands, thermal ablation of tumours located near the gallbladder has been shown to be feasible, although associated in most cases with self-limited iatrogenic cholecystitis.
- Thermal ablation of lesions adjacent to hepatic vessels is possible because flowing blood usually protects the vascular wall from thermal injury. In this case, however, the risk of incomplete treatment of the neoplastic tissue close to the vessel may increase due to heat loss by convection.

### Physician Credentialing

Before treatment, all patients with liver tumours who are considered for RFA should undergo a thorough clinical evaluation by a multidisciplinary team, including an interventional radiologist, a hepatologist, an oncologist, a surgeon, and an anesthesiologist. The core of physiological knowledge required for the interventional radiologist includes understanding liver anatomy, liver tumour diagnosis, and radiologic and non radiologic treatment options.

### Imaging Guidance and Monitoring

Targeting of the lesion can be performed with ultrasound, computed tomography (CT), or magnetic resonance imaging (MRI). The guidance system is chosen largely on the basis of tumour visibility, operator preference, and local availability of dedicated equipment, such as CT fluoroscopy or open MRI systems. The transient hyperechoic zone that is seen on ultrasound within and surrounding a tumour during and immediately after RFA can be used as an approximate guide to the extent of tumour destruction. It is not sufficient to evaluate immediate treatment effectiveness, and follow-up imaging is mandatory. MRI currently is the only imaging modality with validated techniques for real-time temperature monitoring.

### Anesthesiology Care

Thermal ablation is usually performed with the patient under intravenous sedation or general anaesthesia with standard cardiac, pressure, and oxygen monitoring. American Society of Anesthesiologists (ASA) score (Appendix) can be used to assess patient physical status before RFA. Patients with ≤ASA III score can be treated.

### Posttreatment Assessment and Follow-Up

Contrast-enhanced CT or MRI are recognized as the standard modalities with which to assess treatment outcome. CT and MRI results obtained 4–6 weeks after treatment show successful ablation as a nonenhancing area with or without a peripheral enhancing rim. The enhancing rim that may be observed along the periphery of the ablation zone appears to be a relatively concentric, symmetric, and uniform process in an area with smooth inner margins. This transient finding represents a benign physiologic response to thermal injury (reactive hyperemia initially and fibrosis and giant cell reaction subsequently). Benign periablational enhancement must be differentiated from irregular peripheral
enhancement due to residual tumour that occurs at the
Treatment margin. Compared with benign periablational
enhancement, residual unablated tumour often grows in
scattered, nodular, or eccentric patterns. Contrast-enhanced
ultrasound can be performed after the end of the procedure
and may allow initial evaluation of treatment effects.

Later follow-up imaging studies should be aimed at
detecting local tumour progression, development of new
hepatic lesions, or emergence of extrahepatic disease. A
recommended follow-up protocol includes CT or MRI
studies at 3, 6, 9, and 12 months after treatment and at
6-month intervals thereafter for the next 3 years.

Contraindications

Contraindications for RFA are as follows:
1. tumour located <1 cm from the main biliary duct (due
to risk of delayed stenosis of the main biliary tract);
2. intrahepatic bile duct dilation;
3. anterior exophytic location of the tumour (due to the
risk of tumour seeding);
4. bilioenteric anastomosis; and
5. untreatable/unmanageable coagulopathy.

Clinical Results: HCC

Technique Effectiveness

RFA yields satisfactory local tumour control in treating
small HCCs, with a complete ablation rate on imaging of
approximately 90% in tumours >3 cm [4–8]. Histological
data from explanted liver specimens in patients who have
undergone RFA showed that tumour size and presence of
large (≤3 mm) abutting vessels significantly affect local
treatment effect. Complete tumour necrosis was patholo-
gically shown in 83% of tumours <3 cm and 88% of
tumours located in a nonperivascular space [9]. Compari-
son with percutaneous ethanol injection (PEI) in five ran-
donized trials [4–8] showed that RFA has a higher local
anticancer effect than PEI, thus leading to better local
control of the disease (Table 2). Consequently there is no
room per PEI in HCC amenable to RFA.

Survival

Five randomized trials compared RFA with PEI for local
ablation of early-stage HCC (Table 2). The two European
trials failed to show a statistically significant difference in
overall survival between patients who received RFA
compared with those receiving PEI [4, 8]. However, sur-
vival advantages were identified in three Asian studies
[5–7]. These data were recently pooled in two indepen-
dent meta-analysis, and the survival benefit of patients
with small HCCs who received RFA was confirmed [10,
11]. Therefore, RFA is the preferred percutaneous treat-
ment for patients with early-stage HCC on the basis of
more consistent local tumour control and better survival
outcomes.

Recently, the long-term survival outcomes of RFA-
treated patients were reported (Table 3) [12–17]. In
patients who underwent RFA, survival depended on the
severity of underlying cirrhosis and tumour stage. Patients
in Child–Pugh class A with early stage HCC had a 5-year

| Author          | No. of patients | Tumour size            | Complete ablation (%) | Treatment failure (%)a | Three-year overall survival | P     |
|-----------------|-----------------|------------------------|-----------------------|------------------------|-----------------------------|-------|
| Lencioni et al. | 52              | 1                      | 91                    | 8                      | 81                          | >0.05 |
|                 | 50              | HCC < 5 cm or          | 82                    | 34                     | 73                          |       |
|                 |                 | 3 HCCs < 3 cm          |                       |                        |                             |       |
| Lin et al.      | 52              | 1–3 HCCs               | 96                    | 17                     | 74                          | 0.014 |
|                 | 52              | <4 cm                  | 88                    | 45                     | 50                          |       |
| Shiina et al.   | 118             | 1–3 HCCs               | 100                   | 2                      | 80                          | 0.02  |
|                 | 114             | <3 cm                  | 100                   | 11                     | 63                          |       |
| Lin et al.      | 62              | 1–3 HCCs               | 97                    | 16                     | 74                          | 0.031 |
|                 | 62              | <3 cm                  | 89                    | 42                     | 51                          |       |
| Brunello et al. | 70              | 1–3 HCCs               | 96                    | 34                     | 59                          | >0.05 |
|                 | 69              | <3 cm                  | 66                    | 64                     | 57                          |       |

* Includes initial treatment failure (incomplete response)
and late treatment failure (local recurrence/progression)
survival rate of 61 to 77%, whereas patients with a single tumour ≤2 cm had a 5-year survival rate of 68%.

**Clinical Results: Colorectal Cancer Liver Metastases**

**Technique Effectiveness**

Many studies have investigated the use of RFA in the treatment of limited colorectal cancer hepatic metastatic disease in patients who were excluded from surgery. Two early studies reported rates of complete response that did not exceed 60–70% [18, 19]. Subsequently, owing to the advances in RFA technique and probably to the treatment of smaller tumours, reported rates of successful local tumour control after RFA treatment increased substantially. In two series, RFA allowed eradication of 91% of 100 metastases and 97% of 74 metastases, respectively [20, 21].

**Survival**

Recently, data on long-term survival of nonsurgical patients with hepatic colorectal metastases who underwent RFA have been reported (Table 4) [22–28]. In particular, in three series including patients with ≤5, each ≤5 cm, the 5-year survival rate ranged 24–44% at 5 years [22, 23, 26]. When RFA was performed in patients with small (<4 cm) solitary hepatic colorectal metastases, a 40% 5-year survival rate was demonstrated [29]. These figures are substantially higher than those obtained with any chemotherapy regimens and provide indirect evidence that RFA therapy improves survival in patients with limited hepatic metastatic disease. This conclusion is supported by the interim analysis of a randomized controlled trial comparing chemotherapy plus RFA versus chemotherapy alone in colorectal cancer metastatic to the liver [30].

**Complications**

Early major complications associated with RFA occur in 2.2–3.1% of patients and include intraperitoneal bleeding, liver abscess, intestinal perforation, pneumothorax and haemothorax, bile duct stenosis, and tumour seeding (0.5%); the procedure mortality rate is 0.1–0.5% (Table 5). The minor complication rate ranges from 5% to 8.9%. The most common causes of death are sepsis, hepatic failure, colon perforation, and portal vein thrombosis, whereas the most common complications are intraperitoneal bleeding, hepatic abscess, bile duct injury, hepatic decompensation, and grounding pad burns. Minor complications and side
Specific major complications per session | Reported rate (%) | Suggested threshold (%) |
--- | --- | --- |
Hemorrhage requiring transfusion | 1 | 2 |
Bowel perforation | 0.3 | 0.6 |
Abscess | 0.3 | 0.6 |
Hemothorax | 0.1 | 0.2 |
Tumour seeding | 0.5 | 1 |
Hepatic decompensation | 0.3 | 0.6 |
Bile duct injury | 0.1 | 0.2 |
Grounding pad burns | 0.1 | 0.2 |
Death | 0.5 | 1 |

Appendix A: American Society of Anesthesiologists (ASA) Physical Status Classification System

I Normal healthy patient
II Patient with mild systemic disease
III Patient with severe systemic disease
IV Patient with severe systemic disease that is a constant threat to life
V Moribund patient who is not expected to survive without surgery
VI Patient declared brain-dead whose organs are removed for donor purposes

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