

Radiofrequency Ablation

Physician Information

Multiple techniques exist for tissue ablation, including radiofrequency ablation (RFA), percutaneous ethanol injection (PEI), microwave, laser, cryotherapy, and focused ultrasound. Each technique has strengths and weaknesses with unique problems. Learning where other techniques have failed may help avoid repeating similar problems. All methods cause cell death by coagulation necrosis. Knowledge of the underlying mechanism of thermal tissue ablation, and the specific heat effects upon tissue, improve the physician's ability to predict ablation volume and plan for clean treatment margins.

Local, minimally-invasive tissue ablation is an attractive tool for the cancer patient, especially for disease in the liver. There is no existing effective treatment for the vast majority of patients with hepatic metastases. Most primary liver tumors are unresectable at the time of presentation. Recurrence is common, even in candidates undergoing curative resection. Local treatment preserves uninvolved liver parenchyma, has potentially fewer systemic complications and side-effects than systemic treatment options like chemotherapy, and avoids the morbidity and mortality of major hepatic surgery.

Percutaneous ethanol injection (PEI) has proven clinically effective in the treatment of hepatocellular carcinoma (HCC). Long-term survival rates of PEI-treated patients with HCC are similar to those patients treated surgically. The other ablative methods, like RFA should be equally effective at prolonging survival in select patients. RFA may also allow an increase in the rate of curative liver resection.

In PEI, ethanol is injected directly into the tumor in multiple treatment sessions. PEI works much better for HCC than for liver metastases. This is because most HCC occurs in the setting of cirrhotic liver disease, typically due to chronic hepatitis. In this situation the tumor is "soft," whereas the surrounding liver parenchyma is "hard." This promotes the distribution of ethanol within the tumor, particularly when the HCC is encapsulated. Patients with liver metastases typically have normal (soft) underlying hepatic parenchyma, whereas the metastasis is "hard" and infiltrative, a situation that promotes the egress of ethanol from the lesion into the normal liver. Large HCC's are more effectively and completely treated percutaneously than are large colorectal metastases to the liver. Most RFA clinical trials to date have concentrated on RFA of smaller hepatic lesions (<3 cm), although RFA may be effective in the treatment of HCC's up to 5 cm, especially if encapsulated. PEI has been used in conjunction with embolotherapy, and some would advocate combining PEI and RFA for larger liver metastases (4 to 6 cm). It seems that RFA requires fewer treatment sessions and may have a lower recurrence rate than PEI. However, the capsular or exophytic HCC may also be amenable to PEI or combination PEI and RFA, with or without embolotherapy. Laparoscopic RFA may also be useful for tumors in difficult locations.

Radiofrequency ablation is currently the frontrunner among the many choices for local tissue ablation. (Decadt, B. and Siriwardena, A. K. Radiofrequency ablation of liver tumours: systematic review. *Lancet Oncol* 2004;5: 550-560. reference only, no link) RFA may be better than other ablative techniques because it is fast, easy, predictable, safe, and relatively cheap. In RFA, a needle electrode (14-17.5G) with an insulated shaft and a non-insulated distal tip is inserted into the lesion with imaging-guidance. The patient is made into an electrical circuit by placing grounding pads on the thighs or back muscles. The energy at the exposed tip causes ionic agitation and frictional heat, which leads to cell death and coagulation necrosis if hot enough. If the tip is too hot, the vaporization and "charring" (like a burned hamburger with a raw center) may cause decreased energy absorption and less treated tissue volume. The impedance and temperature at the tip are monitored, and the greater output is adjusted to decrease "charring" and thus increase the volume of tissue treated.

The active tip may be different lengths or configurations. Ultrasound is most commonly used for guidance, followed by CT and lastly MR. The procedure may be safely performed on an outpatient basis with local lidocaine (or bupivacaine) anesthesia, and conscious sedation with Midazolam and Fentanyl. In complex cases some prefer general anesthesia and overnight observation; this is also true for large lesions. Each treatment session has about 10 to 30 minutes of RFA, depending on the device used. At the end of a single session, the tract may be cauterized on the way out if the lesion is particularly vascular.

Recent advances in technique have resulted in larger volumes of tissue ablated, which may translate into the ability to treat larger lesions. This has been accomplished with relatively low complication rates, and little collateral damage. Various methods for increasing energy and heat disposition have been attempted in the laboratory and in clinical practice. The most commonly used methods include the coaxial umbrella, the internally-cooled probes, and multiple probes.

RFA is similar, but not identical, to electrocautery. RFA has been used for over ten years for various clinical applications including treating arrhythmias, osteoid osteoma, and nerve ganglion ablation. The current and potential clinical applications are numerous. Patient selection criteria are controversial for RFA, so check the protocols on the NIH website or call us at 1-800-411-1222 to see if your patient qualifies.

Multiple factors influence the effectiveness of RFA as well as the risks. The proximity to vital structures may influence the risk for collateral damage, for example. The risks are kept to a minimum by attention to detail and complete pre-procedural blood work and imaging. The "oven effect" for RFA of hepatocellular carcinoma or renal cell carcinoma allows for greater heat deposition and tissue burn within encapsulated lesions. The "heat-sink" effect of RFA may occur in treated tumors adjacent to large vessels. The inflow of "cool" blood at body temperature (cool relative to the cooked tissue) may impair the heating of the tumor cells closest to the vessels and may be the site of tumor regrowth or incomplete treatment. This heat-sink effect may also result in dimpling of the treated

sphere of tissues next to the vessel. Blood vessels may also be an energy sink as blood conducts energy better than other soft tissue.

Follow-up imaging may present a difficult problem, as the post-treatment inflammatory rim of rind may be difficult, if not impossible, to differentiate from small recurrence or untreated tumor. Sometimes time is the only way to differentiate tumor from no tumor, however. The natural history of treated tumor / coagulation necrosis in the liver is slow shrinkage over the course of months to years.

Patient selection likely has a great impact on the disease-free survival, and the variability in reported survival rates may partly reflect this. There is evidence to suggest that RFA can provide local short-term control of small liver malignancies. Studies of over 3,000 patients treated with RFA have shown the efficacy of percutaneous RFA for hepatocellular cancer lesions <3cm. Recurrence rates are determined predominantly by lesion size, with lesions <3.0cm, yielding a successful treatment in the vast majority. Complete local response averages 70-75% with tumors between 3.0 and 5.0 cm, and drops to 25% in large tumors over 5 cm in diameter. With successful ablation, 5-year survival rates of 40-50% have been reported for HCC. While local recurrences may be successfully treated, new intrahepatic or extrahepatic disease arises in 25-50% of patients. (Friedman, M., et al. Radiofrequency Ablation of Cancer. CardioVasc. and Intervent. Radiol. 2004; 27:427-434 and. Decadt, B. and Siriwardena, A. K. Radiofrequency ablation of liver tumours: systematic review. Lancet Oncol 2004;5: 550-560.) (The reported rate of major side-effects or complications of RFA in the liver is <2%, most of which do not require surgery. (Livraghi, T., et al. Treatment of Focal Liver Tumors with Percutaneous Radio-frequency Ablation: Complications Encountered in a Multicenter Study". Radiology 2003;226:441-451.) reference only. No link. We are cautiously enthusiastic about the future of RFA, and will see whether these numbers withstand the test of time.

The team approach is vital; the efforts of oncologist, surgeon, and hepatologist are often central to effective treatments. Although RFA is a nascent technique, long-term follow-up studies will result in further refinements in this modality, as well as the combination of RFA with other treatments. As with any new technique, there is a steep learning curve, so be careful with patient selection and start slowly.

Frequently Asked Physician Questions:

WHY RFA?

Cheap, safe, fast, easy and predictable. Fewer sessions than alcohol. Safer than Cryo percutaneously. Can you ablate non-liver tissue? Yes, if you are careful. Collateral damage may be more likely. Realistically define goals with patient and referring oncologist or oncologic surgeon. We have treated kidney, adrenal, spleen, pelvis, superficial, lung, breast, nodal, bone, spine and peripheral tumors for various specific indications. Conscious sedation or general anesthesia? Physician preference. Liver lesions on the capsule or diaphragm as well as larger tumors tend to be more painful, and

may require general anesthesia. General anesthesia has the drawback of not being able to follow breathing instructions. Have the anesthesiologist begin with deep sedation (propofol, remifentanyl). Droperidol is a useful adjunct to the regular versed / fentanyl combination. Toradol is useful for post-procedural pain, although only use one or 2 doses to limit renal toxicity. Bolus the drugs so peak is just as juice is turned up.

Ultrasound or CT?

Physician preference. Precise needle location is vital. Occasionally, using both CT and US may provide the best placement and monitoring during treatment. Ultrasound images 2 to 5 minutes after RFA may be more accurate in defining ablation volume than intra-procedural images. Watch during entire treatment - Needle location may shift. MR may provide thermal-sensitive sequences.

How often to follow-up imaging?

Physician preference. Same-day enhanced imaging is done to document treatments and lack of complications. Follow-up imaging depends on tumor (location, growth rate, histology, organ, concern for incomplete treatment). 4 to 8 weeks post, and 6 months post is one method.

Which system?

Physician preference. There are strengths and weaknesses to each, making the availability of all systems desirable, but often impractical. We have all available generators, and choose based upon patient- and tumor-specific issues (location, importance of minimizing collateral damage, proximity of large vessels, desired treatment volume, importance of uniform lesion formation, bleeding risk, respiratory motion, probe pathway).

Is RFA FDA-approved?

The 3 systems each have FDA 510K clearance for "soft tissue ablation". To what this exactly applies is unclear. At least 2 of the 3 have similar clearance for unresectable liver tumors. Hippocratic quote: Hippocrates said what is not cured by the knife may be cured by fire, but he also said "do no harm".

What to do with the post-procedural fever?

Low-grade fever may occur in the first few days after RFA, especially with large ablations. A mild post-RFA syndrome may occur, which is generally much less symptomatic than the typical post-chemoembolization syndrome or post-tumor lysis syndrome. Treat and culture fevers above 101. Drain abscess or blocked biliary ducts (rare).

What about prophylactic antibiotics?

Controversial - 50/50 at RSNA 2000 roundtable. We use Ampicillin and Gentamycin, or Cipro +/- metronidazole, or just Unasyn or cefoxitin pre-RFA and we follow up with a week of antibiotics (Cipro 500 BID +/- metronidazole) in patients with ascites, choledochoenteric anastomoses, sphincterotomy, prior hepatic arterial chemotherapy or focal biliary dilatation, or in patients with central or portal lesions or with large lesions,

or with kidney tumors touching the collecting system. The only possibly RFA-related deaths we have heard of occurred from peritonitis in patients without antibiotic coverage.

How about hydration?

Hydration pre- and post-procedure should be as aggressive as the patient's medical condition allows. Aggressive hydration may limit renal toxicity or ATN from contrast or tumor lysis-related phenomena, and may decrease the symptoms of post-embolization.

The central liver lesion:

There are more risks and complications associated with treating cholangiocarcinoma as well as centrally located liver lesions. Biliary obstruction is the concern. Large vessel abutment may also limit successful tumor eradication. Targeting vessel may help, but may increase risk.