

RADIOFREQUENCY ABLATION IN ONCOLOGY: PRINCIPLES, TECHNIQUES AND CURRENT APPLICATIONS

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Abstract: Radiofrequency ablation (RFA) is a technique that causes tissue necrosis by a process of heating, when high frequency current passes through tissue, thereby causing thermocoagulation. It is a relatively new treatment modality where thermal energy is used for destroying tissue. In radiofrequency ablation a high frequency alternating current (400 to 900 KHz) is delivered to the tumor tissue via a needle electrode. By ionic agitation, frictional heating of the tissue and thermal coagulative necrosis occurs causing cell death. Mammalian cells undergoes death within 4-6 minutes at temperatures above 49°C, which is near instantaneous above 60 degree C, while at 105°C the cells boil, intracellular water vaporizes and tissue gets charred. It is an attractive option for local tumor control in patients who are not surgical candidates or who have failed conventional therapies. RFA has been conventionally used to treat metastases from colorectal cancers and HCC. Currently its role is extended in treating primary and secondary lung tumours, bone tumours, early stage breast cancer and small kidney tumours not suitable for surgery. It is the treatment of choice for osteoid osteoma.

Key words: Radiofrequency ablation, Tumour ablation

INTRODUCTION

Heat has been used in ancient Hindu medicine and by the Greeks as heated stones and metal bar to stop bleeding. D'Arsonval in 1891 first introduced radiofrequency current as a clinical tool in the form of electrocautery and medical diathermy. Radiofrequency ablation (RFA) is a technique that causes tissue necrosis by a process of heating, when high frequency current passes through tissue, thereby causing thermocoagulation. It is a relatively new treatment modality where thermal energy is used for destroying tissue. RFA has been conventionally used to treat metastases from colorectal cancers and HCC¹. Currently its role is extended in treating primary and secondary lung tumours, bone tumours, early stage breast cancer and small kidney tumours not suitable for surgery. It is the treatment of choice for osteoid osteoma.

PRINCIPLE

In radiofrequency ablation a high frequency current (400 to 900 KHz) is delivered to the tumor tissue via a needle electrode. As the current alternates rapidly the ions in the vicinity of the needle tip rapidly change direction (ionic agitation). This causes frictional heating of the tissue, thermal coagulation and cell death by coagulative necrosis. Most mammalian cells do not survive temperature exceeding 42°C. Death begins to occur within 4-6 minutes at temperatures above 49°C and becomes near instantaneous above 60 degree C. At 105°C the cells boil, intracellular water vaporizes and tissue gets charred². This charring and gas formation due to heat deposition near the needle tip is a disadvantage since it

drastically reduces the current flow and limits the size of ablation.

Different manufacturers use different techniques to control the charring so as to increase the size of ablation. It can be achieved by perfusion of saline into the tissue to sustain conductivity (Electrotom, Berchtold, Tuttlingen, Germany). Alternatively the needle tip can be kept cool by inflow of chilled saline (Cool tip, Radionics, Burlington, MA). Machines with multiple retractable electrodes which when deployed physically occupy a larger volume of tissue are also in use resulting in a larger ablation zone. (RITA Medical Systems, Mountain View, CA). Combining strategy with concurrent chemotherapy has yielded larger ablation volumes in experimental studies^{3,4}.

Presence of a large vessel adjacent to the tumour prevents adequate hyperthermia due to rapid heat loss in the flowing blood (the "heat-sink" effect). It explains increased incidence of residual or recurrent disease in the vicinity of a large vessel. Vessels above 3 mm in diameter cannot be coagulated². Proposed standardised terminology for heat sink effect is perfusion mediated cooling⁵. In contrast, encapsulated tumours like hepatocellular carcinoma (HCC) are more amenable to ablation as they allow for greater deposition of heat due to compartmentalization of thermal energy (the "oven effect").

TECHNIQUE

The procedure is safely performed on an outpatient basis under conscious sedation. Prior confirmation of the lesion by biopsy or fine needle aspiration cytology (FNAC) and its localization on an imaging study is necessary. The RF needle is inserted into the lesion under CT (or ultrasound) guidance and an earthing pad is applied on the patient's legs or

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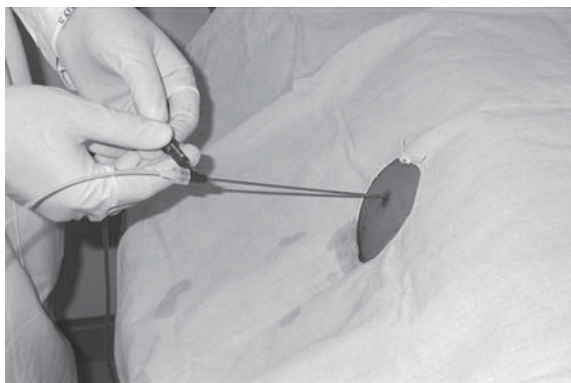


Fig 1. RF needle position during treatment

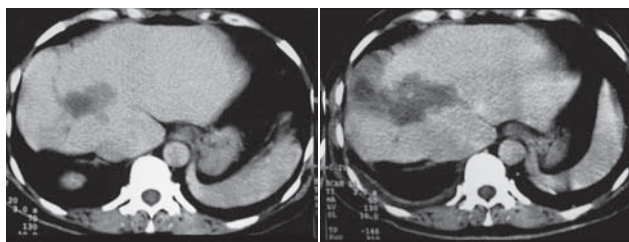


Fig 2. Hepatic metastases from colorectal cancer. Pre and post RFA appearance.

Note the larger ablated zone in the image on right

abdomen (fig 1). The needle electrode and the earthing pad are then connected to the high frequency generator and the patient becomes part of an electrical circuit. The typical ablation session last, for 10-20 minutes, depending on the size of lesions. Lesions with diameter up to 3-5 cm can be treated in a single session. Larger lesions may need multiple insertions. Route of insertion is usually percutaneous although it can also be done laparoscopically or even per-operatively (Open method). Percutaneous approach is preferred as it is least invasive, can be performed on out patient basis and the procedure can be repeated if needed. Follow-up is done with a CT-scan (or MRI) after 24hours, after a month and then at 3 monthly intervals, along with tumour markers to detect residual disease or recurrence. Post-treatment CT-scan should show a completely non-enhancing hypodense area with diameter larger or equal to the pretreatment diameter and with no enhancing focus (fig 2). Although early in the course, a peripherally enhancing rim may be seen due to inflammatory response of the normal tissue and is referred as benign periablation enhancement⁵. The natural history of treated tumour is slow shrinkage over many months to a year. Residual disease or recurrence is indicated by appearance of abnormal enhancing focus on CT scan or MRI.

CURRENT APPLICATIONS

Current indications for RFA include colorectal metastases to liver, liver only metastases from breast cancer, HCC which

is not suitable for surgery, bone metastases for control of pain, osteoid osteoma, small renal tumours particularly in a single kidney or a patient not suitable for surgery due to co morbid conditions, primary and secondary lung tumours usually in association with radiotherapy. RF ablation is also used for nerve ablation to achieve pain relief when tumour infiltrates nerves.

RFA is a safe and quick alternative to surgery with a curative potential. The effectiveness of RFA treatment is significantly dependent on tumour size. Lesions up to 3 cm undergo complete ablation and necrosis while the larger lesion requires multiple RFA treatment to prevent recurrence. For both the local and systemic control of the disease, RFA can be combined with other modalities like chemotherapy.

RF ABLATION IN LIVER

Liver metastasis: Patients with liver metastasis do not survive beyond one year if left untreated, most commonly due to liver failure by extensive hepatic involvement. Reduction in the tumour load in liver prolongs the survival. Long-term survival can be achieved in such patients if the metastatectomy is performed (90% at 1 year and 20-40% at

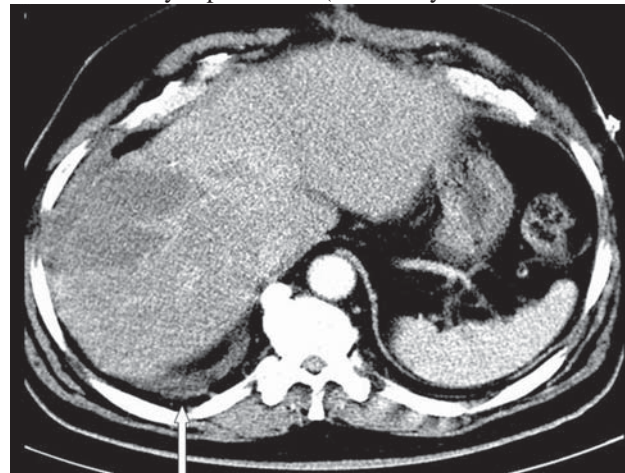


Fig 3. Pleural effusion (white arrow) developed after ablation(black arrow)

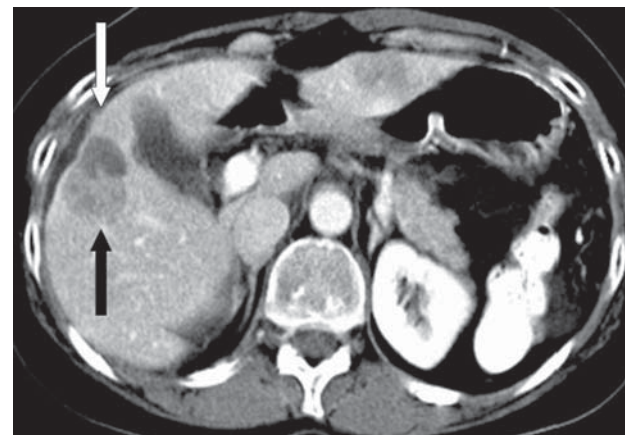


Fig 4. Local recurrence (black arrow) after 12 months at the margin of ablated lesion(white arrow)

5 year). However, only 5-10% of patients are suitable for surgical resection due to the advanced age, extra-hepatic involvement and co morbid conditions. In patients of carcinoid syndrome who have paraneoplastic symptoms, marked symptomatic relief can be achieved after ablation of metastatic deposits in liver. Local recurrence is particularly more common with lesions of diameter larger than 3 cm (fig 4).

RFA of liver lesions is an extremely safe procedure and can be performed on an out patient basis. Some complications of RF ablation are listed below :-

1. Post ablation syndrome: It is a tissue lyses-related phenomenon characterized by transient “flu like” symptoms, low-grade fever, lethargy and sweating⁶, usually self-limiting and common after large tumour volume ablation.
2. Thermal Injury: This includes skin burns at ground pad site or collateral damage to internal organs adjacent to the ablation site.
3. Pleural effusion: It is reactive phenomenon and is usually mild and transient. It is commonly seen in lesions close to the diaphragm (fig 3).
4. Haemorrhage: This can be prevented by correcting the coagulation profile and by ablating the needle track.

Hepatocellular Carcinoma (HCC): RFA was primarily developed for treating hepatocellular carcinoma. HCC have poor response to chemotherapy and radiotherapy. Surgical resection has been considered the only potentially curative option but the majority of patients are not amenable to resection due to the large size, location near major intra-hepatic blood vessels, underlying cirrhosis or a multicentric disease. RFA is a safe and quick alternative to surgery with a curative potential.

After RFA treatment, median survival is 44 months with 10% local recurrence , which is comparable to that found in surgical series. Early recurrences (within 2 years) are due to both local and new lesions while late recurrences (after 2 years) are due to new lesions. Local recurrence rate is less than PEI while the total recurrence is similar to that reported after surgery or PEI. Due to the “oven effect”, encapsulated HCC has least recurrence rate among all liver tumors treated with RFA. RFA is particularly indicated in certain special situations like cirrhosis which has friable liver and the multicentric form of HCC, which largely rules out a surgical intervention. RFA is therefore being used as first line of treatment in HCC patients with cirrhotic background.

RFA has many advantages over a surgery including low complication rate, reduced cost and increased patient compliance⁷. It is simple, safe, and an effective treatment modality. It is less risky and has low morbidity & mortality as compared to surgery. Most of these procedures are performed without general anesthesia on outpatient basis. As compared to percutaneous ethanol injection, RFA

produces a more predictable volume of necrosis and is not impaired by hard consistency of metastatic tissue. PEI requires greater number of sessions (approximately 5 to 8) resulting in poor patient compliance and increased morbidity. RFA treats only the macroscopic disease unlike systematic or hepatic arterial infusion chemotherapy and it does not address the microscopic disease or macroscopic tumor other than the one treated. RFA is designed to work in conjunction with surgery, radiotherapy and chemotherapy and is not intended to replace these modalities. RFA can debulk large tumors, which can be treated with chemotherapy. Post RFA chemotherapy prevents recurrences due to occult micrometastases.

RF ABLATION OF LUNG TUMOURS

Lung cancer has long been the most prevalent cause of cause of cancer death in men in the United States, and it has recently become the most common cause of cancer death in women, even surpassing breast cancer⁸. Surgery provides the highest cure rate in patients with non-small cell lung cancer (NSCLC); however, the majority of these patients have advanced disease at diagnosis and are not candidates for a surgical procedure due to advanced disease in the lungs, poor cardiac function, and poor pulmonary function of the patient. Regarding metastasis to the lung from non-pulmonary tumors, the median survival is equally as disappointing. Radiofrequency (RF) ablation of lung cancer is a potential alternative to surgical resection for patients with tumors⁹.

The prognosis for most people diagnosed with lung cancer is relatively poor, only 15% of patients are alive five years after diagnosis. RFA in lung cancer is considered for early stage disease in patients who are not candidates for surgery. However some of the complications of RFA in treating lung cancer are pneumothorax (35%), empyema and bronchial fistula.

RF ABLATION IN RENAL CELL CARCINOMA (RCC)

There have been numerous developments in minimally invasive treatments for RCC, as compared with the traditional standard of open complete nephrectomy. These developments include partial nephrectomy, laparoscopic complete or partial nephrectomy, and ablation therapies such as cryoablation and radio-frequency (RF) ablation^{10,11}. With respect to tissue characteristics, the kidney is surrounded by fat that serves as a heat insulator; this allows higher ablation temperatures to be achieved and maintained in tumors surrounded at least in part by fat .Consequently, exophytic tumors appear to be more easily treatable¹². On the other hand, near the renal sinus, the central portion of the kidney contains large vessels that serve as heat sinks, limiting tumor necrosis.

Therefore, on the basis of their size and location, small exophytic RCC tumors are the ideal tumors for treatment with RF ablation. Among tumors larger than 3 cm, those

with a central component near large vessels are less likely to be treated with technical success than are those without such a component. Even in the absence of complete ablation, RF ablation may play a role in palliation of disease in patients who find dialysis unacceptable. This palliative role of RF ablation in the treatment of RCC is an interesting area for further study, especially for large tumors with a central component.

RF ablation of RCC is a very promising technique and is most successful in treating small (<3 cm) exophytic tumors, although tumors up to 5.0 cm can be completely ablated. Tumors with a central component in the renal sinus require more ablations but can be successfully treated with multiple visits for repeated ablations. Longer-term studies of RF ablation of RCC left in situ will provide additional guidance for the most appropriate selection of patients for this treatment. Ideal case for RFA in RCC is an exophytic tumour which is less than 3 cm in size and has a safe percutaneous route.

The complications of RFA in kidney can be ureteral stricture formation, bowel injury and haemorrhage. Bowel can be displaced away from the intended ablation site by injecting 5% dextrose solution. Ureteral protection should be considered when RF ablation is to be performed in a tumor near the ureter.

RF ABLATION IN PRIMARY BREAST CANCER

In 1990, the National Institute of Health (NIH), USA, recommended breast conservation as the appropriate form of primary surgery in most women with early stage breast cancer. Current debate is however revolving around the ability of sentinel lymph node biopsy replacing axillary dissection. As and when the need for axillary dissection gets a backseat there would exist an opportunity to treat the primary breast tumor with a minimally invasive percutaneous technique. Currently the most promising of such non invasive techniques is RF ablation^[13]. In a study carried out at M.D. Anderson Cancer Centre (Houston, Texas, USA), it has been conclusively established that tumors upto 2cm in the human breast were completely destroyed by RF ablation¹⁴. Currently, breast cancers upto 1.5cm, with a few exceptions, are treated by RF ablation alone as an alternative to surgery. Core biopsy prior to RF Ablation will be a prerequisite to establish the diagnosis and the prognostic profile. RF ablation would thus be equivalent to a non surgical lumpectomy.

RF ABLATION OF BONE TUMORS

Radiofrequency ablation of bone tumors is potentially applicable for metastatic lesions causing pain. It is performed percutaneously under CT or fluoroscopic guidance. The tumour bone interface is the site that should

be treated. RFA is the procedure of choice for treating osteoid osteoma.

SUMMARY

Radiofrequency ablation of tumours is simple, safe, and an effective treatment modality. It has added advantages over a surgery in low complication rate, reduced cost and increased patient compliance. It is less risky and has low morbidity & mortality as compared to surgery. The procedure can be repeated if necessary and can be combined with other available treatment modalities. RFA is preferred over other techniques available for local control of tumours. Since image guidance is the key to a successful RF ablation, radiologists need to play the principal role in its applications and should accept the challenge in an emerging opportunity to be associated with management of patients.

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