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• REVIEW •

Radiofrequence ablation of liver cancers

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Abstract

Primary and secondary malignant liver cancers are some of most common malignant tumors in the world. Chemotherapy and radiotherapy are not very effective against them. Surgical resection has been considered the only potentially curtive option, but the majority of patients are not candidates for resection because of tumor size, location near major intrahepatic blood vessels and bile ducts, precluding a margin-negative resection, cirrhotic, hepatitis virus infection or multifocal. Radiofrequence ablation (RFA), which is a new evolving effective and minimally invasive technique, can produce coagulative necrosis of malignant tumors. RFA should be used percutaneously, laparscopically, or during the open laparotomy under the guidance of ultrasound, CT scan and MRI. RFA has lots of advantages superior to other local therapies including lower complications, reduced costs and hospital stays, and the possibility of repeated treatment. In general, RFA is a safe, effective treatment for unresectable malignant liver tumors less than 7. 0 cm in diameter. We review the principle, mechanism, procedures and experience with RFA for treating malignant liver tumors.

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INTRODUCTION

Hepatocellular carcinoma (HCC) is one of the most common solid cancers in the world, with an annual incidence estimated to be at least one million new patients[1].The mortality was secdonary to lung cancer in urban and gastric carcinoma in countryside in China[2,3]. Furthermore, the liver is second only t o lymph nodes as a common site of metastasis from other solid cancers, especially abdominal cancer[4]. It is not uncommon, particularly in patients with colorectal adenocarcinoma, for the liver to be the only site of metastatic dise ase[5]. Patients with liver metastases from colorectal carcinoma or other cancers seldom survive more than 1 year if untreated[6,7]. Surgical resection of HCC, hepatic metastases of colorectal cancer, and patients with liver- only metastases from other types of primary tumors can result in significant long-term survival benefit in at least 20-40% of patients[8-12]. Besid es these, surgical palliation through tumor cytoreduction in patients with sympt omatic neuroendocrine tumor (carcinoid, functioning islet cell) with liver metastases can ameliorate the symptoms related to excess hormone production and release.

Surgical resection has been considered the only potential curtive option, but on ly 5-20% of newly diagnosed HCC or colorectal cancer liver metastasis pati ents undergo a potentially curative resection[13, 14]. Patients with dis ease confined to the liver may not be candidates for resection because of multif ocal disease, proximity of tumor to key vascular or biliary structures that prec ludes a margin-negative resection, potentially unfavorable biology with the pre sence of multiple liver metastases, or inadequate functional hepatic reserve rel ated to coexistent cirrhosis. Thus, for so few patients with primary or metastat ic hepatic malignancies confined to the liver who are not candidates for surgica l resection, Surgeons and oncologists have turned to explore novel treatment app roaches to control and potentially cure the liver disease. Systemic chemotherapy for HCC and liver matestases results in less than 25% of patients; Complete r esponses are rare and significant improvements in survival are not sure. Althoug h hepatic artery infusion of chemotherapeutic agents for unresectable disease ha s led to 40% to 55% response rates in the liver, a survival advantage has b een difficult to demonstrate[15-18].

Localized treatment was used to HCC and colorectal cancer liver metastasis and b ased on the principle that decreasing the volume of viable tumor or preventing new growth can lead to longer survival and potential cure in selected patients, provided that diffuse micrometastatic disease is not present. These ablative tech niques include percutaneous ethanol injection[19-21], focused ultrasou nd[22-24], cryoablation[25-28], hyperthermia (ie, microwave tu mor coagulation[29-31]), laser photocoagulation[32-34], and ra diofrequency ablation[35-37] (RFA). Thermal energy produces destruction of tumor cells. When tumor cells are heated above 45-50℃, intracellular pro teins are denatured and cell membranes are destroyed through dissolution and mel ting of lipid bilayers[38-40]. RFA is a newly developed localized therm al treatment technique which was very useful in HCC and liver metastasis.

THE BACKGROUND AND MECHANISM OF RFA

The early usage of heat to treat tumors was back to early Egyptian and Greek whe n they used heat to cautize ulcer and superficial neoplasm. The first experiment in RF ablation of living tissues is credited to d'Arsonval, who demonstrated th at an alternating electric current greater than 10kHz could pass through livin g tissue without causing neuromuscular excitation. Beer and Clark used RF coagul ation in human cancers in early 20th century[41]. Coley suggested that that tumors were more sensitive to the effects of hyperthermia than normal cells and that tumors could not dissipate heat by augmenting blood flow as could adjacent normal tissues. RF techniques have gained acceptance as standard method for making well-controlled thermal lesions in the fields of neurology and cardiology since then[42-44]. It has been used in a variety of neurosurgical procedures aimed at ablating foci of spontaneous neuronal activity, in endoscopic techniques employed in gastroenterology, and in the ablation of aberrant conduct ion pathways in the heart for the treatment of dysrhythmias. Until the early 1990s, it is the technological modification of RF machine has made in to be used in focal thermal injuries deeper inside the body. More recently, Rossi and McGahan separately pioneered the application of RFA to primary and metastatic lesions i n the liver[45,46].

The so-called RF thermal ablation works by converting RF waves into heat. A hig h-frequency alternating current (100 to 500kHz), mostly 460kHz, passes from an uninsulated electrode tip into the

surrounding tissues and causes ionic vibr ation as the ions attempt to follow the change in the direction of the rapidly a lternating current. This ionic vibration causes frictional heating of the tissues surrounding the electrode, rather than the heat being generated from the probe itself. The goal of RFA is to achieve local temperatures such that tissue destr uction occurs. In general, thermal damage to cells begins at 42℃, with exposu re times required for cell death at this temperature ranging from 3 to 50 hours depending on the nature of the tissue. As the temperature is increased, there is an exponential decrease in the exposure time needed for cellular destruction. A t temperatures above 60℃, intracellular proteins including collagen denature, the lipid bilayer melts and cell death becomes inevitable. Thermal coagulation begins at 70℃ and tissue desiccation at 100℃, producing coagulation necros is of tumor tissue and surrounding hepatic parenchyma[46-50]. Tissue he ating also drives extracellular and intracellular water out of the tissue and re sults in further destruction of the tissue due to coagulative necrosis. Besides these, different studies have shown that hyperthermia can cause accelerated emig ration and migration of peripheral blood mononuclear cells, activation of effect or cells, induction and secretion of cytokines, expression of heat shock protein s, and increased induction of apoptosis[51,52].

RFA EQUIPMENT

Three primary RF devices, which worked on the same pricinples, are available in the world. The differences among the devices are the variations in probes and ge nerator designs.

The device made by RITA Medical Systems constites of a 50W alternating electric current generator and a 15-gauge needle electode. The needle electode has a mov able hub and 8 retracting curved electodes from the tip of the needle. Each tips of the needle contain a thermocuple that can register the temperature of the he ated tissues.

The device made by Radionics consists of a straight-tip internally cooled needl e electrode. The tip of the needle is cooled by perfusing its inner chamber with chilled saline which can prevent scorhing of the adjacent tissues and to increa se the size of the thermal injure. The device can be operated with not only a single electode but also with 3 electodes which placed in a triangular configuration. The device made by Radiotherapeutic is similar to the RITA device, consisted a n eedle with a movable hub that can deploy 10 curved needle tips. The multiple pro ngs are reported to produce a more uniform spherical injury than the devices wit h fewer prongs. But, this device does not have the temperature surveillance in the tips of the needles.

RFA PROBE

The first RFA probes were single, monopolar needles in the world. Because the RF energy delivered via the monopolar electrode decreases in proportion to the squ are of the distance from the electrode, coagulative necrosis was restricted to a maximum diameter of 1.6cm in which temperatures reached 80℃. Besides this, the surface temperature of the proximal and distal ends of the probe was higher than that in other parts. Thus, using a monopolar electrode results in an ellipsoid, ra ther than spherical, zone of necrosis, making evaluation difficult since most tu mors are spherical in shape. High temperatures at the surface of the electrode c ause a further limitation in size. Once the adjacent tissue reaches a high tempe rature and desiccates, the resulting tissue coagulum markedly reduces the propag ation of RF current and heat through the tissue, yielding a smaller zone of coag ulative necrosis[52].

One method to increase the zone of ablation is to use standard 0.9% saline or hypertonic 5% saline through the needle electrode during RFA. The infused saline solution acts as a liquid electrode to increase the area of RF current conduc tion around the needle tip[53]. Miao used 5% saline infusion into swin e liver before and during RFA. Both the electrode tip temperature and tissue imp edance decreased and coagulation diameter increased from less than 1.0cm to gr eater than 5.0cm[54].

Another technique to improve the volume of ablation involves the use of chilled perfusate into the lumen of electrodes. Lorentzen infused cool (room temperature) water into a specially designed electrode and noted a significant increase in delivered energy and ablation size in the *ex vivo* calf liver[55]. Goldb erg noted that both energy deposition and coagulation necrosis were significantl y greater with electrode cooling. This was also the case with *ex vivo* and *in vivo* muscle models. Studies in animals have also suggested that the combination of internally cooled electrodes and interstitial hypertonic saline infusion may result in a larger area of ablation than either technique alone[51, 56].

We can also use a second electrode within a few centimeters of the active electr ode to increase the diameter of necrosis. In ex vivo experiments, this bipolar arrangement demonstrated that heat was generated not only at the active electrode , but also adjacent to the ground electrode and between the two electrodes. The resulting focus (5cm) was therefore larger than that produced by traditionals ingle monopolar probes. The necrosis area produced by bipolar electrodes is stil l elliptical rather than spheroid, however, again making evaluation of its effec tiveness difficult[45,57].

Multiple active single probes can be clustered in an attempt to increase the coa gulation volume as well. Goldberg *et al*[60] investigated the effects of RFA via three electrodes placed 0.5cm apart from each other. This resulted in significant increases in the diameter of coagulation necrosis (2.9 to 7.0cm and 1.8 to 3.1cm, respectively) versus standard monopolar techniques. The use of c lustered electrodes requires multiple passes and positioning and it is often lab orious and difficult to ensure proper configuration. Although at times still used, this method has largely been supplanted by the development of multiprobe array electrodes[58].

The most promising and currently the most widely used technique for RFA is the m ultiprobe array system. This system can be placed into the target tissue with the array retracted. Using ultrasound guidance, the array is then deployed and che cked for proper positioning of all needles. These deployed multiple array needle s create a series of electrodes with an overall diameter ranging up to 3.5 to 7 cm across which RFA current can be passed. Using this multiprobe needle with a standard RFA protocol, a 4-6cm tumor can be completely ablated with the array fully deployed. In general, for lesions less than 2.5cm in diameter, the nee dle electrode is placed parallel to the plane of the ultrasound probe. For larger tumors, either a larger multiprobe array or multiple deployments of the needle electrode are required. The treatment is planned such that the zones of necrosi s overlap, keeping in mind that the entire volume of the tumor plus a margin of uninvolved tissue needs to be ablated.

RFA TECHNIQUES AND PROCEDURES

RFA of liver tumors can be performed percutaneously, using laparoscopic guidance, or as part of an open surgical procedure. The choice of treatment approach is individualized in any given patient. RFA is performed primarily by the liver sur geon and radiologist. The percutaneous approach differs from the laparoscopic and open surgical techniques only by the degree of hepatic exposure.

Patients with one to three small (<3.0cm diameter) cancers located in the peri phery of the liver are considered for ultrasound-guided or CT-guided percutane ous RFA. Lesions located high in the dome of the liver near the diaphragm are no t always accessible by a percutaneous approach. Furthermore, local anesthesia or monitored sedation is required for most patients treated percutaneously because of pain associated with the heating of tissue near the liver capsule. Patients treated percutaneously are usually discharged within 24h of

their RFA. Sonogra phy is used to localize the lesion to be treated. A percutaneous approach has been used in patients with small, early-stage hepatocellular cancers with coexist ent cirrhosis, and in patients with a limited number of small metastases from ot her organ sites[59,60].

A laparoscopic approach offers the advantages of laparoscopic ultrasonography, w hich provides better resolution of the number and location of liver tumors, and a survey of the peritoneal cavity to exclude the presence of extrahepatic disease. Using laparoscopic ultrasound guidance, the RFA needle electrode is advanced percutaneously into the target tumors for treatment. The laparoscopic ultrasound permits more precise positioning of the RF needle multiple array near major blo od vessels. Laparoscopic approach was used for patients with no prior history of extensive abdominal operations, and one or two liver tumors <4.0cm in diamete r located centrally in the liver near major intrahepatic blood vessels[61,62].

The majority of patients underwent RFA of hepatic tumors during an open surgical procedure. This approach is preferred in patients with large tumors (>4.0-5.0 cm diameter), multiple tumors, if tumor locates next to a major intrahepatic blood vessel, or if a laparoscopic approach is impractical because of dense post -surgical adhesions. In contrast to percutaneous RFA treatments, it is possible to perform temporary occlusion of hepatic inflow during the intraoperative RFA procedure. Hepatic inflow occlusion facilitates RFA of large or hypervascular tu mors and tumors near blood vessels. The amount of blood flow to a tumor is known to be a critical determinant of temperature response to a given increment of heat. Because heat loss or cooling effect is principally dependent on blood circul ation in a given area, temperature response and blood flow are inversely related. By temporarily occluding hepatic inflow during RFA, the cooling effect of bloo d flow on perivascular tumor cells is minimized[63]. The inflow occlusio n increases the size of the zone of coagulative necrosis and enhances the likeli hood of complete tumor cell kill, even if the tumor abuts a major intrahepatic blood vessel[64].

The RFA needle can be placed under computed tomorgraphy (CT) or ultrasound guida nce (percutaneous RFA) or ultrasound guidance (percutaneous, laparoscopic, or op en RFA). Ultrasound can be used with all techniques of RFA, and offers several o ther advantages as well, including real-time capabilities, vascular visualizati on, availability, speed, and low cost. The probes are usually placed at the deep margin of the tumor and subsequently repositioned anteriorly at intervals appro priate to the size of the needle array. Once the needle is localized in the gene ral vicinity of the tumor, the needle tip is placed into the desired portion of the tumor using a freehand technique. The abalation is started with the power se tting at 25W, and the setting is automatically advanced to 50W over about 30 sec onds. As the temperature at the tips of the deployed prongs exceeds 95℃, the times start to calculate. The temperature should be keep between 95-110℃ at least 10min to get full destory[51,65].

IMAGING TECHNIQUES IN RFA

Accurate imaging is essential for successful in situ tumor ablation. Tumors that are not seen can not be targeted, and residual foci of untreated tumor will continue to grow. With respect to tumor detection, and despite remarkable progr ess in US, CT and MR imaging over the past several years, no currently available imaging technique is perfectly sensitive for the detection of liver tumors, which means that some lesions will undoubtedly be overlooked with all imaging techniques. Generally, these overlooked lesions are small and will grow to a size that allows them to be detected, targeted and treated. Because currently available imaging techniques also may not precisely depict tumor margins, however, small foci of untreated tumor may not be identified. These will continue to grow in size and result in "local recurrence" after treatments that initially appeared to be successful. Improved imaging techniques should result in not only improved detection of additional lesions but also more accurate determination of tumor margins. Recent and ongoing developments in contrast agents for US and MR imaging coupled with technical innovations in US, CT, and MR imaging may provide the much needed improvements. Additional research will be needed to determine their effect on the efficacy of in situ tumor ablation with RF.

In situ tumor ablation is virtually always performed with imaging guidance. Currently, US is most commonly used for guidance in probe placement, owing to its flexibility, widespread availability, relatively low cost, and real-time imaging capabilities. RF ablation can also be performed with CT or MR imaging guidance; however, until recently, the static nature of CT and the complexity of the MR imaging environment have limited their use. The recent development of CT fluoroscopic systems may result in a larger role for CT in the future. Similarly, the developments of open-architecture MR imaging systems and MR-compatible interventional equipment have resulted in increased interest in the use of this modality to help guide interventional procedures. Preliminary experience now suggests that MR imaging may be useful for in situ ablation procedures with RF[66-68].

Imaging is used not only to help detect potentially treatable tumors and guide p robe placement but also to monitor the effects of therapy. When procedures are performed with US guidance, hyperechogenicity is generally seen surrounding the probe tip during the application of RF energy. This has proved to be only marginally useful for monitoring the effects of therapy because the hyperechoic zones correspond only roughly to the regions of eventual tissue necrosis. Furthermore, these changes evolve rapidly over time and can disappear within minutes of ablation[69-71]. Acoustic shadowing from more superficial treated areas can also preclude visualization of deeper portions of the tumor if one is not careful to treat deeper areas first. The use of US contrast agents may improve the accuracy of US with respect to monitoring the acute effects of therapy[72,73]. Contrast-enhanced CT, which is probably the most widely used technique for the follow-up of treated lesions, is less useful for the immediate assessment of treatment results. CT is not particularly helpful for confirming successful treatment or identifying a small focus of untreated tumor. MR imaging appears to be more accurate than US or CT for monitoring the acute affects of[66-68].

Follow-up imaging is very useful to assess the result of RF and the recurrence of new tumors, although sometimes it is very difficult. CT and MRI were showed more effective than ultrasound for monitoring the RFA ablation in animal studies. If the follow up imaging is performed soon after the procedure, a peripheral hype remic halo surrounding an area of hypoattenuation devoid of parenchymal enhancem ent is usually seen with spiral CT or MRI. Occasionally a hyperdense central are a corresponding to the needle tract is also seen. The interpretation of the foll ow-up CT scans required radiologists experience to prevent both diagnosis and u nderdiagnosis of the residual or recurrent tumor. The ablation process cause a h yperemic response in the liver parenchyma surrounding the ablation. The hyperemic prevents an accurate assessment of the completeness of the ablation in the early post-ablation period. The hyperemia usually resolved within 1 month after the procedure. After this time, persistent or new peritumoral hyperemia is considered an indication of recurrent tumor. Recurrent hypovascular tumors are detected as an enlargement of ablation area, or a subtle double-density halo developing around the margins of the treated area. All areas suspicious for tumor recurrence should be assessed by percutaneous biopsy.

RFA OF PRIMARY LIVER TUMORS

Primary liver cancer is a highly vascular cancer. A vascular sink phenomnon may contribute to the extended ablation times. Most of the

early reports on the use of RFA for HCC came from Rossi *et al*[74] in Italy in 1995. They repo rted their results with percutaneous RFA in twenty-four patients (16 men and 8 women; age range, 53 to 79 years) with 36 hepatocellular carcinoma nodules of not more than 3.0cm in diameter underwent radiofrequency interstitial thermal ablat ion treatment with the intent to achieve a cure. In each patient, the thermal ne crosis volume achieved was about double the tumor volume. During the mean follow -up interval of 24.8 months, 13 of 24 patients had recurrences, 9 of whom under went further radiofrequency thermal ablation treatment. Radiofrequency thermal a blation was again repeated in two patients who showed a second recurrence.

Marone *et al*[75]. reported percutaneous RF results using cooling sal ine in the tube of 13 cirrhotic patients with 19 hepatocellular carcinoma in 199 8. None of the patients had portal thrombosis or extrahepatic spread. They used a radiofrequency generator (100W power) connected to an 18G perfusion electr ode needle with an exposed tip of 2-3cm. The circuit is closed through a disp ersive electrode positioned under the patient's thighs. A peristaltic pump infus es a chilled (2-5℃) saline solution to guarantee the continuous cooling of t he needle tip. The needle was placed into target lesions under US guidance. Comp lete necrosis as assessed at dynamic CT (no enhancement during the arteriographi c phase) was achieved in 16 of 19 nodules (84%). No side-effects occurred. Du ring the follow-up (median: 11 months) no death occurred and five patients had recurrent hepatocellular carcinoma appearing either as single nodule or as multi nodular liver involvement? In a large series from Curley *et al*[76], 149 discrete HCC tumor nodu les in 110 patients had been followed for a minimum of 12 months(median follow- up 19 months) after RF. Percutaneous, laparscopic or intraoperative RFA was performed in 76 (69%) and 34 (31%) patients, respectively. Median diameter of tu mors treated percutaneously (2.8cm) was smaller than lesions treated during la parotomy (4.6cm, $P<0.01$). Local tumor recurrence at the RFA site developed in four patients (3.6%); all four subsequently developed recurrent HCC in oth er areas of the liver. New liver tumors or extrahepatic metastases developed in 50 patients (45.5%), but 56 patients (50.9%) have no evidence of recurrence. There were no treatment-related deaths, but complications developed in 14 pati ents (12.7%) after RFA.

RFA OF COLORECTAL CANCER LIVER METASTASES

The liver is the most common site of distant metastasis from colorectal cancer. Colorectal cancer is the fourth most commonly diagnosed cancer and second leading cause of cancer death in the world. Nearly half of patients will develop liver metastases during the course of their disease, with 15-25% having liver meta stases at the time of primary diagnosis and another 20% of patients developing metachronous liver metastases[10,11]. About one-fourth of patients with liver metastases from colorectal cancer have no other sites of matestases and can be treated with regional therapies directed toward their liver tumors. But o nly a minority of the patients are candidates for surgical resection. RFA, one o f the regional therapies, may be offered to patients with unresectable liver metas tases.

Most of the early reports on the use of RFA for colorectal cancer liver metastases also came from Rossi *et al*[74] in Italy. In 1996, they reported their results with percutaneous RFA in 50 patients, in which 11 patients had 13 me tastases ranging from 1 to 9cm in diameter. Monopolar and bipolar needles were utilized and multiple probe insertions and treatment sessions were performed. There were no associated complications or deaths. Of the 11 patients with metasta ses, two underwent subsequent surgical resection, of which one had complete tumor necrosis by histopathologic examination. At a median follow-up of 22.6month s, 10 of 11 patients (90%) were alive, but two (18%) had a local recurrence and seven (64%) had persistent or distant disease. Only one patient (9%), th erefore, was alive without disease. These studies suggested that although RFA was effective in preventing local recurrence of metastases, it may not affect the progressive course of the cancer.

Solbiati *et al*[77] reported on 117 patients with 179 metastatic lesi ons undergoing RFA with a mean follow-up of 3 years (range, 6 to 52 months). Co mputed tomographic follow-up was performed every 4-6 months. Recurrent tumors were retreated when feasible. Estimated median survival was 36 months. Estimated 1, 2, and 3-year survival rates were 93%, 69%, and 46%, respectively. Su rvival was not significantly related to number of metastases treated. In 77 (66 %) of 117 patients, new metastases were observed at follow-up. Estimated medi an time until new metastases was 12 months. Percentages of patients with no new metastases after initial treatment at 1 and 2 years were 49% and 35%, respec tively. Time to new metastases was not significantly related to number of metast ases. Seventy (39%) of 179 lesions developed local recurrence after treatment. Of these, 54 were observed by 6 months and 67 by 1 year. This study suggests th at long-term local control can be achieved in a majority of patients, but that the development of new metastases limits improvement in overall survival.

Wood *et al*[78] reported 231 tumors in 84 patients treated with 91 RFA procedures. The majority of patients had metastatic lesions (213 lesions in 7 3 patients) and 51 of the 91 treatments consisted of RFA alone. The other 40 inc luded RFA combined with surgical resection, cryoablation, and hepatic artery inf usion of chemotherapy. Of the 91 RF treatments, 39 were ablated at laparotomy, 27 by laparoscopy and 25 percutaneously; tumors ranged in size from 0.3 to 9.0c m. There were seven major complications including three deaths, one (1%) of wh ich was directly related to the RFA procedure. Ten patients underwent a second R FA procedure (sequential ablations) and, in one case, a third RFA procedure for large (one patient), progressive (seven patients), and recurrent (three patients) lesions. At a median follow-up of 9 months (range, 1-27 months), 15 patients (18%) had developed a local recurrence. Of the remaining 69 patients, 34 were alive without disease, 14 were alive with disease, and 21 died of their disease ; new hepatic tumors or extrahepatic disease therefore had developed in 35 patie nts. The average hospital stay was 3.6 days overall.

RFA OF OTHER LIVER METASTASES

Most of the papers discussed so far consisted of both primary liver tumors and c olorectal cancer liver metastases. RFA for liver tumors has also been evaluated for specific tumor types.

Livraghi *et al*[79] reported on 24 patients with 64 metastatic breast lesions ranging in size from 1 to 6.6cm. The liver was the only site of disea se in 16 patients, while the other eight patients had stable metastatic disease elsewhere. The patients were treated with the percutaneous approach utilizing mo nopolar or clustered electrodes. Minor complications were noted in two patients and no deaths were reported. Complete necrosis was achieved in 59 (92%) of 64 lesions. Among the 59 lesions, complete necrosis required a single treatment ses sion in 58 lesions (92%) and two treatment sessions in one lesion (2%). In 1 4 (58%) of 24 patients, new metastases developed during follow-up. Ten (71%) of these 14 patients developed new liver metastases. Currently, 10 (63%) of 16 patients whose lesions were initially confined to the liver are free of disea se. One patient died of progressive brain metastases. Although a preliminary stu dy, these results do suggest that RFA for selected patients with metastatic brea st carcinoma confined to the liver can be as effective as RFA for colorectal and other metastatic tumors to the liver.

Neuroendocrine tumors metastatic to the liver often produce symptoms secondary t o hormone production. Although only a minority are curable by surgical technique s, significant symptomatic relief can be obtained by surgical procedures. For th ose patients who are not surgical candidates, RFA may provide a viable therapeut ic alternative. Siperstein *et al*[80] reported 18 patients with 115 n euroendocrine tumors were ablated with RFA. The mean lesion size was 3.2cm (ra nge, 1.3 to 10cm) and the average number of lesions ablated per patient was six (range, one to 14). There were two complications consisting of arterial fibril lation in one patient and an upper gastrointestinal bleed in another. Fifteen pa tients (83%) with 100 lesions were followed for a mean of 12.1 months (range, 3 to 35months). Local recurrence was detected in three patients (20%) and si x (6%) lesions and three patients died during follow-up. However, data regard ing potential symptom improvement were not reported.

FOLLOW UP OF RFA

Initial imaging serves as an indicator of complete treatment, and provides a bas is for subsequent studies. However, the resolution and accuracy of current imagi ng techniques preclude identification of residual microscopic foci of malignancy at the periphery of a treated lesion. Hence, these viable tumor foci, if present, will grow and result in "local recurrence".

Multiphasic helical CT and contrast-enhanced MR imaging play a central role in the long-term assessment of therapeutic response, allowing confident discrimina tion between ablated and residual viable tumor. CT and MR studies are obtained a t 3-4 months intervals and are combined with tumor marker (serum CEA, AFP, CA19 -9) levels to detect local or distant recurrences. In general, sampling error a nd the histopathologic findings of thermally ablated tissue are too variable to render fine needle aspiration or core biopsy reliable indicators of the presence or absence of residual disease. US has proved valuable for immediate assessment of ablative results during the RF session, still in patients under general anes thesia, allowing for an immediate refinement of the ablation, if needed. US is a lso valuable for long-term follow-up and detection or confirmation of recurren ces; in many patients contrast-guided retreatment has been performed in order to precisely direct RF energy on recurrence areas[81-83].

ADVANTAGE AND DISADVANTAGE OF RFA

RF thermal ablation has several advantages over other therapies for primary liver cancer and metastasis liver cancer. It can be used as a percutaneous procedure , under the guiding of ultrasound, CT scan and MRI, done in local anesthesia, in out-patient department. The complications and morbidity are lower than hepatic resection and cryosurgery. RFA can be retreated in the patients whose tumors re cur at the margin of treatment or have new tumors develop elsewhere in the liver . It has similar results as hepatic resection because it destroyed the tumors co mpletely as taking it out in liver surgery, which is superior to ethanol injecti on. RF requires less sessions than other ablation procedures such as ethanol inj ection.

Although RF has a lot of advantages in the treatment of primary and metastasis liver tumors, it still has a few disadvantages and complications. These complicat ions included symptomatic pleural effusion, fever, pain, subcutaneous hematoma, subcapsular liver hematoma, and ventricular fibrillation. The severe complication is treatment-related death. As with all methods related to tumors, the outcome of RF thermal abalation will be related to the skill of physician performing the procedure. Exact placement of the ablation needles require considerable skill and some degree of guesswork by the radiologist and surgeon, which may be the most experienced in interventional procedures. Recurrence at the treatment margin may result from an inability to adequately kill the tumor the hepatic parenchym a adjacent to the treated tumors. The abundant portal venous blood flow present in normal hepatic parenchyma act as a heat pump, which makes the creation of the rmal injury in normal liver more difficult than that it is in liver tumors. RF a lso caused skin burn in percutaneous procedures, hemorrhage, diaphragmatic necro sis, hepatic abscess, hepatic artery injuries, bile ducts injuries, renal failure, coagulopathy and liver failure, which were severe and eventually fatal.

CONCLUSION

Despite the considerable progress that has been made to date, a number of challe nges remain for the future. These include the development of techniques that can increase the volume of tissue destroyed at a single treatment session, the deve lopment of more suitable and accurate imaging tests, and a better understanding of how to integrate in situ ablation techniques into the overall care of patient s with different specific neoplasms.

Although long-term observations are still not available, RFA will definitely give the surgeon a helpful hand and offer the patients a better prognosis. But, RF A is unlikely to be curative for most patients, it can relieve the symptom of pa tients and improve the quality of live of patients. RFA has been shown to be safer and better tolerated compared to other ablative techniques, such as cryotherapy, laser ablation and microwave ablation, has been associated with fewer local recurrence. However, surgical resection remains the gold standard for treating m etastatic and primary liver tumors. RFA of unresectable liver tumors provides a relatively safe, highly effective method to achieve local disease control in some liver cancer patients who are not candidates for liver resection. RFA also shown some better respect in combination with surgical resection, hepatic artery catheter and regional chemotherapy. With the development of RFA equipments and techniques, the treatment of a large primary and secondary liver cancer and malignant tumors at other body sites will be feasible and effective. The most interesting feature of RFA is the minimal-invasiveness with zero mortality rate, signif icantly lower complications, reduced costs and hospital days compared to surgery and other local therapies. Furthermore, with combination of other procedures, RFA will improve the survival of patients with cancer.

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