Percutaneous RFA of unresectable HCC in 282 patients-our experience

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Purpose

The aim of this retrospective study is to report our center’s experience in the therapeutic outcome and early and late complication rates in a large series of 282 patients (322 lesions) with unresectable HHC who underwent CT-guided RFA.

Hepatocellular carcinoma (HCC) is a common malignancy, with an increasing incidence worldwide due to infection with hepatitis B and C virus and alcoholic liver disease (Fig 1). Surgical resection remains the treatment of choice, although only a small number of patients may undergo it at the time of diagnosis. Percutaneous radiofrequency ablation (RFA) is a relatively new, minimally invasive technique that is considered the best treatment option for patients with HCC in whom surgery is contraindicated.

The improvement of equipment and the increased expertise of interventional radiologists have greatly contributed to a high level of treatment efficacy and a low incidence of complications of image-guided RFA. Reduced mortality, morbidity and hospitalization are considered major advantages rendering RFA as a promising alternative, not only in controlling malignant disease, but also in improving survival rate for patients with limited but unresectable disease.

Image-guided tumour ablation can be performed with a variety of imaging modalities (ultrasound, computed tomography, magnetic resonance imaging, fluoroscopy). Although ultrasound is the most common image guidance in liver RFA, we prefer the CT guidance for electrode placement. We believe that correct needle localization, which is very important to RFA and must be precise to the millimetre, is better achieved under CT guidance. Since CT can better ensure adequate positioning of the RF device and our experience obtained in RFA is greater with CT than with ultrasound, we perform ablation under CT guidance.
Fig. 0: Fig 1. CT in a male patient, with cirrhosis who developed an HCC; operation was unattainable. Pretreatment arterial phase CT image reveals enhancing hepatocellular carcinoma nodule.

Methods and Materials

In our department, 282 patients (231 males, 51 females; age range: 44-76 years; mean age: 62 years) with 322 lesions of HCC underwent CT-guided RFA from February 2002 to February 2007. All patients were diagnosed by biopsy at least on one lesion. The diameter of the tumors ranged from 1.5cm to 5cm. Prior to RFA sessions a-fetoprotein values were normal (< 20ng/ml) in 110 patients, slightly elevated (20-200ng/ml) in 91 and markedly elevated (> 200ng/ml) in 57 patients.

In this study we used three different RFA systems with an expandable needle electrode and one with a perfusion electrode, all monopolar systems. The RITA Medical Systems (Mountain View, CA, USA), the Boston Scientific (Watertown, MA, USA; formerly Radio Therapeutic Corporation, Mountain View, CA, USA), and the MIRAS (Invatec S.r.l., Roncadelle, Italy) are expandable type devices.

Prior to therapy all patients had undergone laboratory examinations (hematocrit, white blood cell count, blood coagulation tests, values for hepatic function and a-fetoprotein levels): a platelet (PLT) count <50,000/ml or international normalized ratio (INR) >1.3 is a contraindication for RFA and should therefore be corrected. Coumadin and aspirin must have been ceased at least for 3 days. Ascites should be controlled. Patients with portal vein tumor thrombosis or extrahepatic metastasis were excluded. Finally, the benefits and the risks of the technique were fully explained and written informed consent was obtained from every patient.

Forty-five minutes before the procedure all patients received the analgesic and antidepressant treatment consisting of one pill of 3 mg bromazepam (Lexotanil® Roche) per os and 75 mg d-propoxyphene hydrochloride (ZIDERON® Norma Hellas S.A) intramuscularly. At the puncture site local anaesthesia was achieved with an injection of a 10-15 ml 1-2% lidocaine hydrochloride solution both intradermally and into deeper tissues.

CT-guided RFA was started by placing the patient in the supine position. Using a Somaton Emotion Duo (Siemens Medical Solutions, Germany) a pre-procedure CT scan was obtained. A radiolucent net device with radiopaque guides, in touch with the skin, was placed and 5-mm collimation CT of the desired area was performed. The lesion’s exact location and depth, in relation to the overlying skin, were determined on the acquired CT slices, and marked with a permanent ink marker. The shortest, most vertical and safest path was chosen. The net was removed. The skin at the needle entry site was prepared with povidone iodine 10% solution. A 22G needle for syringe use was inserted into the skin, and three contiguous CT images were obtained to ensure that the chosen point was the appropriate one. Local anaesthetic (2% lidocaine hydrochloride) was then instilled through this needle for skin and subcutaneous tissue anaesthetization. The needle was removed and an incision with a surgical blade was made to facilitate electrode cannula insertion.
After patient preparation was completed, two dispersive electrodes were applied to the patient’s abdomen or thighs. Subsequently, the device was inserted from the exact skin entry site in a stepwise fashion, while the trocar tip was controlled each time with three contiguous 5-mm CT images. If the lesion was small and was unable to be visualized well on plain CT, needle placement was based on nearby anatomic landmarks and the correlation to preablation CT images. In a few cases, where uncertainty existed regarding the correct needle position, a small bolus of contrast media was given and the area scanned during the procedure. Once the tip was seen on CT images at a correct position, the electrode was deployed slowly. When final confirmation of the correct positioning of the tip of the device was obtained (Figs. 2-4) with additional 3-mm contiguous CT images, the dispersive electrodes and the device were connected to the RF generator.

A pulsed RF energy was applied for 13 to 20 min, depending on the size of the lesion, its location and its vascularity. The duration of the ablation was predefined according to the manufacturer’s instructions and modified during ablation if necessary. When the tumor was larger than 3 cm in diameter, one single insertion of the electrode was performed, but during the procedure the angle of needle trajectory was changed in order to ablate another site of the lesion avoiding multiple electrode passes. After the ablation of the lesion was completed, low pulsed RF energy was applied for the ablation of the track. This operation was necessary to avoid tumor seeding.

To evaluate the immediate response of the lesion to the ablation and check for immediate complications, dual-phase dynamic contrast enhanced CT was performed after the electrode’s removal (Figs. 5, 6). For the outpatients, observation for 3 hours was mandatory; the inpatients were hospitalized for 24 hours. The immediate (<3 hours) and the delayed complications were recorded. Major complications were defined as those that, if left untreated, might threaten the patient’s life, lead to substantial morbidity, or result in hospital admission or substantially lengthened hospital stay. All other complications were considered minor. All patients were dismissed after detailed instructions were given. The follow-up period ranged from 6 to 68 months (mean, 29 months) and included a dual-phase dynamic contrast enhanced CT at 1, 3 and 6 months post-RFA and every 6 months afterwards (Figs. 7, 8). The tumors were considered as ablated completely, if no viability was found on dual-phase dynamic contrast enhanced CT at 1 month after RFA. Alpha-fetoprotein measurement was also part of the follow-up.

The diagnosis of recurrence was made by dual-phase dynamic contrast enhanced CT during follow-up compared with the previous CT examinations, while magnetic resonance imaging was performed to confirm the recurrence, when necessary. HCC recurrence was classified as either local tumor progression when occurred adjacent to the treated site or intrahepatic distal recurrence when a new nodule observed remote from the margin of the ablative lesion. Tumor recurrence that emerged during follow-up was treated with RFA, if the same initial inclusion criteria were still satisfied. If the patient did not meet
the initial requirements for RFA or if multicentric HCC the decision of the treatment was made by the referring oncologist.

Survival analysis was performed on the patient’s group and survival probabilities were calculated using the Kaplan-Meier method. For survival rates, the time from the first RFA treatment to the last follow-up CT examination or death was used. For recurrence rates, the time from the beginning of RFA treatment to the first follow-up CT examination that revealed either local tumor progression or intrahepatic distal recurrence was used.
Fig. 0: Fig 1. CT in a male patient, with cirrhosis who developed an HCC; operation was unattainable. Pretreatment arterial phase CT image reveals enhancing hepatocellular carcinoma nodule.

Fig. 0: Fig 2. RFA electrode inside the malignant lesion located in segment VII; RFA electrode has been inserted into the tumor under CT guidance.

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**Fig. 0:** Fig 3. Hepatic lesion in the left lobe; RFA electrode inside the lesion.

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**Fig. 0:** Fig 4. HCC in the left lobe in a patient who underwent RFA; because the lesion was small and was hardly visualized on plain CT, needle placement was based on nearby anatomic landmarks and correlation to preablation CT images. Electrodes are inside the lesion.

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Fig. 0: Fig 5. CT image immediately after RFA of the patient shown in Fig. 1 demonstrates no enhancement of the tumor, evidence of a good response to the RFA.

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Fig. 0: Fig 6. Immediate CT scan after contrast media administration of the patient shown in Fig. 3; the lesion does not enhance.

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Fig. 0: Fig 7. Follow up CT scan after contrast media administration of the patient shown in Fig. 2 after 3 months; the lesion is hypodense, evidence of a complete ablation

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**Fig. 0:** Fig 8. Six months follow up CT scan after contrast media administration of the patient in Fig. 4; note the hypodense appearance of the lesion indicative of complete ablation.

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Results

The first month follow-up revealed total necrosis in 281 tumors. The ablation success rate after the first RFA based on the CT findings were 87.3% (281/322 lesions). In this study, 12.7% (41/322 cases) of the patients had tumor residue, of which 32 cases (78.1%) were those with tumors larger than 3cm. All residual tumors were managed with a second RFA session.

The survival rates at 1, 2, 3, 4 and 5 years were 94.8%, 86.6%, 73.1%, 64.2% and 51.1%, respectively.

Minor (those not requiring medical intervention) complication rate was 2.8% (9 of 322 sessions) and consisted of subcapsular haematoma (n=6), reactive small pleural effusion (n=2) and partial liver infarction (n=1). All complications were observed on dual-phase dynamic contrast enhanced CT which was performed after the electrode removal. No delayed complications were recorded. In our group of 282 patients who were treated percutaneously with 322 RFA sessions, no major complications were encountered. No mortality was observed and no carcinoma seeding was identified.

Post-ablation syndrome occurred in 120 cases (37.3%) of the 322 RFA sessions. Post-ablation syndrome is a known situation consisting of transient flu-like symptoms. Symptoms comprise fever (94%), malaise (70%), chills (35%), delayed pain (29.5%) and nausea (11.7%). On average, the symptoms are present 3 days after ablation and last 5 days.

A post-RFA reduction of alpha-fetoprotein was noticed in all patients who had elevated values at the beginning.

During the follow-up period, the local tumor progression rate was 22%, while the recurrence rate of new intrahepatic nodules was 48%.
In conclusion, percutaneous RFA of primary liver tumors is a rapidly evolving treatment for unresectable lesions. We believe that with continuous technology improvement and increasing clinical experience, RFA may achieve even better results and possess prominence in the treatment of early, unresectable and recurrent HCC. Although surgical resection remains the gold standard treatment of HCCs, this standard may be challenged in the near future, as more results emerge from long-term studies of RFA.


### Personal Information

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